Validation Master Plans as Commitment Documents

Justin Pawlik

“Validation Strategy and Planning” discusses various topics associated with strategic aspects of validation useful to practitioners in validation and compliance. Experienced practitioners in validation and compliance often comment that strategy and planning are the most important activities associated with validation. We intend this column to be a useful resource for daily work applications. The key objective for the column: Useful information.

Reader comments, questions, and suggestions are needed to help us fulfill our objective for this column. Manuscripts or case studies submitted by readers illustrating validation strategy and planning are also most welcome. Please send your comments and suggestions to column coordinator Stephen Perry at stephen.perry@kymanox.com or to coordinating editor Susan Haigney at shaigney@advanstar.com.

KEY POINTS DISCUSSED
The following key points are discussed in this article:

• A validation master plan (VMP) is more than a plan for validation; it is a commitment from the organization to achieve compliance during validation
• A VMP is a forward-looking document that must contain a plan for maintaining the validated state of systems after initial qualification
• Every VMP should contain three general commitments: a commitment from management, a commitment to how compliance is achieved, and a commitment to plan validation
• It is a regulatory expectation that there is a commitment from management, which is necessary for any effective validation program
• The commitment from management is a policy statement that describes the organization’s values, global objectives, and global approaches for achieving compliance
• The statement of the commitment to achieving compliance is comprised of the groups responsible for validation, the documentation created to support validation, and a high-level description of the activities performed to meet the requirements for compliance
• Including a high-level description of the validation activities helps to explain the organization’s interpretation of regulations and guidances and define the terminology used by the organization
• The VMP contains a commitment to plan all aspects of validation, including scope, schedule, and validation lifecycle management
• The VMP helps good manufacturing practice inspectors understand the company’s level of commitment by describing the validation approach and outlining the setup and organization of all validation activities
• Validation lifecycle management is a statement of commitment from the organization to maintain its validated state and support the forward-looking nature of the VMP.

INTRODUCTION
In the pharmaceutical, biotechnology, and medical device industries, it is paramount that the products manufactured are done so under strict guidance and supervision. Quality systems are put into place to

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ensure the safety and efficacy of the product. Validation ensures that systems, equipment, and processes are reproducible and reliable. The validation master plan (VMP) is the primary document that houses all aspects of the validation process and conveys management’s overall intent, including defined policies, validation scopes, scheduling of required work, and responsible persons.

A VMP is more than a plan for executing validation. It is a commitment from the organization to ensure that the validated systems satisfy regulatory expectations. The individual sections in a VMP include different policy statements that outline various commitments from the organization. While the VMP is used to plan validation and outline the commitments from the organization, it is also a forward-looking document. A VMP must include a commitment for maintaining the validated state of systems in the future, as well as achieving a validated state for systems in the near-term.

COMMITMENTS IN A VMP
The VMP is viewed by regulatory agencies and auditors as a commitment document and is frequently one of the first documents requested in audits. A VMP is an overall commitment to ensure that systems, equipment, and processes are validated and in compliance with governmental regulations and company policies. It demonstrates that the products manufactured from those systems and processes meet safety and efficacy requirements for the end customer. The following are specific commitments made in a VMP:

• A commitment from the management of the organization
• A commitment to how compliance is achieved
• A commitment to properly planning all aspects of validation.

The Commitment From Management
A VMP must, first and foremost, contain a commitment to compliance and validation from the management of the organization. The overall commitment from management is a policy statement that describes the organization’s values, global objectives, and global approaches for maintaining the validation quality system. Documenting this information is consistent with International Conference on Harmonisation (ICH) Q7, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, which states: “The company’s overall policy, intentions, and approach to validation…should be documented” (1).

Management’s commitment to achieving compliance is a regulatory expectation which can be accomplished through an effective validation program. ICH Q10, Pharmaceutical Quality System (2), 21 CFR § 820.20 (3), and the International Organization for Standardization (ISO) 9001 (4) quality assurance model all refer to the need for a commitment from management in order to achieve compliance. The specific topics included in the policy section of a VMP form the management’s overall commitment to validation.

