This article discusses two life cycle documents: the User Requirements Specification (URS) and the Functional Specification (FS).

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GAMP Life Cycle Documents as Effective Communications Tools

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Introduction

Imagine a resource from which engineers, designers, and end users can draw practical information that compiles the good practices, procedures, and technical competence of top operators and researchers, and has validation significance. This compilation of best practice may be found in the GAMP Guidance, a comprehensive reference of good practice, tailored specifically to automated systems. An article covering all aspects of GAMP could not be justified if limited to a few pages or less; therefore, this article covers two key life cycle documents:

- the User Requirements Specification (URS)
- the Functional Specification (FS)

The User Requirements Specification (URS) is intended to define end user expectations with regard to features, functions, and overall appearance of proposed process equipment and associated operations. The Functional Specification (FS) is intended to provide a working interpretation of the URS and an implementation strategy by external consultants or contractors. Unlike the Code of Federal Regulations, neither the URS nor FS are directly enforced by FDA mandates. Nevertheless, the development and adherence to both makes practical sense with regard to speedy development, competitive engineering, and the FDA-enforced validation practices.

URS and FS Defined

Before the URS and FS can be defined in accordance to GAMP guidance, it is important to understand the association they have with the stages of development or "life cycle" of a particular product line. The series of life cycle documents prepared up to and throughout validation, start-up, and commissioning, beginning with the URS and FS, represents only one stage of overall product development, and does not stop at the successful completion of Performance Qualification (PQ) testing. However, since much of the work is required to essentially "break the ground" of a new production line (or product line enhancement), many entities with a broad range of differentiated tasks are often involved, thereby requiring some mechanism to organize the thought processes and communication among players; and as a tool to coordinate the construction effort. Following PQ and throughout the useful life of the product line, the end user is generally responsible for the continuation, refinement, and maintenance of these life cycle documents although some external consultation or support may be retained. Therefore, the life cycle concept as defined by the GAMP guidance is "an approach to computer system development that begins with identification of the User Requirements, continues through design, integration, qualification, user validation, control and maintenance, and ends only when the commercial use of the system is discontinued." The significance of the FS is emphasized as a key component to life cycle documentation due to its inseparable link to the URS.

According to the GAMP Guidance, the URS "describes what the equipment or system is *supposed* to do, and as such is normally written by the user. The URS may be sent to suppliers as part of the vendor selection process. This version should include all essential requirements (*musts*), and if possible, a prioritized set of desirable requirements (*wants*)." Therefore, the URS is essentially a document that is generated (directly or indirectly) by the end user, often with assistance from an external consultant working on behalf of and sensitive to the performance issues expressed by the end user. It defines the key aspects of system per-

formance following start-up/commissioning as verified by PQ, often initiated during Site Acceptance. Following end user sign-off and distribution, the end user is generally bound by the "agreed-upon" terms and conditions, as detailed in the URS throughout the detailed design and validation periods.

The FS, on the other hand, "describes the detailed functions of the equipment or system, i.e., what the system *will* do. An initial version of the FS may be produced as part of the supplier response. Further revisions of the FS are prepared in conjunction with the user. The FS links to OQ which tests all the functions specified," communicated by those typically responsible for interpreting the URS in an effort to satisfy the objectives of the end user. Therefore, the FS represents the effort generally put forth by those contracted by the end user (or contractor representing the end user) to engineer, design, and build equipment and/or systems to meet end user expectations as outlined in the URS. The assessment performed by the end user of such effort generally occurs during Factory Acceptance Testing (i.e., at the site of development) through the execution of Operational Qualification (OQ) test protocols assembled by validation consultants, auditors, or groups within the end user hierarchy.

Both the URS and FS are vital documents essential to a successful validation program -- the details of which are typically outlined in the Validation Master Plan (VMP). The relative positions of these key life cycle documents (underlined) are illustrated in Figure 1.

Since the author of the FS is typically a contractor hired by the end user to satisfy the objectives of the URS, a traceability matrix is usually advised to objectively identify and link all characteristics and propositions of the FS to the requirements detailed in the URS. Although not generally required, the preparation of a matrix is strongly encouraged to help ensure the FS is an accurate and complete interpretation of the URS. An effective matrix example (Table A) is one that is structured in tabular form, listing all requirements of the URS, followed by a brief description of the methods, procedures, and tangibles (i.e., hardware and software) proposed by the FS to address each item. A 'checked by' column should be included for verification.

URS and FS Enforcement

Although the URS and consequently the FS are not enforceable through FDA validation policy (i.e., 21CFR Parts 11, 210 and 211), they are widely accepted and frequently referenced by FDA compliance auditors in determining the "validatable" state of a process unit, control system, or entire operation. By using the GAMP life cycle documents as communication tools to collect and refine important information pertinent to end user performance expectations and operational requirements, elements of the FDA enforcement can be derived through validation-specific detail as referenced in the URS and FS. These "enforcement factors" add "bite" over standard "Scope Documents" and "Operational Guidelines" most often applied as communication tools.

Since the End User may often lack the time and focus on any particular project (often due to other priorities and/or resource allocation issues), one may perhaps agree that it can be quite a challenge to secure the assistance of those within an end user hierarchy most closely associated with the operation and maintenance of associated equipment. As a consequence, the dissemination of reliable and complete information on end user-anticipated performance regarding new or revised operational equipment more often than not falls short of an accurate and comprehensive reflection of the actual needs of the ultimate users.

