eBook
Guide to Validation 4.0 and a Digital Transformation of Quality

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Introduction

Validation 4.0 is a key component to Quality 4.0 and Pharma 4.0™. In order for it to be successful, organizations require an in-depth understanding of their products and processes, their data, integration, and documentation. Understanding the organization's products and processes is critical in order to better concentrate efforts towards finding and implementing appropriate controls to improve quality. Additionally, the organization's data needs to be integrated across the organizational functions and visible to those who need to utilize it. Additionally, documentation needs to go digital and be centralized by the organization.

In this eBook we discuss what Validation 4.0 is and how it relates to Quality 4.0. We also review some of the key considerations when looking to incorporate it into the organization. Additionally, we look at the benefits and challenges of incorporating it into the organization as well as a model to assist with the implementation.

Topics:

Validation 4.0 and Quality 4.0 in the Life Sciences Industry

Industry 4.0 and Quality 4.0

A new industrial revolution has resulted from technological advancements during the last decade. The fourth industrial revolution, often known as "Industry 4.0," is a term used to describe this period. The exponential proliferation of disruptive technologies, as well as the changes that these technologies are bringing to the Life Sciences industry and the markets that they serve, are driving the revolution.

Quality 4.0 is a concept used to describe the status of quality and organizational excellence in the future. This is part of the Industry 4.0 framework. This is leading organizations to enhance their quality best practices as well as adopt new digital disruptive technologies required for this new Quality of the Future. To support aspects of Quality 4.0, traditional validation practices are also undergoing a major shift – leading to the term Validation 4.0.

The Role of Validation 4.0

For Industry 4.0 to succeed in the Life Sciences industry, there needs to be a new mindset relative to validation across the value chain. It needs to incorporate new technologies that enhance product quality and the safety and efficacy of drugs and medical devices for the patient. There needs to be a transition to a data-powered technology driven approach to compliance.

The objective of Validation 4.0 is to provide a risk-based method for process performance qualification that involves a uniform, coordinated and unified approach to computer system validation . It is based on the Pharma 4.0™ operating model and includes a thorough control plan, as well as digital maturity and data integrity by design. This approach will aid in the support and facilitation of existing and future pharmaceutical industry improvements.

Key Focus Areas to Consider with Validation 4.0

In order to evolve the organization and enhance the process towards Quality 4.0 and Pharma 4.0, organizations need to consider how to approach Validation 4.0. It requires an in-depth understanding of the products and processes, data, integration, and documentation.

Quality by Design

The more the organization understands regarding the key aspects of their products and processes, the better they can concentrate their efforts towards finding and implementing appropriate controls to improve quality. The approach should focus on incorporating design aspects and controls into the value chain at various phases and continuously rather than a holistic check towards the end of the process, thus attempting to mitigate risks throughout the process.

Data Integrity by Design

Data is centric to the organization. It needs to be visible to those that need to access it and leverage it across the organization. Validation is impacted by bad data and specifically when data is not integrated across functions of the organization. Integrated data is critical to Validation 4.0.

Integrated Environments

Current technologies like IoT have provided a means to capture and make visible key information across the entire value chain. This information is key to ensuring Validation 4.0.

Modern Documentation

A critical area to consider regarding validation is documentation. Going away from a paper-based approach to a digital approach where all the data is centralized versus in multiple places is imperative.

Validation 4.0 - The Benefits to the Life Sciences Industry

The objective of Validation 4.0 is to provide a risk-based method for process performance qualification that involves a uniform, coordinated and unified approach to computer system validation. It is based on the Pharma 4.0™ operating model and includes a thorough control plan, as well as digital maturity and data integrity by design.

The Benefits of Validation 4.0

Validation 4.0 ensures new technologies are adopted and validated to meet patient safety and product quality criteria and follow the Pharma 4.0™ operating model. Given that Validation 4.0 enables Pharma 4.0™, there are a number of benefits that Life Sciences organization will see including:

Improved Quality

By focusing on the critical thinking and the risk management required to validate the various technologies like smart devices within the ecosystem, it assists in ensuring optimal quality is met. The validation includes visibility into the data exchanged through support networks of suppliers, CDMOs, CMOs, and other external organizations that are part of the value chain.

By incorporating the guidelines of Validation 4.0 organizations can ensure a high level of data integration across the organization as well as with suppliers. It can also enhance visibility and resiliency of the value chain.

Lowers the Cost of Operations

In leveraging new technologies as part of the Pharma 4.0™ framework and incorporating the guidelines of Validation 4.0, the organization can lower the overall cost of Quality across the organization.

