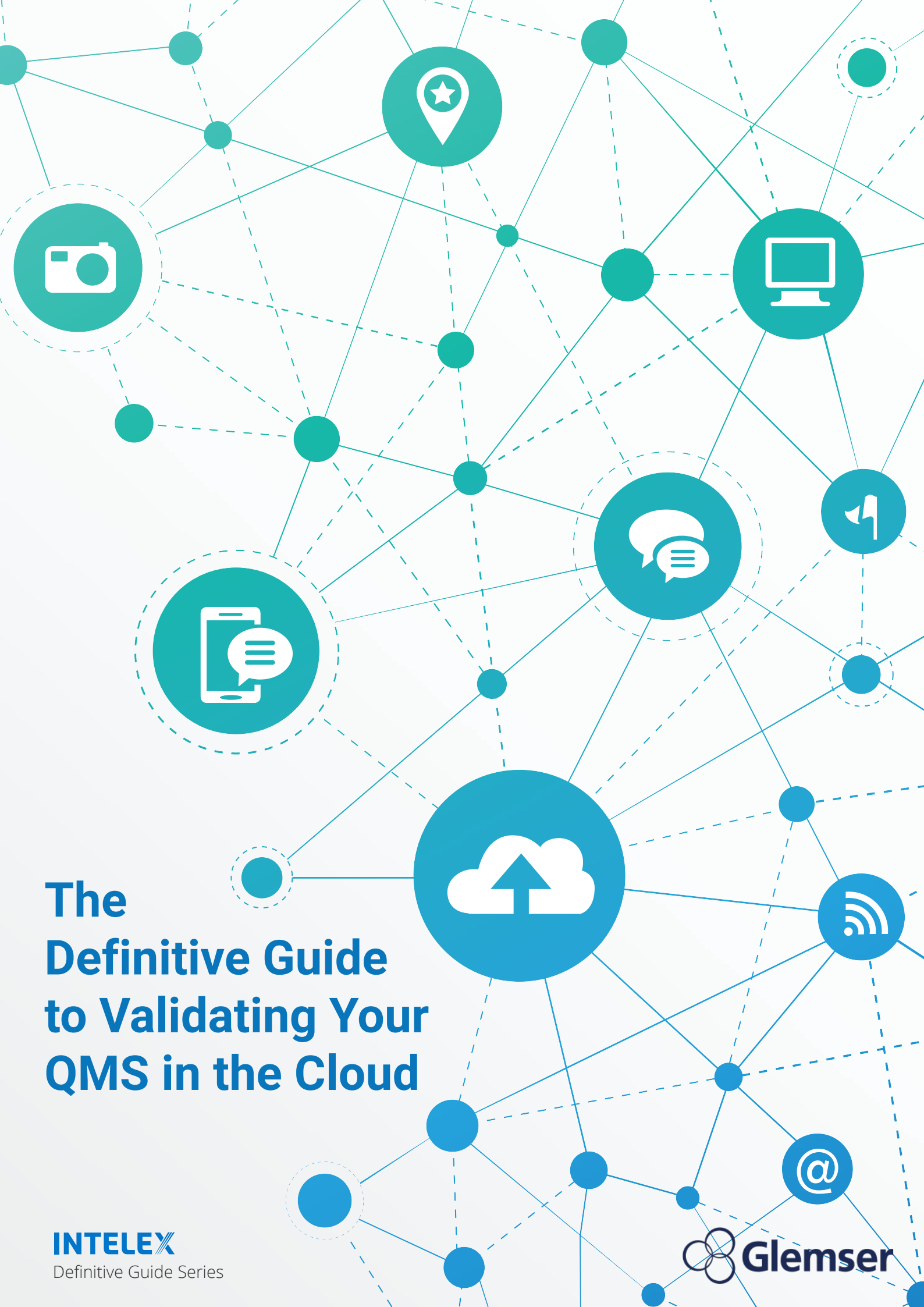

The Definitive Guide to Validating Your QMS in the Cloud

INTELEX
Definitive Guide Series

Glemser

INTELEX Glemser

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CHAPTER 1: The Validation Imperative

Validation – a requirement of the regulations

With every trip to our local pharmacy, grocery store or corner variety shop, we pass hundreds of products that have reached the shelves only after a lengthy process designed to ensure their quality. A medical thermometer manufacturer, for instance, subjects its product to rigorous, government-mandated testing before it can offer it for sale. Similarly, a cheese-maker ships its cheddar or mozzarella to grocery stores only after it has met countless quality checks.

