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Ways out of the Validation Jungle

Validation from a Process Equipment Manufacturer's Point of View

In the pharmaceuticals industry, machinery and systems need to be validated. So far, so good. While it is true that there are numerous recommendations, instructions, and guidelines, putting these into practice will frequently be a painstaking and expensive effort. A Validation Master Plan developed in good time is indispensable so that it will be possible for both sides to control costs.

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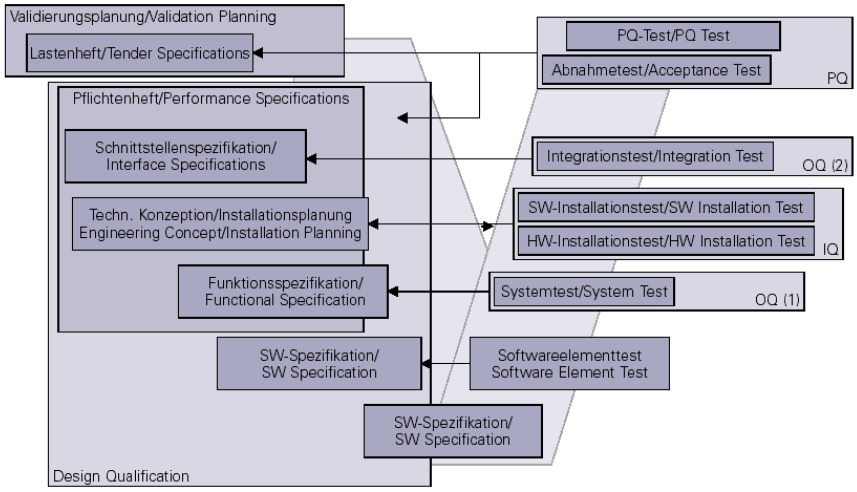
In the sector of the pharmaceuticals industry, the qualification and validation of systems, plant, and apparatus is common practice. Business enterprises intending to design and operate a manufacturing facility, and to sell their products on the US market, will inevitably be subject to supervision by the FDA (the Food and Drug Administration). The objective is essentially to ensure that a machine or system will produce a product of a quality that remains constant, and, in particular, that documentary evidence of this will be available. The main expenditure incurred in the validation or qualification of a piece of equipment or apparatus will primarily result from implementation in terms of electrical engineering and there, particularly, in providing documentation relating to computer-assisted process instrumentation and control engineering. Sections below will therefore relate especially to the qualification and documentation of computer-based systems and apparatus.

In a large number of cases, users will be confused about the way the qualification documents have been drawn up because an FDA guideline only says 'that' validation will need to be carried out, but will



Das V-Modell **The V-model**

consistent guidelines applicable to the validation of computer-based systems. The guidelines not say anything about the 'how'. Accordingly, the requirements imposed by system operators on plant contractors will as a matter of course be very different in practice.

Some bodies are dealing with the development of observed and applied most frequently in the chemical and pharmaceuticals industry is certainly GAMP (Good Automated Manufacturing Practice), release no. 4. Since compliance with these guidelines, however, is not mandatory for acceptance by the FDA, there remains ample room for interpretation even in that case. In practice, one will in most cases find a mixture consisting of operators' own standards and documentation drawn up on the basis of general guidelines.

Ultimately, however, the operator of a facility to be validated will be responsible for establishing guidelines on the course of action to be taken in validating.

In any such case, an operator may either create and use a quality plan of his own (also referred to as a Validation Master Plan) or proceed in accordance with guidelines in general use. The only requirement will be success in obtaining FDA acceptance, and the ability to submit sufficiently documented evidence of the functioning of the facility.

Problems in Practice

In practice, a production unit using process engineering will as a rule be a combination of several pieces of equipment and systems. Validation, however, will ultimately need to be carried out for the complete unit, with responsibility resting with the system operator.

Hence, it is even prior to procurement that an operator will have to establish an internal Validation Master Plan for the course of action to be taken in validation, so as to be able to set consistent requirements when purchasing the various pieces of equipment. The objective should be to obtain from individual apparatus and machinery vendors documents laid out and organized as consistently as possible, which can then be consolidated into a complete and transparent set of documents. If, however, a Validation Master Plan is not on hand yet when equipment is being procured, the system operator will have to rework the documents received so as to ensure compliance with standards set subsequently, or will need to claim subsequently from sub-suppliers any missing documents, or demand the performance of testing not conducted to that date. Experience shows, however, that any subsequent reworking or preparing of documents will invariably entail more time spent and, hence, more costs than a documentation customized from the beginning. In extreme cases, it may even be necessary to rewrite completely the structure of software already created so that it will be possible for the required tests to be performed.