First, the VMP must broadly define the organization’s values with respect to validation. Just as a child’s values are developed from parents, so too are the values of employees developed from management. Defining the organization’s values regarding validation creates an environment where validation is viewed as an essential quality system. Validation is not simply an activity that is complete when all required tests on the systems have been executed and passed.

Outlining the organization’s policies and values in the VMP is important because they describe the validation philosophy by which the organization operates and monitors its commitment to compliance and validation. Since the VMP is typically requested by inspectors prior to or during an audit, including this information in the VMP demonstrates management’s commitment to validation.

The VMP must also include management’s global objectives for validation. These objectives outline the goals for the validation program. Goals that are written down have a much higher probability of being achieved than those that are not. Goals for validation are no different. Including the objectives for validation in the VMP is a commitment to achieving those goals from the management of the organization.

In addition to including global objectives for validation, the VMP must include global approaches for ensuring that the validation program is both effective and accurate. Every system must be monitored and controlled after implementation to make certain that it continues to operate as intended. A frequency schedule for evaluating validation status should be applied to each area based on criticality and quality risk. Including a plan for maintaining the validation program reaffirms management’s commitment to validation.

The Commitment To How Compliance Is Achieved
A commitment from management to compliance and validation is expected to be contained in a VMP.
However, it is not the only policy statement that must be included. The VMP must also include a commitment to how compliance will be achieved. The VMP is one of several quality systems that help to ensure that compliance is achieved. Other systems include training and auditing. The methods listed below are included in the VMP:

- The groups responsible for ensuring compliance is achieved during validation
- The documentation that must be created to support validation
- The validation activities that must be performed to meet the requirements for compliance.

The VMP must outline who will be responsible for ensuring completion of validation efforts. Effective and compliant validation is not the responsibility of just one person or group; it requires multiple resources from multiple departments within an organization. Validation may also require outside resources such as consultants or subject matter experts. Identifying responsible persons for completion and approval of validation activities provides a high level of commitment and enhances accountability.

Since outside resources may be needed to complete validation, additional steps may be required. For example, if an outside supplier is providing material for a process, that supplier would need to be qualified before the material could be utilized in a process. Including this supplier as a responsible party in the VMP displays the commitment to achieving compliance to inspectors reviewing the VMP.

Documentation is an essential component of any successful validation. Many documents will need to be created to support validation efforts, and these documents must be listed in the VMP. Annex 15 to the European Union (EU) Guide to Good Manufacturing Practice lists documentation as data that must be included in a VMP (5).

The following are examples of documents that may be required to support validation and should be listed or referenced in a VMP:
- Specifications (i.e., user requirements specification, functional requirements specification)
- Standard operating procedures (SOPs) (i.e., preventative maintenance SOP)
- Supplier documentation (i.e., certificates of compliance)
- Supplier audit reports
- Protocols (i.e., installation qualification protocol, process validation protocol)
- Protocol reports (i.e., installation qualification summary report).

Including the documentation required to support validation in the VMP is a statement of the commitment to how compliance will be achieved during validation.

Achieving compliance in validation also involves activities that will be performed during validation to meet the requirements for compliance. As such, a high-level description of these activities must be included in the VMP and serve as another policy statement of the commitment to how compliance will be achieved during validation.

While the specific details of each activity performed for validation will be described in other documents, the VMP should include the high-level details of the activities to be performed. The inclusion of this high-level detail serves the following purposes:

- **Explains the organization’s interpretation of regulations and guidances.** The regulations and guidances provided by the many regulatory agencies are not specific instructions on how to perform various activities. They are generally high-level requirements that point in the correct direction. The implementation of these regulations and guidances is left up to the individual organizations. The interpretation of these documents can vary from one organization to another. Describing the high-level details of validation activities allows inspectors to become acquainted with and understand the organization’s individual interpretation of the governing regulations and guidances.