It's not something the everyday consumer thinks much about. But without this crucial element of the manufacturing process, we would never be able to trust the quality of the many products whose high standards we take for granted. It's quite easy to envision the catastrophes that would result.

Core to the process of ensuring quality is the concept of validation. This is the process whereby pharmaceutical manufacturers provide objective, documented evidence that their processes, equipment and computerized systems are checked and validated to ensure the quality of their medicines and medical devices.

Central to the validation journey is the required documentation produced with each step. To satisfy regulators, companies must record evidence to prove what work was done and when, including elements such as designs, tests and test-script executions.

The form of that evidence has evolved over the years. Until the 1990s, it was primarily paper. As products, particularly in the pharmaceutical and medical device manufacturing space, became more complex and subject to ever-expanding regulatory requirements, companies found themselves drowning in seas of paper. For many organizations, the task of documenting their work was becoming as expensive as the actual work itself.

The solution rested in computer software and the components of the validation process that digital offerings could automate. For instance, hard copy documents, drawings, records and other collateral that was used in the validation of many different products could now be created once, stored electronically, and pulled out whenever necessary. Despite some early resistance and confusion – how could an electronic signature be as legally binding as a good old-fashioned pen and ink one, for instance – the electronic model caught on. The digital spreadsheet ruled the quality validation landscape.

In today's well-established Internet age, a new model has emerged. Still electronic, it is defined by where the validation collateral resides and who controls the different parts of the new architecture. It's known as the Cloud model, and this paper will provide an in-depth look at how it works and the many improvements it offers manufacturers charged with validating their products.

Documentation and traceability – ensuring your software is doing what it should

Traditional on-premise validation of a QMS typically utilizes a "V Model" workflow (see Figure 1). The process begins on the top left, with the left side defining a series of required deliverables. Once these are mapped out, you can configure and develop the system. Finally, as illustrated on the right arm of the model, the system is tested, with these actions being traced back to the previous planning stages.

The model helps organizations answer key questions about the project, such as:

- What are you trying to accomplish?
- What are the roles?
- What documents are you going to generate?
- Who approves them?
- What process will you follow to develop this application?

The model helps ensure that the system will be able to effectively handle a regulated action that occurs in the everyday process of doing business. A manufacturer, for instance, would use the model to guarantee that a product recall request could be carried out. Proving that this can be done is imperative if the firm is ever audited by a regulatory body. The product lot number on an affected customer's invoice would have to match the one on a materials batch record. This kind of detail is an example of what is tested during the workflow on the right arm of the V Model.

The total time required to complete all steps in a V-Model varies by project size, but Dr. Ray Glemser, CEO and executive consultant of Glemser Technologies, an IT services and solutions firm serving the life sciences industry, says six to 12 months is typical for traditional large on-site systems, with two to four months of that being dedicated to testing.

