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Risk-Based Equipment Qualification: A User/Supplier Cooperative Approach

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This article presents an efficient cooperative approach to Commissioning and Qualification (C&Q) for manufacturing equipment and covers the entire life cycle for the specification, design, manufacture, installation, commissioning, qualification, operation, and maintenance of the equipment in a risk-based approach. This article reflects the current status of the work in progress conducted by the GAMP Italia Equipment Validation Workgroup. The main topics covered in the article are:

- **holistic risk-based approach covering business, safety, and quality risks**
- **involvement of the supplier in the risk management process and risk analysis**
- **support from the supplier in the C&Q activities (risk-based)**
- **team building**
- **time savings**
- **trends**
- **good engineering practice**

GAMP Italia and Equipment Validation Group

GAMP Italia is a local Community of Practice that was introduced to the ISPE community in December 2005, during the ISPE Milan Conference.

The mission of GAMP Italia is to improve the communication among users, suppliers, consultants, regulatory authorities, and academia, helping life sciences companies streamline their validation processes through a more consistent application of good practices and the GAMP guidance on both the supplier's and user's side.

GAMP Italia operates in accordance with the general objectives of the International GAMP Forum and reports to the GAMP Europe Steering Committee, like other regional groups (GAMP Nordic, GAMP D-A-CH, and GAMP Francophone).

The Equipment Validation Group is the first working group started within GAMP Italia and is composed of members coming from equipment manufacturers, consultants, end users (pharmaceutical companies), and academia.

The group is currently preparing document templates useful for supporting qualification of different standard and non-standard equipment.

Background

Most equipment currently available on the market is the result of a very long and uninterrupted improvement process that started many years ago and brought to the current design.

There is a significant difference between the purchase of a **standard system**, as opposed to the development of a **bespoke or custom made** equipment. Pharmaceutical users in most cases are just buying and installing standard pieces of equipment. The design of new parts or new functionality is often negligible, or limited to a small part of the process. Nonetheless, users are currently spending significant human efforts and financial resources in commissioning and qualification activities that are sometimes excessive and redundant, quite often including a mere repetition of verifications already performed by the manufacturer.

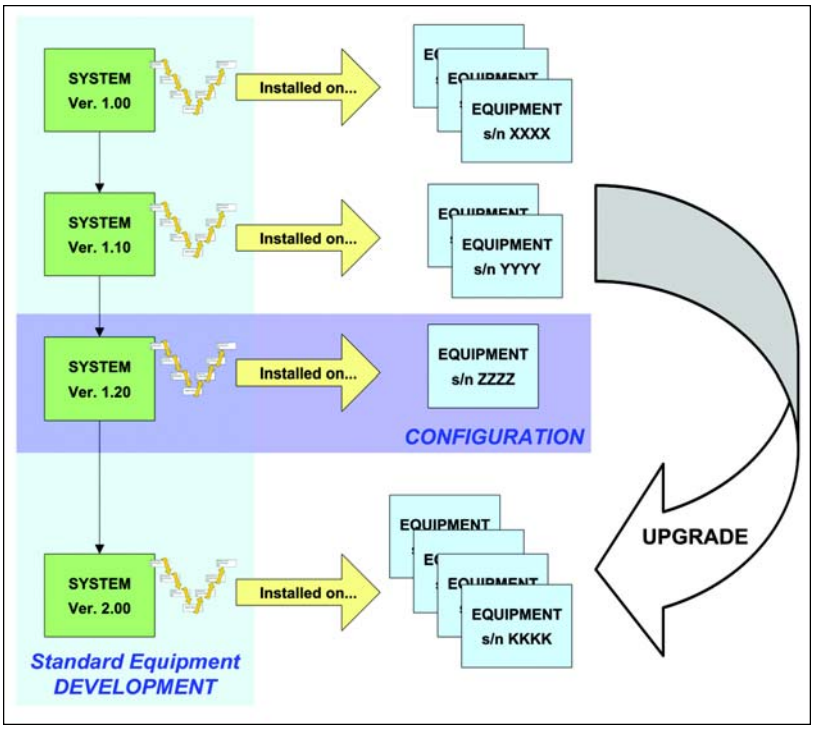

Figure 1. Standard equipment development Life Cycle.

Inefficiencies also arise from the variable formulation of different requirements (from different users) for the manufacture of the same standard equipment (from the same supplier). This may easily lead to different validation approaches and sometimes to very different set of documents on behalf of the supplier. A more uniform approach and a risk-based definition of the requirements can result in a significant savings in time and effort spent for both parties.

Risk-based qualification can improve quality and reduce validation efforts. ISPE is actively suggesting this approach, which is now being used more and more extensively.[8,9]

Risk management can be significantly enhanced with the supplier support, because they have a deep knowledge of the systems they produce. This approach can ensure faster, cheaper, more complete, and reliable results.

Indeed, **C&Q activities can be significantly abbreviated when the supplier is involved since the early stages of the process** and the efforts done during the product development and subsequent manufacturing are taken into account.

The main objective of the Equipment Validation Working Group operating within GAMP Italia is to suggest a more profitable role of the supplier during the entire equipment life cycle from specification and purchase, through manufacture and delivery, commissioning and qualification, use, maintenance, and even retirement.