In practice, however, it is precisely that quality plan for the implementation and procedure of validation that in many cases will not have been stipulated in detail at an early project stage (i.e., when equipment is being purchased).

On the one hand, this will be a consequence of the fact that a large number of system operators still lack experience in the validation of systems and, therefore, knowledge of the necessity of having a Validation Master Plan. On the other hand, however, the financial implications of defining validation guidelines subsequently are often underestimated, and no great significance is attached to such guidelines at an early project stage.

Therefore, a Validation Master Plan defined individually by a plant contractor will be the decisive guideline as to the type and scope of the tests performed and documentation prepared. A plant contractor, then, will invariably need to adapt to the individual requirements of each customer and to a customer's Validation Master Plan. In practice, projects will be implemented in close cooperation between a system operator and a plant contractor. During important project phases, project execution/implementation will be monitored, controlled, and accepted by the subsequent system operator. It is only in this way that a system operator will be able to ensure consistently documented comprehensibility of the functions of individual pieces of equipment and, hence, the entire installation.

Different Demands

Practical experience has demonstrated that for many customers, requirement profiles in respect of "pre-validated equipment" are very different. There is almost every conceivable level — from simple requirements that hardly go beyond the usual scope of a standard documentation (functional description, software listing, test protocols) to comprehensive software documentation where each individual function is to be documented and tested. If one intends to proceed strictly along the lines of the GAMP guideline, the expenditure incurred for many applications will be very large, and funding will frequently turn out to be impossible in practice. Therefore, either extreme will be encountered rather infrequently. In most cases, demand will be at some intermediate level, in conformity with the GAMP guideline.

For a large number of operators, detailed and comprehensible documentation of the functional reliability of newly-developed, customized software will be sufficient. Detailed design and test specifications of standard-software modules used therein may be dispensed with in many cases if the future system operator accepts utilization and documentation from out of the plant contractor's standard library of software modules.

In respect of the demonstrated functional reliability of standard-software modules, reference is in such cases made to the quality certification for software developments as issued to the automation department of a plant contractor. Modules used successfully in a running plant may also serve as

A quality plan should define, and provide for, the following items relevant to quality:

Quality system: organizational structure; provisions to be applied in the event of deviation; quality limits; responsibilities; requirements as to documentation; requirements as to employee training

- **Concept Phase**

Inputs: user requirements specification, project plan, R&I scheme, functional requirements document

Tasks: developing an R&I scheme; preparing a concept; defining functional requirements

Outputs: report, summary of deviations observed

- **Design Phase**

Inputs: standards, system requirements specification; hardware documentation

Tasks: verifying system requirements; verifying hardware documentation; developing a design

Outputs: report, summary of deviations observed

- **Implementation Phase**

Inputs: software listing

Tasks: verifying the software listing, playing-on of software

Outputs: report, summary of deviations observed

- **Factory Acceptance Test**

Inputs: factory acceptance test plan

Tasks: performing the tests

Outputs: report, summary of deviations observed

- **Site Acceptance Test**

Inputs: site acceptance test plan

Tasks: performing the tests

Outputs: report, summary of deviations observed

evidence of the functional reliability of a standard-software library.

A Possible Concept from Practice

In practice, it turns out that it is one of the most frequent problems at the early stages of projects that a system operator does not yet have, or has not precisely defined yet, a Validation Master Plan. For a plant contractor, this means that on the conclusion of a contract, it will be difficult to estimate costs and expenditure, and to provide for a contractual limit. In such cases, a plant contractor will be well advised to be able to present a detailed validation concept of his own.

Summary

Validation and acceptance by the FDA will primarily consider product quality, and not a piece of equipment or the production unit itself.

Thus, it is not a readily validated piece of equipment that can be supplied but only a "pre-validated" package qualified in accordance with the requirements set by the subsequent system operator for validation. For the implementation and scope of validation, the Validation Master Plan to be prepared by the operator will be authoritative. Since in practice such guidelines will frequently not be available yet at an early project stage, it will make sense for plant contractors to develop their own quality concepts for the project implementation of "pre-validated systems", which can be followed by the operators of machinery and systems.

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