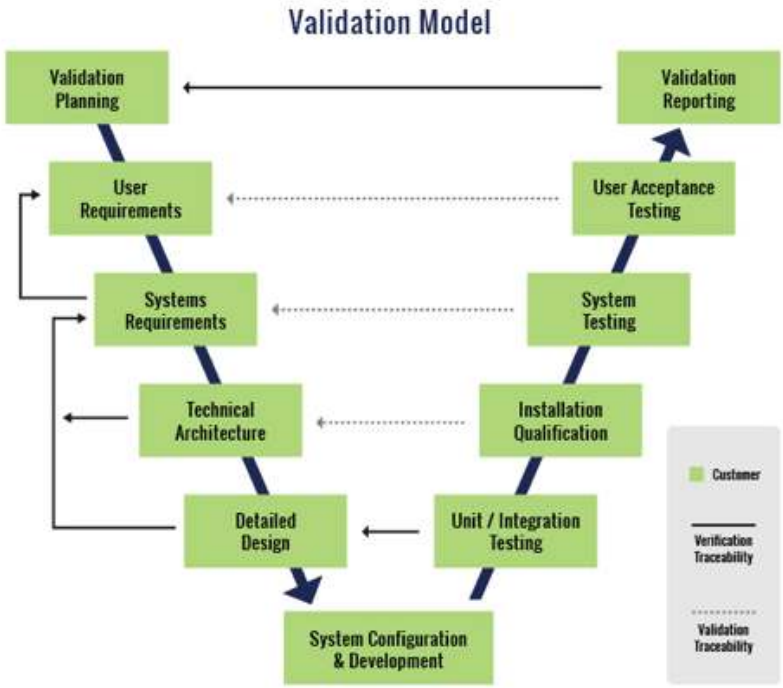
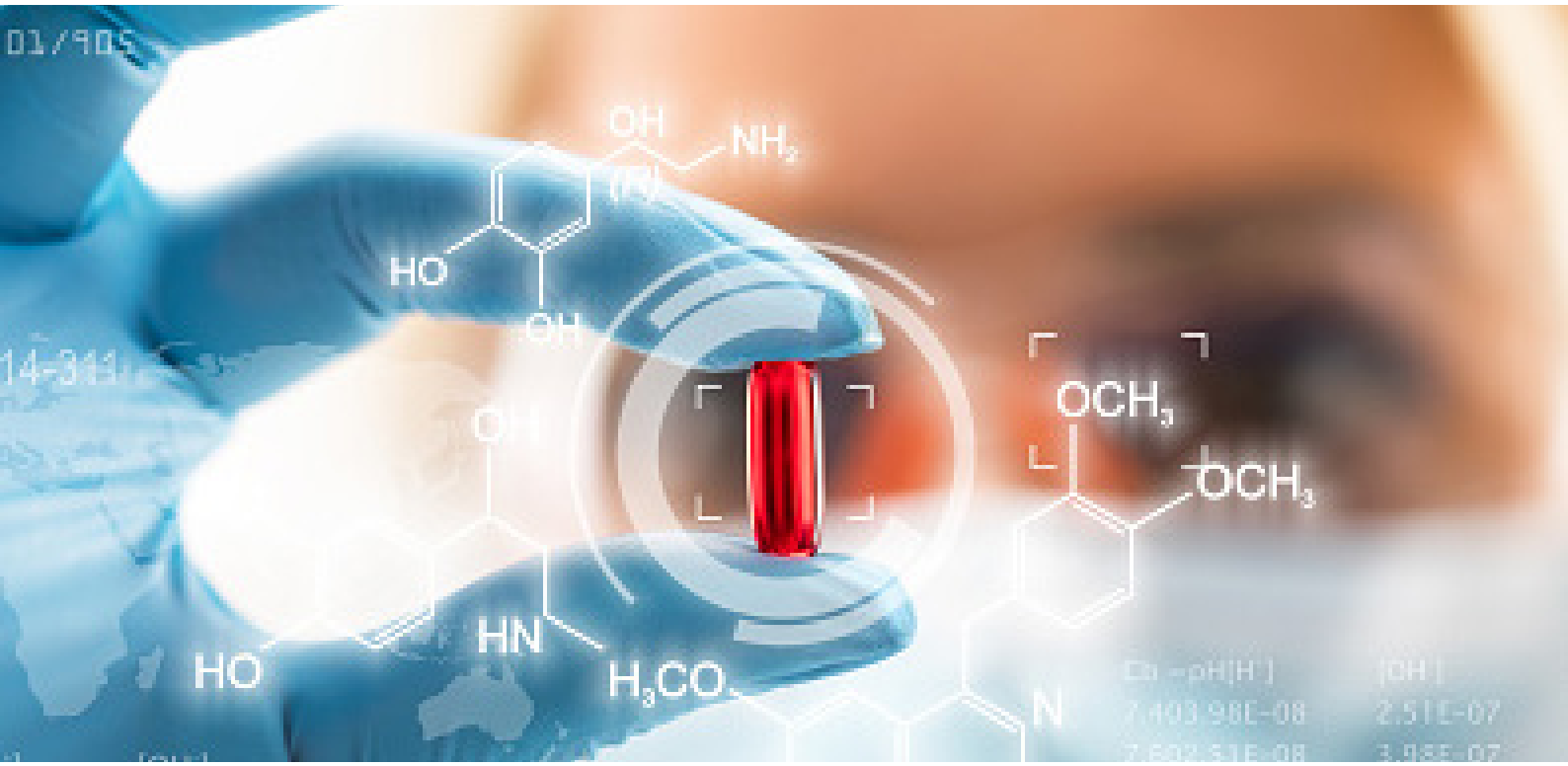


Figure 1 - QMS Validation Model

FDA audits and consequences

Following the Validation Model helps organizations feel confident that their operations will stand up to the stringent requirements of U.S. Food and Drug Administration (FDA) auditors. Failure to meet requirements can result in consequences of varying degrees of severity, depending on the nature of the offense and an outfit's history with the FDA.