Considering the current high level of automation in the industry, it is important to look at **computerized systems** and **process control software**, either embedded or standalone related with the equipment. The importance of computer control systems is emphasized because in some cases, the equipment is completely dependent on the proper behavior of the software. Computer systems may include PLC or microcontrollers and Human-Machine Interface (HMI), supervisory PC (e.g., SCADA systems, statistical process control), as well as interfaces with other remote systems like Manufacturing Execution System (MES).

Therefore, the discussion includes both computer validation and equipment qualification in an integrated approach.

More complex and potentially GxP critical scenarios are on the horizon due to the emerging **Process Analytical Technology (PAT)** applications that may bring new computer systems operating in strict connection with the equipment to ensure product quality. The proper identification and management of Critical to Quality Attributes and the relevant Critical Process Parameters may significantly help develop a PAT-ready equipment and extend the ICH Q8 Design Space concept into the equipment process variables.[10]

Basic Concepts

Good practices help ensure high quality products. Properly designed and manufactured products are safe, robust and reliable, well documented; therefore, they should be easy to qualify and/or validate.

This is true for both pharmaceutical products and the equipment used to manufacture the products.

Commissioning, qualification, and validation activities are only the final stage of a long process, and can be more easily and successfully performed if the entire development life cycle of the equipment is considered, supporting best practice and the concept of "Quality by Design" (QbD) when these are pursued by the manufacturer of the equipment. This approach closely relates to good engineering practice, which is endorsed by the ISPE Baseline® Guide on Commissioning and Qualification.[8]

There is a strict similarity between GEP and GMP: in both cases, quality should be achieved by design, and not just tested at the end of the process. Embedding quality into an equipment design is mostly a supplier's responsibility in a cooperative and trustworthy relationship with the user.

A **risk-based approach** requires the identification of critical items, distinguishing them from "ordinary" items, and dealing with them in a differentiated manner. Criticality may refer to different aspects of the product or process: quality, safety, and business being the most common areas of interest.

Critical items and key documents should be identified from the beginning of the project (i.e., explicitly documented in the User Requirements Specification), properly traced to standard offerings of the supplier and managed during the design and manufacture of the equipment, and then carefully verified during C&Q in a conscious and efficient manner. C&Q should concentrate on critical items, according to a sound risk evaluation methodology, and following a structured risk management process.

Standard, non-critical parts (e.g., non contact parts, functionality with no or little impact on product quality) can be implicitly qualified during manufacturing if the supplier is capable of demonstrating suitable **maturity** in the design and manufacturing. Verifications performed during FAT and SAT can be used as a proof of the good design and good manufacture, without the need of repeating the same tests over and over.

The expertise and knowledge of the supplier and the activities performed during manufacturing should be used to avoid redundancy.

Development Life Cycle

A practical risk-based approach should consider the **"real" life cycle of the product development** (as opposed to the life cycle in the delivery of a single instance of the standard equipment). Most manufacturers today have very standard equipment, designed for a large market and highly modular. This is quite common for instance with automatic machines like capsule fillers and tablet presses, and packaging lines, etc. The "design" of the equipment for a single customer is largely a matter of choosing the right model and assembling together the appropriate optional parts. Practicing good engineering practice is largely sufficient to qualify many elements of standard equipment.

Equipment Categories

To simplify the management of equipment qualification/

validation, it may be useful to distinguish the following main classes of equipment:

- standard equipment with no configurable parts or functions
- standard configurable equipment, having two possible levels of configuration:
  - definition of which standard parts are to be included
  - setting of parameters for the parts included
- custom or bespoke apparatus (prototypes of new equipment, custom built) specifically developed by the supplier to meet a set of specified user requirements

Standard configurable equipment may contain some custom parts that should be identified and treated as bespoke apparatus.

Development vs. Configuration

The development of new products (standard equipment) follows a complex life cycle, normally defined in the supplier's Quality Management System. A good reference is the V model included in GAMP Guide.[2]

The product is released on the market following an incremental life cycle with many different releases during the product life span. The entire process, limited to software portion for simplicity, may be summarized in Figure 1.

The large variety of customer requirements results in a very high level of modularity within the same equipment. Different models, different optional units, and a large amount of variable parameters are normally available in a standard equipment.

A new version of the equipment and/or its relevant control software is delivered to the Customer only when the development process has been completed. This includes the management of functional and technical specifications, and the execution of all defined test cases. New custom (bespoke) functions may become part of the evolving standard.

Therefore, the standard product development line is **orthogonal** to the configuration process, needed to tailor the general product to the customer specific requirements.

Software for a single piece of equipment is quite often upgraded during the operation period, even long after the start-up, for instance when new products are to be manufactured. The life cycle for the delivery of a single system from a combined user and supplier viewpoint can be seen in Figure 2.

The knowledge of the actual product life cycle and the differentiation between the management of standard parts vs. bespoke parts is fundamental for an appropriate risk management.