Lowers the Risk

By leveraging Validation 4.0 strategies, the organization can also lower the overall risk. By incorporating the new technologies of Pharma 4.0™ and leveraging Validation 4.0 guidelines the organization can better mitigate risk. This requires an approach that focuses on incorporating design aspects and controls into the value chain at various phases and continuously rather than a holistic check towards the end of the process, thus attempting to control and mitigate risks throughout the process.

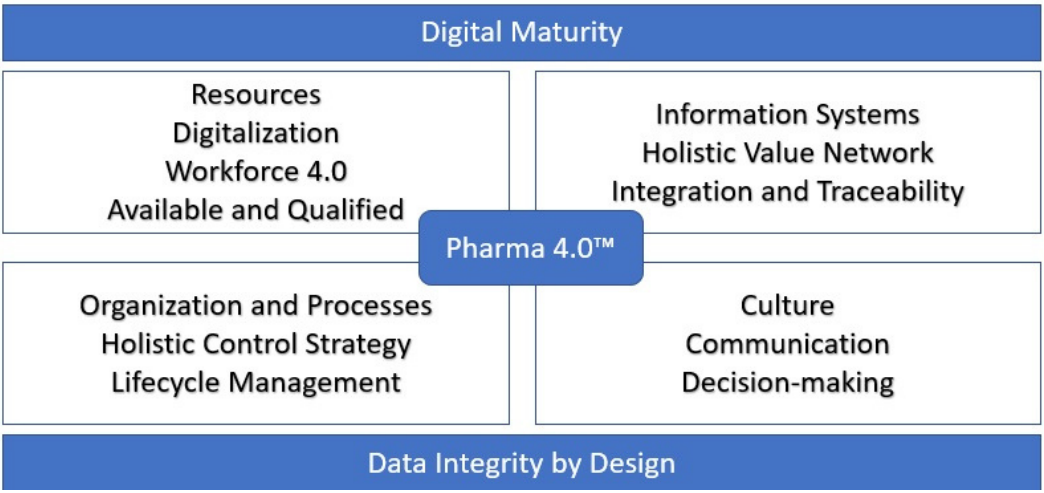
Provides a Faster Time to Market

Validation 4.0 also assists in helping the organization to get products out to market faster. By leveraging technologies of Pharma 4.0™ and the Validation 4.0 guidelines, the organization can better control the quality and safety in real-time and manage any deviation, thereby augmenting a faster time to market of products.

Better Visibility Across Value Chain

By incorporating the new technologies of Pharma 4.0™ along with the guidelines of Validation 4.0, the organization will have a complete and concise view across the value chain in order to ensure better control of the various internal and external processes.

Validation 4.0 – The Challenges of Implementing



Pharma 4.0 Structure as defined by ISPE https://ispe.org/initiatives/pharma-4.0

Pharma 4.0™ and Validation 4.0, as part of the plan, requires resources, information technology, a holistic control strategy, and a cultural shift of the organization. All areas need to come together to ensure that the business can make progress towards improvement and achieve the objectives. This can lead to challenges given the extensive impact on the organization.

Challenges Impacting the Implementation of Pharma 4.0 and Validation

People, Culture, and Skillset Challenges

Manufacturers and regulators will need to make cultural adjustments and innovate to manage the myriad of data, computing, and automation hazards on the way to full adoption of Pharma 4.0™ and Validation 4.0 guidelines and the technologies required to get there. In order to achieve optimization, knowledge and training gaps will have to be addressed in the adoption of a new paradigm and industry infrastructure based on digitized and interconnected enterprise systems that rely on computational power, communications technologies, cybersecurity, and advanced controls.

For example, to implement AI and other advanced technologies in pharmaceutical manufacturing, a variety of expertise beyond traditional biology, chemistry, and process engineering will be required. Data scientists, computational and systems engineers, IT specialists, and AI experts, for example, will most likely be needed. At least initially, regulators and business may be fighting for the same tiny pool of talent in these areas. New labor force training standards are undoubtedly on the way, and comprehensive training programs will be required.

There will also be a need to understand the operation of smart devices that will enable monitoring and operating from a distance by operators and supervisors. These technologies will simplify the changeover, setup, and maintenance and the life cycle management. There will also be a need for the workforce to operate cross functionally, integrating several disciplines.

Incorporating best practices and new technologies into the business is required. The difficult part is changing the culture and persuading individuals to accept a new way of doing business after having done things a certain way for many years. Organizational Change Management will be necessary (OCM).

OCM is the “application of a systematic process and set of tools for driving the people side of change to accomplish a desired outcome," according to Prosci, the global leader in change management best practices research. Additionally, strong communications, with a leadership team eager to drive positive experiences through technology, will be required.

Planning and Process Challenges

Because the potential for Pharma 4.0™ is so great and so wide-ranging, many pharmaceutical companies are racing to implement the technology and haven’t defined their primary goals and what problems they're seeking to solve.