- **Recommendation** – Important feedback provided to companies with a good FDA relationship. An issue is noted in an audit file with the expectation that it be addressed by the next audit.
- **483 form** – A formal notice sent to the head of a company's Quality department, with a response due within 30 days. This a low-key public record similar to a misdemeanor.
- **Warning letter** – A public letter sent to a company's CEO with a plan due within 30 days. This is similar to a felony offense and may result in a second and third warning letter.
- **Consent Decree** – This is a legal action taken by the FDA through the U.S. courts and is similar to a warning letter. An overseer who reviews a Quality remediation can be involved in more complex cases. The results of a Consent Decree can be severe: fines, shutting down of portions of an operation, or suspension of licenses. An infrequent Consent Decree issued by the FDA raises industry awareness of the seriousness of a particular offense. Because this action constitutes an actual lawsuit and is played out in the U.S. court system, the spotlight is particularly bright on the recipient. Some cases have taken years to play out.



Three approaches to define a QMS

QMS Elements

In this definition, we can think of a QMS as the relationship between roles within an organization and a set of procedures.

One set of roles falls under the Executive element. These business decision makers can hold various titles, including CEO, chief quality officer, a division president or vice-president of quality.

Ideally, leaders will be well-informed of their company's Quality efforts. They will also be part of a Quality steering committee that meets regularly to review quality metrics, such as adverse events or incidents, and deviations in processes. This analysis in turn leads to corrective actions and an understanding of any patterns that, once corrected, can help the firm enjoy better quality results, delivered more consistently.

Another key area of involvement for executives is at the supply chain level. Leaders should participate in audits of their own company's supply chain and those of their customers, of which they are a part. These audits generate findings and observations that can shed light on any underlying trends that are affecting quality, either in a positive of negative way.

A second set of roles is encompassed by a company's Quality and Compliance arm. Different functions have a hand in ensuring product quality, some more directly that others. The typical players are:

- **Systems**, those who manage the enterprise technology infrastructure that has an impact on quality
- **Validation**, which involves testing applications and ensuring they are compliant
- **Training**, which involves creating specialized testing for staff on compliance training and quality systems
- **Compliance**, the group that tracks government regulations and ensures the company is satisfying them
- **Information Security**, which is charged with ensuring all data is protected from outside threats – a growing area of importance given the number of cyber threats that are now part of operating over the Internet.

A third set of roles under a company's Quality umbrella focuses on Operations. Departments in this area work to ensure the functions of production are carried out with maximum efficiency. Two specific departments – Infrastructure (physical assets such as machinery) and Technical Operations (IT) – have many elements that require detailed Quality testing.

In most companies, there is a tug-of-war between Operations and Quality, where the former group is driven to meet production targets, and the

latter, which concentrates on quality, sometimes counterbalancing the Operations group's desire to get wares off the line and into buyers' hands.

"That's the way organizations work," Glemser says. "The tension between these competing perspectives are basically institutionalized. These are competing forces. Quality issues can arise with too much focus on achieving output objectives. . But over time, they come to meet in the middle. And you need both of those in organizations, in order to really find the right balance."

That balance will shift, as outfits are faced with different business challenges and changing regulatory environments. It's ultimately up to the Executive to make sure the balance does not shift too far in either direction.

"If something goes wrong, it's typically viewed as a failure of the CEO and leadership to support Quality," Glemser adds.

The other main bucket of QMS elements is known as the Quality Framework, which codifies what needs to be done to ensure organization-wide quality. It encompasses **Strategy**, laid out in a Quality policy that is typically aligned with regulations; management of **procedures** such as audits and reviews and business continuity planning; and management of **foundational elements** that help track what was done when – things such as electronic documents, records and signatures.

QMS processes

A second way to define a Quality Management System is the QMS Processes model. It starts by defining your customers' requirements (on the left side of Figure 2) and what goods and services you will provide to satisfy them. Once the product is created and distributed, a process of continuous improvement then takes place to ensure ongoing quality. It involves measurement and analysis of customer feedback, reallocation of resources to improve the product (if required) and distribution of the updated offering.