A Holistic Risk Management Approach

Risks may arise in different areas:

- Quality

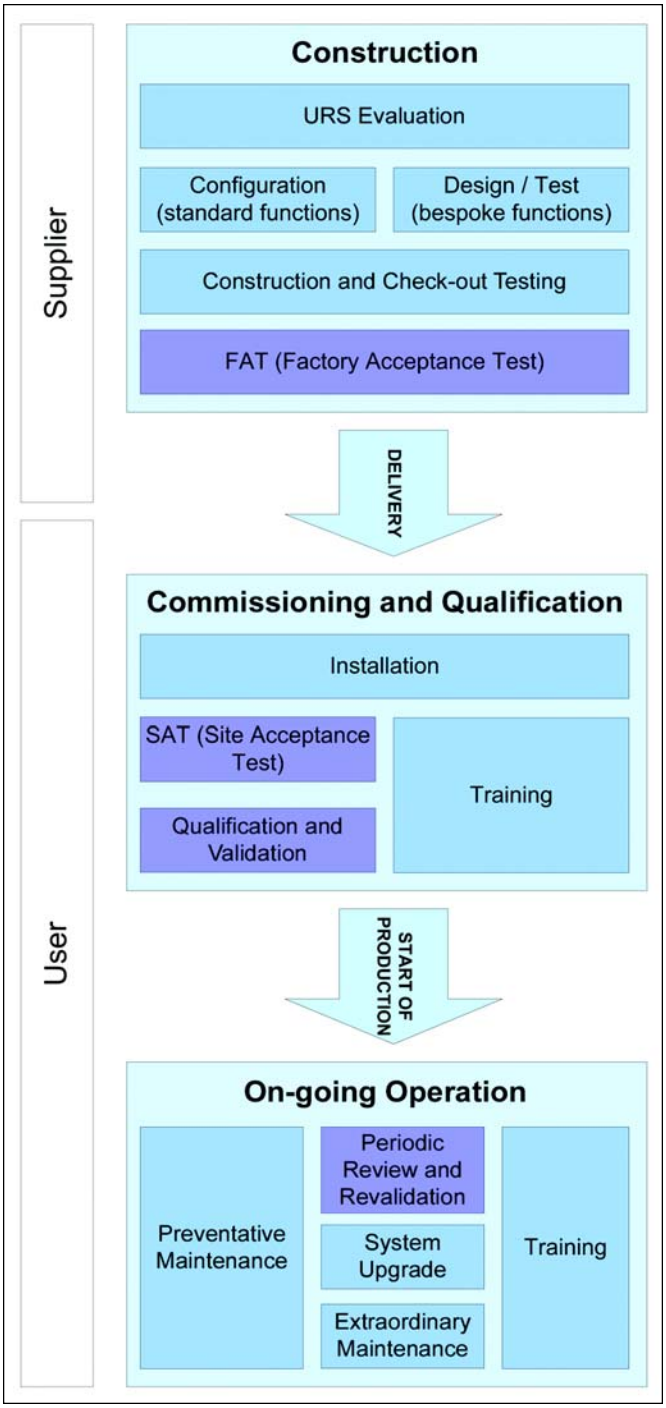

Figure 2. Delivery life cycle for a specific user.

- Safety
- Business

Product Quality Aspects (GxP)

In this case, what matters in the pharmaceutical industry is the quality of the final product delivered to the patient. In this area, all GxP requirements are included. The quality hazard impact can be evaluated according to:

- damage to patient (illness, temporary or permanent side effects, death)

- compliance issues with the authorities

Typically, quality aspects are identified by Critical to Quality Attributes (CQAs) for the product.

Safety Aspects (Operator and Environment)

In this case, what matters is the evaluation of the potential damage to the personnel operating the equipment and/or the impact on the environment caused by system malfunctions. The safety hazard impact can be evaluated according to:

- damage to personnel (temporary or permanent injury, death)
- damage to the environment (damage to people who live outside the factory)

Business Aspects

In this case, what matters is the evaluation of the potential damage for the business caused by system malfunctions or lack of availability. The business hazard impact can be evaluated according to:

- cost of components to be replaced and workmanship (direct damage)
- production loss (indirect damage)

Business continuity, line efficiency, down time, size change over, and line set-up are important items in this perspective.

A description of an overall risk management process is shown in Figure 3.

Risk Analysis

The results of the analysis depends largely on the impact that the customer assigns to each identified source of risk. The same function could be potentially critical in a specific application and non-critical in a different one. Cooperation between customer and supplier is essential to properly manage risks.

User - Supplier Cooperation

The supplier can provide a large number of support activities and services during the life cycle of a product, under all the different perspectives, offering a significant contribution in the risk management process.

A general risk management flow can be adopted. ICH Q9 established a standard approach for "Quality Risk Management" that is quite general and can be easily adopted for all three areas.