- **Defines the terminology used by the organization.** In validation, there are many terms that are used to describe the activities that will take place: commissioning, installation qualification, operational qualification, etc. However, the terminology may vary from one organization to the next, especially if each organization services a different part of the industry. For example, activities that are included in the installation qualification of medical device companies may be part of the operational qualification for pharmaceutical manufacturers. Defining terminology for validation activities in the VMP familiarizes inspectors with the specific terminology used by that organization.

An overall commitment to achieving compliance, and specifically, how compliance will be achieved, is a critical statement of commitment that must be made in a VMP. This commitment is comprised of outlin-
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ing what groups will be responsible for validation, the documentation that must be created to support validation, and a high-level description of the activities that will be performed to meet the requirements for compliance. Any inspector viewing the VMP will see that the organization is committed to achieving compliance during validation if the appropriate information is included.

Commitment To Planning And Keeping To The Plan
The final commitment that must be made in a VMP is the commitment to planning all aspects of validation. Planning specific components of validation is critical to ensuring the overall system is qualified for its intended use. Annex 15 to the EU Guide to Good Manufacturing Practice (5) states that “all validation activities should be planned.” The commitment to plan validation should include scope, schedule, and the organization’s policy for validation lifecycle management.

Defining the scope of validation in the VMP is the first step to ensuring that the overall system can satisfy the regulatory expectations for compliance. A commitment to planning validation starts with defining the boundaries for validation in the VMP. Depending on the scope, the VMP can be a commitment to ensure compliance for a single piece of equipment or for an entire site. There are also many interdependencies with the various systems in an organization, and the VMP must define what is and is not included in validation. Explaining the boundaries of validation in the VMP is a commitment from the organization to ensure compliance for those systems.

The commitment to planning validation must also include a plan for the primary validation schedule. The validation schedule outlined in the VMP is most certainly viewed as a commitment by inspectors reviewing the VMP. There are several techniques that should be used when planning the validation schedule, as described in the previous installment of this column (6). The most important technique for maintaining the validation schedule is using task dependencies rather than hard dates. Using specific dates for achieving milestones may result in missed deadlines, which can raise red flags for inspectors during an audit.

There may be legitimate reasons for missing milestones during validation, such as delay of a shipment of raw material from an outside supplier. However, because the validation schedule is a commitment from the organization, milestones that are constantly missed during validation may be indicative of a larger problem within the organization. This, in turn, may result in additional scrutiny from inspectors into other parts of the organization, such as its management or quality systems. The validation schedule is a commitment that must be made in the VMP.

The VMP must also contain a statement of the organization’s policy and commitment to plan validation lifecycle management. Every system needs to be monitored and maintained after its initial implementation. 21 CFR § 820.75(b) states that procedures for monitoring and controlling process parameters in validated processes must be established and maintained (7). Planning validation lifecycle management is the commitment to maintain the system’s validated state.

In order to ensure that a system is still capable of producing a product that is high in quality and safe for patients, it must be monitored from time to time. There must be a change control system in place to address any changes that need to be made to the system after its initial qualification. Including the policy and plan for post-validation monitoring in the VMP shows the organization’s commitment to maintaining its validated state.

CONCLUSION
A VMP is a document that serves many purposes for validation. One of its key functions is as a commitment document. The VMP should contain three specific commitments: a commitment from the management of the organization, a commitment to how compliance will be achieved during validation, and a commitment to planning all components of validation and keeping to those plans. Each commitment is not only expected, but is required by various regulatory agencies throughout the world. A VMP will likely be requested by inspectors prior to or during an audit.

Validation is not only an activity that is required to ensure that validated systems operate as intended. Validation is a commitment from all involved parties to ensure that the systems satisfy regulatory expectations, which are in place to ultimately protect the patient.

ACKNOWLEDGMENTS
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REFERENCES
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RESOURCES

ARTICLE ACRONYM LISTING
CFR Code of Federal Regulations
EU European Union
FDA US Food and Drug Administration
GHTF Global Harmonization Task Force
GMP Good Manufacturing Practice
ICH International Conference on Harmonisation
ISO International Organization for Standardization
SOP Standard Operating Procedure
VMP Validation Master Plan