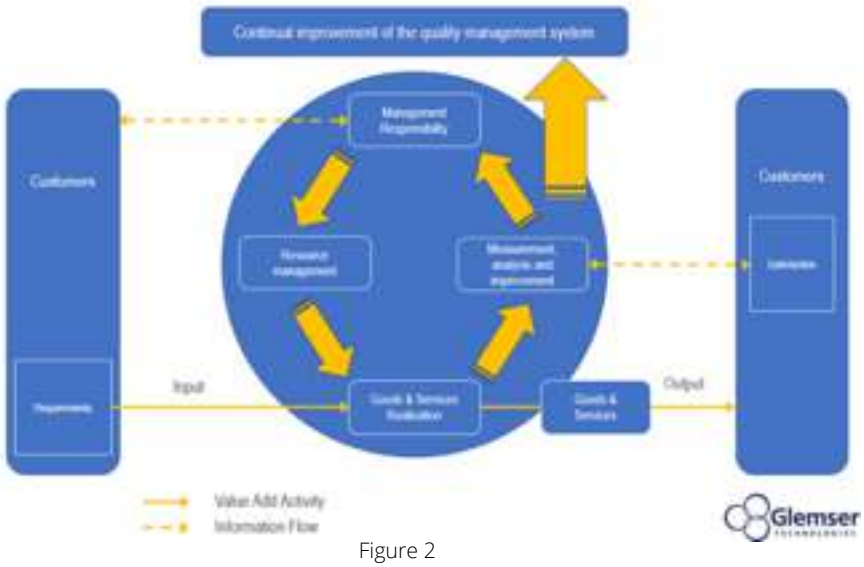


Figure 2

QMS activities

A third QMS definition, known as the Plan, Do, Check, Act model, is based on activities. It follows a popular model used in various business applications beyond Quality. Plan activities focus on such things as the creation of processes and procedures around document control, managing audits, training staff and defining how the products will be managed.

Once the product or service is out on the market, a company's Quality arm moves into the Do phase to ensure continuous improvement. This involves such activities as making adjustments based on customer complaints, tweaking the training that is delivered, and undertaking inspections and revising their focus if required.

Check activities include Root Cause Analysis, looking at Key Performance Indicators and Pareto Analysis (a widely used statistical technique in decision-making used for the selection of a limited number of tasks that produce significant overall effect.) These inform what action items are undertaken in the Act phase. All activities under this model aim to achieve continuous improvement of the quality of an organization's offering.

"This is another way of saying the same thing (as the other two models), except that it takes the customer out of the central part of it and organizes it around understandable quality initiatives and activities that most Quality organizations do," Glemser says.

The Cloud – What is it?

Traditionally, companies have owned and operated their Quality Management System using their own resources – an in-house IT department and fully owned, on-premises computing resources. However, given the increasingly sophisticated nature of QMS software and the high cost of specialized talent capable of managing, maintaining and upgrading it, firms are adopting a new approach known as the Cloud model. Let's look at exactly what it is.

The three players

The Cloud model features three main players: the customer, the software provider, and a middle level participant, the cloud provider. The provider's function is to manage the infrastructure and all responsibilities associated with it for the customer, in its own location, typically known as a data center. For a fee, the customer is relieved of the burden and cost of looking after the infrastructure piece of the QMS puzzle.

Cloud service models

There are three ways that companies can buy cloud services:

- Software as a Service (SaaS) – The most typical model where the customer uses the software provider's applications running on the cloud provider's infrastructure.

- Platform as a Service (PaaS) – The customer creates or acquires applications using tools from the software provider and deploys them onto a cloud infrastructure.
- Infrastructure as a Service (IaaS) – The customer "rents" processing, storage, networks and other cloud infrastructure from a cloud provider on which it can deploy and run any software.

Qualified Infrastructure

For most customers, the big change that comes with moving to the Cloud model is the transfer of their applications, data, servers and associated computing components to another organization. Let's call these assets the Qualified Infrastructure.

Cloud deployment models

There are four Cloud models into which the Qualified Infrastructure can be deployed:

- Private Cloud – Used only by one customer, it is managed by the customer on premise or by a cloud provider;
- Community Cloud – Used by multiple customers, it is managed by a cloud provider in support of a community with shared concerns;
- Public Cloud – Shared by many customers and managed by a Cloud provider;
- Hybrid Cloud – Two or more clouds that remain unique entities but are connected by technology that allows data and applications to be shared between them.