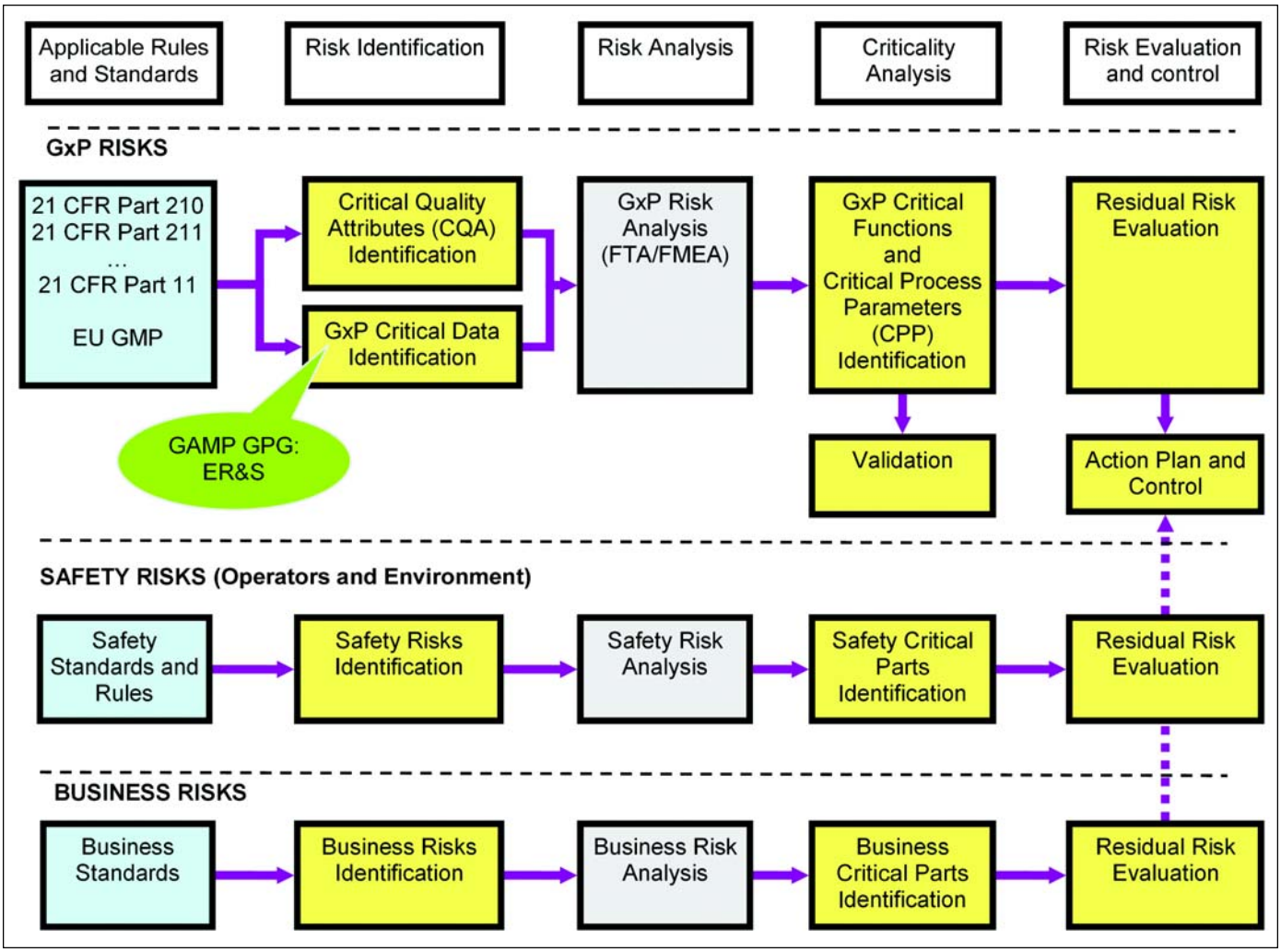

Figure 3. Overall risk management flow chart.

Involvement of the supplier in the process can include a large part of the risk analysis, provided it is based on the information supplied by the user.

In more detail, the sequence of operations can be seen in Figure 4.

The flow of operation also illustrates the embedded Risk Communication process between user and supplier along the entire life cycle, and their different role and responsibility in the risk management process. The following three main phases can be distinguished:

1. **Specification Phase**. It's the responsibility of the user to communicate potential risks and the relevant impact to the supplier so that important items are properly managed during design and manufacturing of the equipment. The supplier should be made aware of unwanted issues impacting the quality of the product, the safety of the operators and the business, and the relevant impact level.

2. **Design and Manufacture Phase**. It's the responsibility of the supplier to identify critical parts (such as mechanical units, components, software functionality, or parameters) and communicate these to the user. The user can then wisely evaluate the risks and provide additional controls or countermeasures where necessary, and finally accept the system design when residual risks are below an acceptable threshold.

3. **Operation Phase**. The operation and maintenance of the equipment should be performed in cooperation with the supplier to maintain constant performances over the time and/or improve the system when necessary.

It should be noted that **while the technical part of the risk analysis can be performed by the supplier, it's a responsibility of the user to evaluate the risks, to provide any required additional controls, and finally to accept the residual risks**. This possible separation of roles has been clarified in ICH Q9.[16]

It's important to distinguish between **elements criticality** and **process (residual) risk**: an element (system component or function) may be critical because it guarantees the product quality, nonetheless, the residual risk for the process can be low due to the high reliability of the element.
However, irrespective of the residual risks, critical parts should be identified because they need qualification/validation.

Standard parts exhibit less risks than custom parts and functions. Under a risk perspective, the explanation is in their improved reliability and lower probability of failure (while the impact remains unchanged).

When the risk analysis is conducted purely for compliance purposes (e.g., to define qualification/validation activities), it can be performed at a high level, without entering into system details such as analysis at component level.

When the risk analysis is required to investigate on specific quality hazards or to cover safety and business risks (e.g., reliability of the equipment), additional difficulties arise on the user's side: the user doesn't have sufficient information and knowledge about the system and the analysis can be very labor intensive and time consuming. One of the difficult items to characterize the system is the probability of occurrence for adverse events since these are quite often related to system components reliability. The manufacturer on the other hand has the necessary knowledge, can guarantee an investigation with sufficient level of detail, and can afford an investment of time and resources on a product that is intended for a wide market and not only for a single user.

It's worth observing that risk analysis performed by the supplier should be somewhat "parametric." The results should in fact be tailored to the specific list of hazards and their impact level, as communicated by the user during the specification phase.

Validation Life Cycle

Based on the Equipment Validation Group experience, the following are preliminary recommendations on the entire life cycle of a generic piece of equipment. Further and more specific suggestions will be included directly in the dedicated documents the group will produce in the future for each equipment type.