If these two important questions are not answered before starting down the path to Pharma 4.0™, the direction will be unclear, and many firms will lose sight of their objectives and goals.

The organization's business processes will undergo significant changes as a result of the major technologies required for digital transformation, and those changes must be acknowledged and understood before they are implemented. The company needs to have a strategy and a plan to get there.

Pharma 4.0™ and Validation 4.0 require an holistic control strategy. A strategy that follows the product from research to development, to tech transfer, and then through to commercial manufacturing. With this strategy there also needs to be a synergy between digital automation and guidelines and an enhancement of the quality manufacturing focus, where Quality Target Product Profiles are required for all products. With this control strategy, the data from machines and components is immediately available without traversing various systems . The operators' remarks can be automatically recorded making the continuous improvement process easy to implement.

Technology Challenges

Transitioning to Pharma 4.0™ and leveraging Validation 4.0 guidelines requires incorporating new technologies and ensuring that everything works together to produce reliable data across the value chain. The technology needs to provide a means to integrate data and eliminate the silos that may exist throughout the organization today. These data silos can exist across process areas, applications being used, and organizational groups. A few examples are business quality data, IT quality data, product quality data, and supplier quality data. In many situations, the data is not being collected using the same method and this incongruent data has a negative impact on the decision process. Many times, this leads to inefficiencies and sometimes costly inaccuracies.

Organizations need to look at technology solutions across the value chain. From the company's business partners and the customer perspective, the organization needs to be able to make informed decisions based on data compiled from various sources and to communicate specific aspects of that data accurately to suppliers, vendors, and customers.

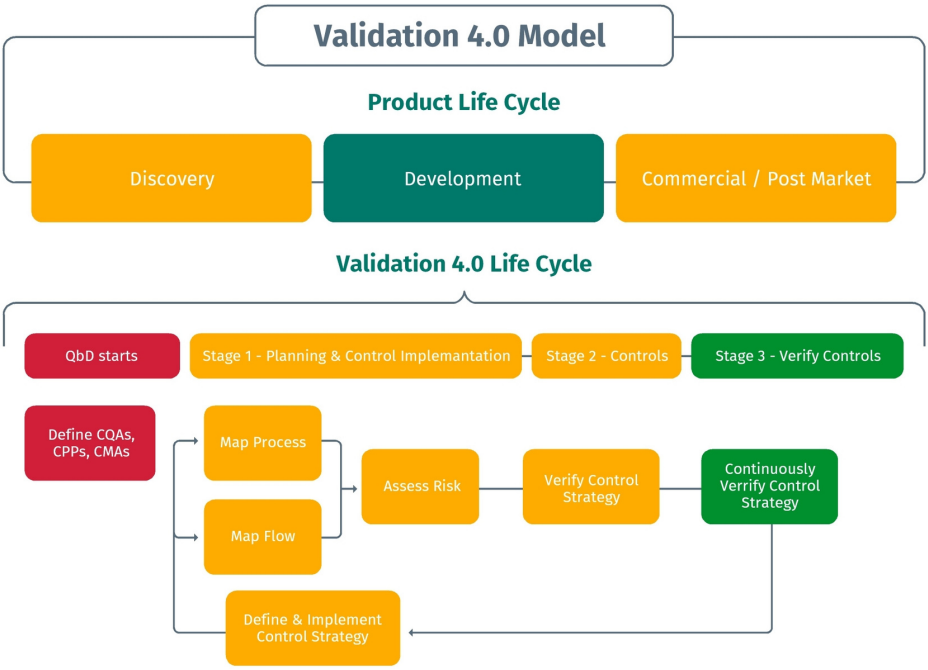
Innovative technologies also necessitate new processes and more regulatory scrutiny. Manufacturers must remain nimble and able to adopt new skills in order to improve manufacturing and provide high-quality products.

To connect the essential instruments and equipment, the technology including tools, devices, and IT systems must be on an open platform with common data standards and, most likely, be cloud-based to enable data sharing. Integration and traceability, as well as automation, rely on information systems that eliminate needless manual or human interaction while also lowering regulatory scrutiny. Leveraging the right technology across the organization that is integrated and provides consistent and accurate information is imperative.

Operating within existing regulatory frameworks can be considered another challenge for Pharma 4.0™ and technical innovation when it comes to regulatory restrictions. Due to a lack of regulatory precedent, the industry may continue to use old practices even though new processes will lower overall regulatory burden and improve quality in the long run.