Chapter 3: The Cloud

Success factors for moving into the cloud

Customers are moving their QMS into the cloud for many reasons:

- **It is easier to finance**, with expenses spread out over a number of years. Because your company is sharing computing resources with other people, the total cost is cheaper overall. The services component will be higher than if things are kept in-house, but expenses such as hardware purchasing/upgrading and employment of increasingly expensive talent to manage the computing resources will be taken off the corporate ledger.
- **It is faster to deploy.** Business benefits are realized much quicker because internal processes, such as reviews, approvals, and the accompanying meetings and endless email chains that typically bog down implementations are no longer part of the equation. According to Glemser, one of the most common pain points identified by his newer clients is that their traditional validation process takes too long, often a period of several months or longer.
- **It offers faster access to the latest and greatest software features.** No longer does the customer need to keep up with newest developments in software and implement those they want. Cloud providers seek to keep pace with industry innovation and ensure the latest advancements are available to customers.
- **It frees up people for other strategic initiatives.** The efforts of precious IT and operational resources previously dedicated to "keeping the lights on" can now be redirected to other, higher-value tasks and responsibilities that can help grow the business, rather than simply maintaining the technology infrastructure.
- **In the Cloud, it is easier to scale up to meet global needs.** Previously, multinational firms would typically roll out components, such as a compliance handling system, gradually throughout the world, perhaps starting in North America and then, months later, to its locations in Europe and Asia-Pacific. With the Cloud, every location can get the same information technology functionality at the same time, increasing efficiency and allowing the company to get the most out of the updated technology.

The (perceived) cloud tradeoff

For many organizations, the obvious gains offered by the Cloud model around Total Cost of Ownership (TCO) are tempered by perceived risks associated with ensuring the integrity and security of their data when entrusting it to a third-party cloud provider. Particularly in the pharmaceutical industry, high-profile, headline-making corporate security breaches generate enough concern to make companies want to keep all data in-house.

According to Glemser, however, the human resources cost associated with keeping information secure is becoming prohibitively high. Top information security talent is being recruited by the likes of governments and top-level

cloud providers like Amazon and Microsoft. Most pharmaceutical companies find it difficult to compete – which is increasingly spurring them to move to the Cloud.

Although pharmaceutical companies are more conservative in their embracing of the Cloud, relative to other industries such as financial services, they are becoming increasingly comfortable with entrusting their data to a third party. A typical approach, says Glemser, will see a pharmaceutical firm begin by putting less-sensitive data in the Cloud, such as marketing collateral, and keeping their core "secret sauce" data behind its own walls.

Regulatory responsibilities in the cloud

Companies that move to the Cloud are still responsible for meeting the same regulatory obligations as in the traditional model. They must:

- Comply with regulatory requirements, including: validating and maintaining the validated state of their QMS; maintaining documented quality procedures; and auditing quality suppliers, including their software providers and cloud provider.
- Maintain data integrity and data security.
- Control changes.
- Back up, recover and restore data.

For their part in the regulatory picture, Cloud providers are responsible for keeping QMS records. Specifically, this involves:

- Keeping accurate and complete copies of records
- Protecting records
- Limiting system access
- Carrying out operational system checks, authority checks (who has what permissions?) and device checks
- Maintaining a policy for accountability
- System documentation
- Ensuring the integrity of electronic records
- Maintaining controls around electronic signatures
- Password controls.

Larger cloud providers like Amazon and Microsoft have been working with life sciences companies for years, Glemser points out. They have created platforms tailored to address the regulatory responsibilities particular to this industry.

What has changed in the cloud … and what hasn't

A key element in any software validation process is the Installation Qualification (IQ). This is essentially a checklist to ensure all elements needed to effectively run the software are in place. Questions to be answered include whether the software was loaded correctly and whether there is enough memory. The Cloud model's architecture introduces new elements that companies must be aware of, as these pertain to the validation process.

Regulatory expectations for cloud providers

The traditional and the Cloud architecture share the same basic structure. It consists of:

- A **development** environment, where applications are created,
- A **test** environment, where the recently developed software is tested exhaustively to make sure it does what it is supposed to do,
- A **production** environment, where the final, live version of the software sits, and,
- A **backup** environment, which houses an identical copy of the final version of the software lest something happen to the in-use version.

The architecture of the Private Cloud model mirrors the traditional architecture. The only differences are that the servers and additional infrastructure pieces are housed on the cloud provider's premises, and that the cloud provider performs the IQ.

One significant difference between the traditional model and the Community and Public Cloud models is in the actual servers themselves. All servers are virtual in these setups, as opposed to being individual machines. These are used so that cloud providers can house exponentially larger numbers of clients than they could on individual servers dedicated to a single customer.