The Equipment Validation Group is preparing document templates useful for reducing the time and efforts in the entire delivery process, including C&Q. Templates are produced in an industry wide perspective and include suggestions for tailoring the document to the specific application case.

The group realizes that producing standard documents is not always possible considering the variety of different mechanical, electrical, and software solutions available on the market. Where a general template can't be produced, the group will prepare a guide for the preparation of the document.

User Requirements

To properly implement a holistic risk-based approach, it is necessary to start defining critical items from the beginning of the process. The user should provide the supplier with the identification of different hazards (quality, safety, and business) and the relevant impact evaluation.
The following are some specific suggestions:

- The User Requirements Specification (URS) should be treated as a contractual document, avoiding conflicts with other technical specification documents. The URS should not be considered a mere part of the validation documentation, but rather the main - and possibly only - specification document for the equipment.

- Ideally, the requirements should be independent from the supplier's product and express customer needs without addressing specific design solutions.

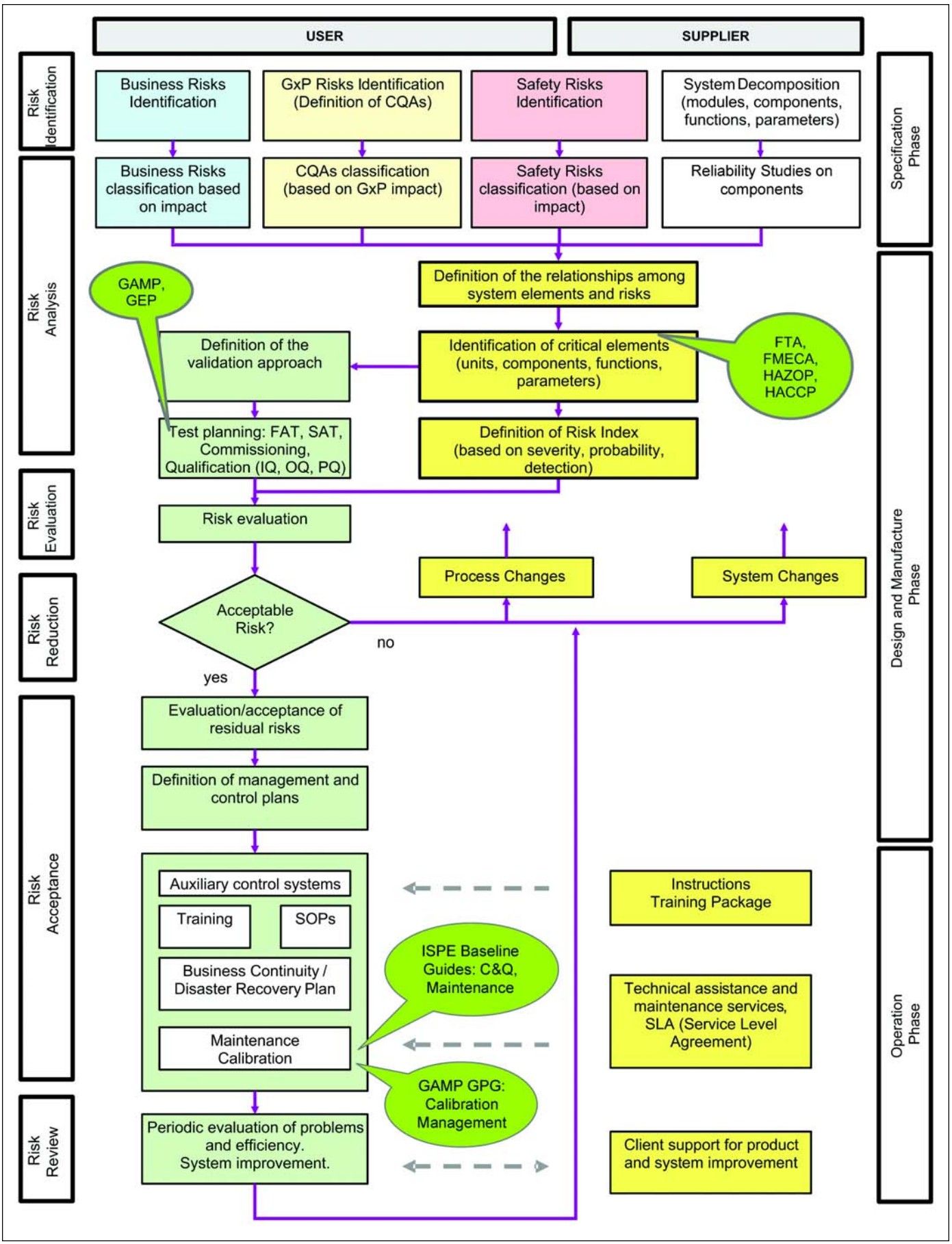

Figure 4. User-supplier cooperation scheme.

- The URS should, as a minimum, cover all mandatory parts, including those necessary to guarantee the final product quality and achieve compliance with the rules. One often neglected part is the definition of the expected quality of the product and the level of allowance for unwanted defects.
- Requirements on equipment safety and business performances also should be included.

- Detailed technical requirements which are typically produced by the user may be included if appropriate in an annex of the URS, as this document usually specifies design solutions rather than equipment performances.

- Ideally, all requirements should be identified with a unique code for easy and unambiguous traceability and classified according to the impact. If possible, impact should be defined in more than one level (e.g., high/medium/low). Business requirements should be classified according to their priority (e.g., mandatory or "nice to have.")