Validation 4.0 Model for a Digital Transformation of the Life Sciences Industry

Validation 4.0 requires a high level of data integration, increased supply chain visibility and resiliency, and that the right processes, skillset and technology are leveraged. In order to ensure success of Validation 4.0 implementation, organizations need to understand how Validation 4.0 maps to the Product Life Cycle (PLC) – ensuring that product quality and patient safety are kept to the highest standards.



Source: Special Interest Briefing on Validation 4.0: Objectives, Working Model, and Relation to QBD

With that in mind, there is a need for a framework that assists in the transition to Validation 4.0 by showing how it maps to the PLC. A Validation 4.0 model highlighting this mapping was discussed in June of 2021 on an ISPE webinar on this topic. This model is the foundation for incorporating Validation 4.0 into the organization. It reviews the PLC stages along with the inter-dependency of some of the activities across the phases.

Product Life Cycle

PLC goes from Discovery, to Development, to Commercialization, and then to Post Market. The Validation life cycle has corresponding steps that provide data and feedback to ensure success. Quality by Design (QbD) attributes such as the Critical Quality Attributes (CQAs), the Critical Process Parameters (CPPs), the Critical Material Attributed (CMAs), and other key considerations would need to be incorporated into the PLC to provide the required visibility as well as monitoring of the overall process.

Quality by Design

Utilizing digital tools as an enabler across all stages of the validation process provides ready access to critical variables, parameters and requirements as they change throughout the process. It is important to note that QbD is not a signal step of the process but rather an iterative approach we use in order to learn more about our product and processes. With QbD, we accumulate information that assists in better understanding the products and processes so as to improve efficiency and optimization across all stages.

Planning and Control Stage 1

Stage 1, in the Validation 4.0 life cycle is the planning & control implementation phase. This maps to the discovery and development stage of PLC. In this stage, the organization's user requirements are captured through process maps and data flows. This involves a digitization of the process leveraging technology. In this stage, the requirements that provide a better understanding of what the organization needs from a process and products perspective are contextualized. Additionally, a risk based assessment is applied that is associated with the process maps and data flows. This is where the risk is measured as it impacts product quality and patient safety. Criticality and vulnerability of the risk are both key considerations relative to this area.

Controls Stage 2

The Implementation of Controls is the next stage, Stage 2, in the Validation 4.0 Life Cycle. In this phase, we have digital tools in place to collect, report, and act on critical data in real-time.

Verify Controls Stage 3

The following stage, Stage 3, is the Verify Controls phase. In this stage, the critical data from the on-going process are continually monitored to provide opportunities for optimization as well as implement any changes to the system based on performance monitoring. The digital monitoring is to ensure that the design of the system to control the process and data is providing an acceptable level of risk. Data is leveraged for continuous improvement and optimization of the process. A continual feedback mechanism is required where the data is collected and analyzed in real-time so that the appropriate action on any discrepancies can be taken.

Summary

Validation 4.0 requires an in-depth understanding of the products and processes, data, integration, and documentation in order to successfully implement. By leveraging the guidelines of Validation 4.0 the Life Sciences organization can receive significant benefits. It can improve quality of the products along with lowering the cost of operations. There will also be a lower risk given the focus on controls throughout the value chain and at various phases to continuously check for issues. Additionally, the organization will have a quicker time to market by leveraging new technologies and Validation 4.0. Along with these significant benefits, there will be visibility across the value chain to ensure things are running smoothly from both an internal and external perspective.

Moving to Validation 4.0 impacts the entire organization. These challenges are in the areas of people, processes, and technology. To move to this new approach, it will require training of the people and a cultural shift to be successful. It will also involve an understanding of the objectives of the move to Pharma 4.0™ and the processes involved and an holistic control strategy. Additionally, it requires an understanding of the new technologies so that everything works together to produce reliable data across the value chain.

In order to successfully incorporate Validation 4.0 into the business, there also needs to be an understanding of the Product Life Cycle (PLC) along with the requirements associated with the processes and data that needs to be digitized so that they can be measured throughout the life cycle. This is required in order to ensure that the product quality and patient safety is kept at the highest level. To do this, we need a Validation 4.0 model that maps to the PLC that we can leverage to assist in ensuring the monitoring of the data and processes via controls.

This model needs to incorporate the appropriate technologies that help us to report, control, and improve the validation process across the life cycle. The validation process also needs to be continuously monitored to verify that standards are kept in place.

About Astrix

For over 25 years, Astrix has been a market-leader in dedicated digital transformation & staffing services for science-based businesses. Through our proven laboratory informatics, digital quality & compliance, and scientific staffing services we deliver the highly specialized people, processes, and technology to fundamentally transform how science-based businesses operate. Astrix was founded by scientists to solve the unique challenges which science-based businesses face in the laboratory and beyond. We're dedicated to helping our clients speed & improve scientific outcomes to help people everywhere.