This, however, creates a challenge when trying to pull information on an individual client for the purposes of an IQ. Where before it was simple for a company to find its data because the servers were their own and no other companies' data was present to create any confusion, in the virtualized cloud, the abundance of data makes it next to impossible to extract pinpointed data for an IQ.

Cloud providers instead capture data from across their virtualized environment that is representative of whatever parameter is being requested to satisfy the requirements of an IQ, such as available memory. This data is then used to help establish that the IQ has been carried out appropriately. According to Glemser, the method is being well received by life sciences companies looking to satisfy regulators.

Who plays what roles

Who does what in the Validation model (see Figure 1) can change when we move to the Cloud (see Figure 3). The customer remains responsible for, on the front end, validation planning and user requirements, and on the back end, user acceptance testing and validation reporting.

The software provider can assume responsibility for system requirements, detailed design, system configuration and development, unit/integration testing and system testing.

The cloud provider can now look after the technical architecture and IQ.

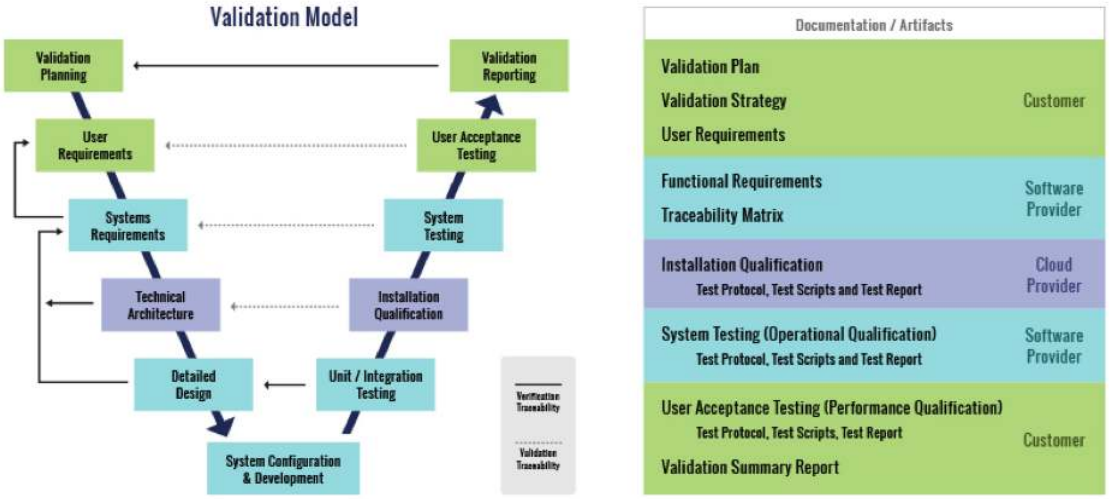


Figure 3

Change control – private cloud vs. public cloud

Life sciences companies can tap into a wealth of innovative software that is being developed at a rapid rate – but it comes at a price. Every time new or improved software is introduced and adopted, it is accompanied by an additional revalidation cost.

In the traditional and private cloud models, customers have full control over software changes. They can review new releases and patches from their software vendors and introduce changes at their own pace.

In the community and public cloud models, the software provider controls software changes. To increase the level of flexibility a customer has over the processes, the concept of feature toggles is becoming more widely used. In this setup, the software provider publishes its upcoming changes before releasing them. The customer then reviews, assesses and accepts the changes prior to deployment.

Using change controls, a company can elect to either turn on a feature and use it or simply leave it turned off. Features are typically organized by either modules or types of documents supported by a department. Examples include controls around document management, training management or complaint management.

Software provider innovation

Important changes are taking place in the way many software providers develop their products, ones that have direct impacts on the validation process.

Waterfall development vs. Agile development

For many years, developers have used the “waterfall” model to create their software. This involves creating a fully developed version of the software before presenting it to customers or internal customer representatives for testing and feedback. Each step – plan, analyze, design, construct, test, deploy and maintain – is done one after the other, forming a waterfall visual. (See Figure 4).

Here, all user requirements are defined before anything is developed.