- Generic requirements like "the software shall be 21 CFR Part 11 compliant" should be avoided. High level identification of GxP critical data which are expected to be handled by the system should be done at this stage of the process.

The main issue for the customer during the requirement phase is to identify the most appropriate supplier and the most appropriate equipment model that can satisfy all the requirements.

Validation Plan

The Validation Plan should be developed by the user considering the actual life cycle of the manufacturer that changes significantly depending on the amount of design activities

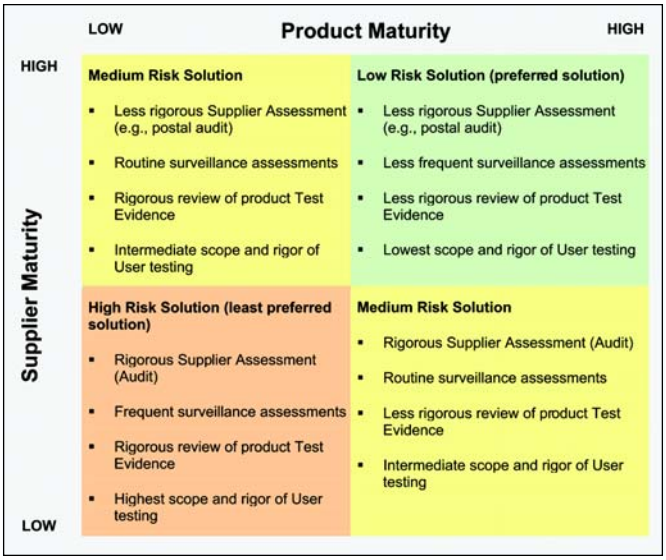

Figure 5. GAMP GPG: Testing of GxP Systems (Figure C1.1: Supplier and Product Maturity Model - Chapter. 1: Minimizing User Testing).

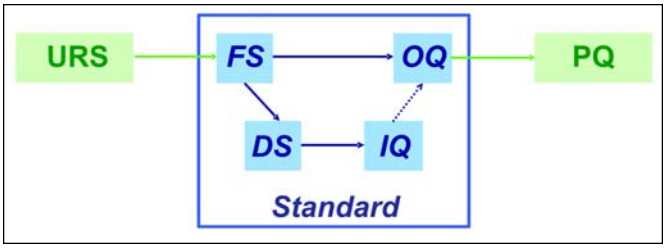

Figure 6. Standard vs. specific documentation.

required to deliver the equipment. Efforts should be based on the overall risk scenario, thus, considering on a global level, aspects related to standard components, supplier, and product maturity.

Overall Risk Scenario

Product and supplier maturity should be evaluated. A good guide is provided in the GAMP Good Practice Guide: Testing of GxP Systems;[6] - *Figure 5*.

Supplier Maturity

The supplier maturity should be evaluated with a detailed analysis of the design, manufacturing, and support processes of the supplier. The supplier audit is the best tool to achieve this goal and it's an important part of the process. To facilitate sharing and comparison of information, the use of standard checklists is highly recommended, such as the one proposed in the Appendix M2 of the GAMP Guide.[3]

Re-use of previously performed supplier audits is encouraged, especially within large organizations, thus, avoiding repetitions and redundancy. A secrecy agreement with the supplier may be necessary.

Product Maturity

Product maturity should be carefully evaluated, considering the level of standardization achieved for the specific equipment. This may require an investigation with the supplier, and a standard survey may prove useful when selecting among different suppliers. Standard and robust products should be preferred to custom solutions, unless strictly necessary. Custom (bespoke) systems normally exhibit much higher risks and should be handled with extra care.

Functional Specifications

Functional Specifications (FS) are documents commonly produced by the manufacturer. FS for a standard equipment can be structured in a standardized "validation package" that often includes Design Specification (DS), plus Installation Qualification (IQ) and Operational Qualification (OQ) protocols - *Figure 6*.

The main issue here is to map variable User Requirements with standard elements (components or functionalities) of the equipment. This is normally done by the supplier during the User Requirements evaluation phase. Different situations may arise when analyzing each User Requirement:

1. The requirement can be satisfied with a standard basic element.
2. The requirement can be satisfied with an optional element.
3. The requirements involves the re-design of an existing element.
4. The requirement involves the design of a new element.

Cases 1 and 2 are very similar: the main difference is generally only at the commercial level, and both can be considered as standard equipment.

Case 3: The re-design should be managed by the supplier under strict change control and the decision should be made to include the change in the standard product or consider this as a customer specific (bespoke) difference. Bespoke components are highly discouraged in the development of standard equipment, but this may be the only way forward.

Case 4: New parts can be designed on demand and still be included in the standard product life cycle, but the risk may be higher for the first installations. Software is normally managed as a standard product, typically highly configurable with many parameters.

To ensure traceability with the User Requirements, each single Functional Specification should be identified with a unique code.

Traceability Matrix

Producing a Traceability Matrix (TM) is very important for C&Q activities. It can help to trace all user requirements, thus, ensuring both complete coverage of URS and test coverage of the critical functions.

Following the GAMP suggestions, TM should report the criticality level of each function. This can help the quick identification of critical functions. Safety and/or business critical functions also should be properly identified in the TM to achieve a holistic system criticality understanding.

In addition to the recommendations from the GAMP Guide,[4] additional information should be included in the TM regarding the level of standardization of the function. Higher risk non-standard functionality can be quickly located in this way.

Design Specifications

Design specifications for standard equipment should describe the equipment, rather than fit specific User Requirements. The main purpose of the documentation is to provide the user with useful information for the operation and maintenance of the equipment. Normally, the supplier is able to demonstrate traceability between standard DS and the relevant standard FS. This traceability also may be included in the standard Qualification/Validation Package.

However, design solutions that are arranged specifically for the user should be identified. Non-standard solutions should be managed with additional care and specific details, especially when they cover critical aspects of the system.

The supplier should provide all the required documents for the parts included in the final equipment. As-built documentation (such as electrical, lubrication, and pneumatic diagrams) is commonly available from the supplier.

Additional documents may be contractually agreed between the user and the supplier in the technical annex of the URS.

Risk Analysis (and/or Risk Management Plan)

The supplier may play a very important role in the risk management process. This has already been covered in the discussion "A Holistic Risk Management Approach."

Under the modern approach of ICH Q9, the risk management concepts along the entire life cycle should replace the pure risk analysis performed in a single phase. Therefore, it is recommended to prepare and follow a Risk Management Plan, rather than a single Risk Analysis document.

It should be remembered that according to the spirit of ICH Q9, risks should be carefully evaluated by the user and residual risks formally accepted.

Before starting the risk analysis process, it is essential to establish the scope: to either evaluate only the quality aspects and define the validation approach, or also to cover safety and business aspects.

In the first case, the risk analysis can be efficiently performed by the user, adopting a top-down technique like Fault Tree Analysis (FTA) to cover specific product quality related risks.

In the latter case, risk analysis should be more detailed and cover system components. This is in general a complex and time consuming exercise that can be effectively performed by the supplier using a bottom-up technique like Failure Mode and Effects Analysis (FMEA). This approach also helps with preparing the list of critical items (GxP, safety, business). Making this information available to the user is an important part of the risk communication process.

Equipment Construction, Commissioning and Qualification

Significant savings can be achieved if efforts are focused on critical items of the equipment and the results of previous testing phases - *Figure 7*.

Check-Out Testing

Consolidated software versions installed on each equipment are tested by the manufacturer according to the development life cycle.

The check-out internal testing phase at the supplier's premises has the purpose to ensure that the equipment is properly built and functioning in all of its components (mechanical, electrical, electronic, and software) and that it satisfies the specific user requirements provided by the customer. The focus of testing activities before the delivery of a standard equipment to a specific user is the proper configuration (selection of items and parameters that satisfy the user requirements), and proper integration in the equipment. These testing activities can be optimized. For instance, if a software algorithm has already been tested during the development process, it is not always necessary to include it

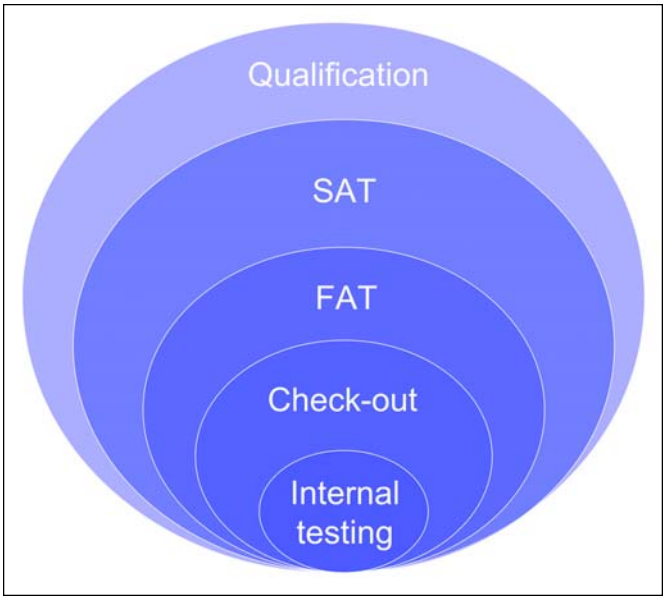

Figure 7. Testing activities.

in the check-out.

Quite often the equipment check-out is ignored during the subsequent steps of the commissioning and qualification, while the evidence of these tests could provide sufficient information and avoid test redundancy.

FAT

A Factory Acceptance Testing (FAT) phase can be executed to check congruence of the system to the purchase order and its proper functioning with the actual customer products. FATs are mainly intended to allow the customer to verify proper construction and operation of the equipment at the supplier's premises; therefore, authorizing delivery to the user's plant. The documentation produced during the FAT may be in part re-used during the subsequent Site Acceptance Test (SAT).

When the supplier has been properly qualified, a significant reduction in testing activities can be done. FAT should concentrate on critical items identified in the previous steps of the process. Testing of standard parts can be evidenced by the internal test results of the supplier, including the final check-out documents.

The execution of FAT may be skipped for standard equipment produced by well-known suppliers, while the user may require the testing documentation (e.g., final checkout results) before authorizing delivery.

Commissioning and SAT

The supplier normally supports the customer during the installation of the equipment, connecting utilities, and performing initial installation tests. The usage of standard check-lists is highly recommended in this stage.