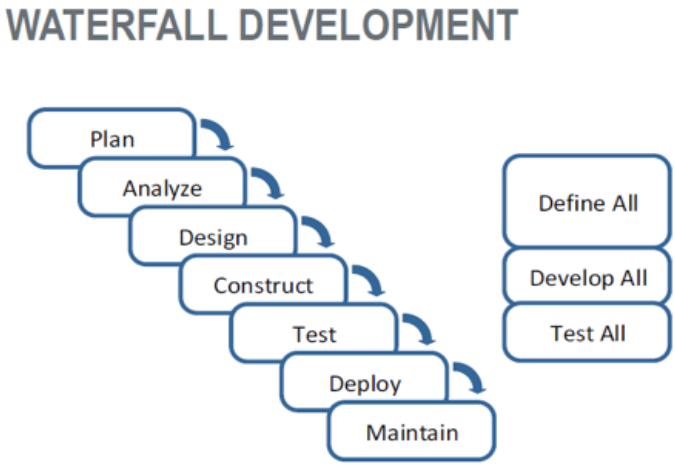


Figure 4

A major drawback to the Waterfall model is that it is often impossible to know all user requirements at the outset of the a software development project. Those that are identified often change during the months-long development cycle. Others do not become evident to users until the completed version is put before them. Developers then must go back to incorporate change requests, adding significant time to the process. Validation at the end also can add months to the release cycle.

To help speed up the process, software developers are increasingly using the Agile Development model (see Figure 5). Here, rather than being created all at once, portions of the software are developed in "sprints" of two- or three-week periods and presented to users for feedback. This is then incorporated into the next sprint, and so on, until a feature complete product is delivered at the end of the cycle.

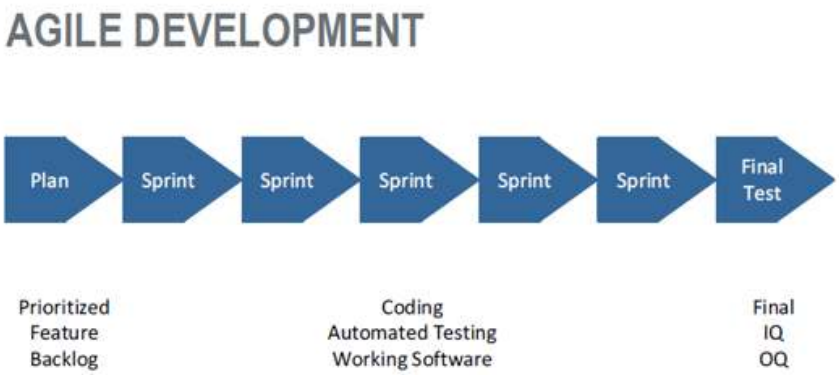


Figure 5

Typically included on the agile development team is a validation analyst, who is checking and validating along the way. This, according to Glemser, can reduce the validation time typically required at the end of the Waterfall model.

Quicker development times are a benefit of the Agile model, but its main objective, Glemser says, is to "get something in front of customers that they can actually use, rather than something we thought they could use 18 months ago with limited input."

Development Operations

Glemser also notes that software developers are taking advantage of a proliferation of exciting new development tools to help them create deliverables more quickly and more accurately. Collectively known as Development Operations, or DevOps, these include automated testing tools, automated build tools and security and quality scanning. As a result, software development shops are today much more robust environments than in the past, with new roles dedicated to specialized tasks.

"It isn't just a couple of people programming anymore," Glemser says. "What's happening in modern software development is that it's like a factory....This isn't your grandfather's software development shop anymore."

The new partnership-based landscape

With more than two parties (customer and software provider) now involved in the validation process (cloud provider now added to the mix), the concept of the typical Service Level Agreement (SLA) changes in the cloud. It's important, Glemser says, for a customer to recognize they are now in partnership with the other two players, who are performing more specialized functions for them.

"These are tied together in what we used to call an SLA," Glemser says. "We are now organizing them into Quality Agreements where the Quality system validation state needs to be maintained by multiple organizations rather than just one. It is very important to get the roles correct, the business relationships established and the procedures in place at the different organizations to support these Quality Management Systems in the cloud."

Looking ahead

Many organizations, Glemser points out, have moved their QMS validation efforts into the public cloud and are realizing significant benefits, including lower costs, the ability to focus on core business concerns rather than merely "keeping the lights on", and access to leading software products and expertise.

"They're not going to turn back, and it's only a matter of time before everybody gets comfortable with it," Glemser says.

Yes, there will always be stragglers, he adds. The life sciences industry, in fact, is one of the most conservative in its willingness to move into the cloud.

"But many industries are already here, and the fact that people are successfully surviving audits while operating in the cloud will continue to push the pendulum to this side."