When the installation has been completed, a Site Acceptance Testing (SAT) phase can be executed to verify proper operation of the equipment at the user's premises, including local interfaces with other systems. SAT efforts may efficiently be reduced re-using the experience and documents already produced during the FAT, focusing on parts and functions that may be compromised by the disassembling, transport, and reassembling process. The supplier may help with indicating which tests are to be repeated at the final destination. Testing of non critical parts or functionality may adequately be covered by the SAT, without any need for a formal qualification. Additional suggestions about the management of commissioning activities can be found in the ISPE Baseline Guide on Commissioning and Qualification.[8]

The supplier supports the customer with plenty of documentation that can be used to develop the specific preventative maintenance plan and the calibration plan. Additional suggestions can be found in the GAMP Good Practice Guide: Calibration Management.[7]

Information from the supplier may be useful to prepare:

- training
- SOPs
- business continuity/disaster recovery planning
- maintenance planning and action procedures

Qualification: IQ, OQ, and PQ

IQ, OQ, and PQ activities should be limited to systems and components with Direct Impact on the product quality. All of the rest of the system may be simply commissioned and managed according to good engineering practice. The identification of critical parts is an outcome of the Risk Analysis.

IQ and OQ may be easily conducted using the standard Qualification/Validation Package normally available from the supplier, covering the majority of physical and functional features of the equipment. This documentation should be produced in accordance with a sound risk-based approach. The execution of IQ and OQ tests may be accelerated with the support of the supplier, especially when using its document set. However, specific URS and relevant Critical Process Parameters also should be addressed by IQ and OQ with additional tests to be integrated into or enclosed to the supplier standard package. The responsibility of the qualification testing is still with the user who should review and approve the documents and witness the execution of the tests. Repetition of tests already performed during equipment check-out, FAT or SAT is normally redundant and should be performed only when the previous tests can be compromised by other activities.

PQ is more specific for the customer application and some level of tailoring from a standard template is quite often necessary. The supplier may optionally contribute in the preparation of this document as well as support the execution of the relevant tests.

Training

Training is another important part of the commissioning and qualification phases. Specific sessions for the different roles involved in the usage of the equipment should be designed by the supplier in order to explain the right things to the right people. The supplier should prepare a suitable risk-based training package with specific instructions about the man-

agement of GxP and safety risks.

On-Going System Operation

Once the equipment is in production, there are still several opportunities for the customer and supplier to keep on the positive cooperative relationship created during the start-up.

The supplier may support the user to perform most critical and complex maintenance checks and operations with specific frequencies.

In addition to these maintenance interventions, the user should periodically review and evaluate the system performances.

As a result of this analysis, the user may decide to perform a periodic revalidation repeating a subset of IQ/OQ tests covering the components and features with higher criticality level in order to demonstrate that the system maintains its validated state. The supplier can still support the customer to identify appropriate tests and execute them more rapidly.

Other services that the supplier can provide during the life-time of the equipment cover the following aspects:

- specific training sessions to new people involved in the equipment operation
- software and/or hardware upgrade and relevant qualification activities (typically performed to comply with updated regulations, to renew obsolete components, or to adopt improvements applied to the product installed on different equipments)
- warranty services
- extraordinary maintenance interventions
- support for equipment relocation from one site to another

Decommissioning

The supplier may support the user even in the final stage of the equipment's life. At system retirement, it may be necessary to safeguard important information that is kept in the system, because the mere backup or recovery procedures could not fit for data migration to a new, different, equipment. The supplier role, in the case, may be helpful in many aspects, including managing obsolete mass storage devices or coding specific software filters.

Quality Audits

The customer may increase his confidence in the supplier during the life cycle: by means of quality audits performed on the development process, periodically inspecting the supplier during the construction phases, controlling check-out results during FAT, and finally during the installation and qualification phases.

The mature supplier uses the results of audits, verifications, and inspections in a pro-active philosophy as drivers for continuous improvement.

Developing standard products, both the supplier and the equipment progressively increase their maturity level, going toward the preferred solution where customer verifications may be reduced in terms of frequency and rigour - *Figure 5*.

Trust is based on the confidence on the supplier quality system and the overall design and manufacturing processes that bring to the final equipment.

Conclusions

To save time and money in the commissioning and qualification activities still guaranteeing the final proper quality level of the equipment and the relevant production, it is basilar to use a risk-based approach that focuses on critical items of the equipment and critical activities of the life-cycle.

The knowledge of the actual manufacturing life cycle may aid in the identification of critical steps in the process, distinguishing the production and assembling of standard parts from the design of custom parts.

Supplier involvement from the early stages of the process can further improve savings. Building a trustworthy relationship between the user and supplier can reduce redundancies and provide significant advantages for both parties.

C&Q efforts can be significantly reduced using mature products and mature suppliers. Using best practices in the design and manufacturing bring the mature supplier closer to the sphere of Quality by Design, improving their products and services.

Glossary

C&Q	Commissioning and Qualification
CQA	Critical to Quality Attribute
DS	Design Specification
FAT	Factory Acceptance Test
FMEA	Failure Mode and Effects Analysis
FS	Functional Specifications
FTA	Fault Tree Analysis
GAMP	Good Automated Manufacturing Practice
GEP	Good Engineering Practice
GMP	Good Manufacturing Practice
GPG	Good Practice Guide
HMI	Human Machine Interface
IQ	Installation Qualification
MES	Manufacturing Execution System
OQ	Operational Qualification
PAT	Process Analytical Technology
PLC	Programmable Logic Controller
PQ	Performance Qualification
QbD	Quality by Design
SAT	Site Acceptance Test
SCADA	Supervisory, Control, and Data Acquisition
SOP	Standard Operating Procedure
TM	Traceability Matrix
URS	User Requirements Specification

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