For the sake of accuracy and coverage of information to be included in a user requirements document, management support is essential to ensure all ultimate users (i.e., operations and maintenance personnel) are involved. This end user-sponsored mandatory involvement should persist throughout the evolution of the URS - a level of involvement mandated by the end user management team whose enforcement policy should not interrupt normal activities of the employees, but should be strongly encouraged such that appropriate measures and precautions are applied (in whatever form that is best for the end user). If human resource allocation shortfalls exist and persist, the end user management team should strongly consider external support that can be readily relied upon to fill these voids. The key objective here is to ensure that the URS is an accurate and complete reflection of the precise end user expectations after project completion. Some time also should be allocated by the end user hierarchy to review the content of the FS to ensure external contractors are not only properly interpreting all provisions of the URS, but possess the capacity and competencies to do so.

URS/FS Evolution

Among the multitude of steps required for project planning and execution, all associated disciplines should find resolve through the evolution of a vehicle tied to regulatory mandates and enforcement. From an automation point of view, the URS is typically the first document to be issued following the Basis Of Design (BOD) and VMP documents that govern the design and validation efforts respectively. During the early phases of project execution, the URS may function more like a "scope of activities" document than a document with validation significance. The evolution of the URS (throughout the project life cycle) progressively adds credibility to the document as a "validation mandate" - to be verified by way of PQ testing during the Site Acceptance Testing (SAT) - accepted by not only the end user, but third-party regulatory auditors as well. The FS, generated after the URS has been drafted, may follow a similar evolutionary trail with emphasis placed on equipment operations (verified via OQ protocol execution) as opposed to performance. In many cases, the end user justifiably places more emphasis on the FS (particularly if the engineering and design of a particular process is placed in the hands of outside contractors) to ensure compliance to the requirements of the end user - even if a URS has not formally been prepared. Note, however, given the circumstance just mentioned, an FS without a formal URS places more risk than necessary on the contractor. Therefore, the evolution of a

URS Part	Description of URS Part	FS Part	Description of FS Part	Checked By
2.1	Control System shall utilize brand X PLC...	2.2	Model "A" PLC from X, Inc. shall be applied to perform sequential logic...	QRS
3.4	Analog I/O shall be 4-20mADC with 24 VDC primary power for...	3.4	The PLC analog I/O cards shall be provided with 250 Ohm precision...	TUV
5.2	All discrete tie-ins from field devices shall be fieldbus...	6.3	The discrete field devices shall be linked together using Devicenet...	WXY
7.1	Control System Historian shall be 21 CFR Part 11 compliant...	8.2	The Historian shall consist of OS/drivers, applications S/W, H/W...	QRS

Table A. Sample matrix.

formal URS, with "FDA bite," is strongly encouraged to improve two-way communications and assist in the solidified notion of shared accountability.

Benefits

The advantages derived through the use of GAMP-supported documents as vehicles to establish initial contact and maintain continuous dialog between the engineering/design and build contractors, and between the contractors and end users alike are numerous; ten of these are listed:

1. URS as Viable Communications Tool

The importance of assembling input from the end user cannot be underestimated. After all, the focus of most any design project, pharmaceutical or otherwise, is to provide the end user the equipment and services they require to sustain a competitive margin in their respective market. Communicating the needs of the end user to those entities with the resources to fulfill the expectations of the end user is often a complex task. This is a particularly viable statement if the end user may not be familiar with the variety of options available or lack the resources to best achieve their ultimate goals. Therefore, the preparation and subsequent utilization of GAMP life cycle documents (at least in principle) are well positioned to "unravel" the complexities of associated information exchanges - primarily through the URS and FS as effective communications media.

2. URS as Primary Reference Document

Considering that the BOD reflects the conceptual expectations of the end user with regard to capacity and approach, the URS (as a working and evolutionary document) should be prepared to provide direction and distinction far beyond the intent of its earlier ancestors (including the VMP). The URS must contain sufficient detail to accurately and effectively direct the authors of the FS to assemble a design consistent with the needs of not only those marketing the products of the end user, but also should include the needs of the operators, maintenance technicians, parties involved with safety/environmental regulatory enforcement, procurement specialists, and onsite engineers. The URS and subsequent FS are essential components in the assurance that detailed design efforts, as described in the Detail Design Specifications and other related life cycle documents, follow the appropriate path toward compliance (to both the end user and regulatory agencies).

3. FS as Key Contractor Document

The FS is the key life cycle document by which external contractors base their designs. Therefore, an accurate, complete, and end user-approved version of the FS is essential. Many external integrators and programmers, for example, impose substantial "cost adders" to their proposed project budgets without formal end user acceptance of the FS and all its constituents. These "cost adders" are justified and often necessary to cover the increased risk of frequent and unsupported "after-the-fact" design changes. Therefore, the allocation of some review time toward FS acceptance often saves the end user considerable costs due to "risk reduction," as well as a reduction in unsolicited change requests. As a side note, the end user should be cautious of any contractor who claims the FS is an unnecessary project component for the sake of "budget reduction" and competitive bidding.

4. Required by Validation Auditors

Although not an FDA mandate per se, most (if not all) entities involved with the validation of automated systems reference the URS and related documents to enhance the efficiency and effectiveness of the validation effort, while reducing the total amount of preparation work, risk, and associated costs. Therefore, the use of GAMP guidance encourages the end user to directly involve those responsible for the operation and upkeep of the equipment and systems engineered and specified.

5. URS/FS and the Divisions of Responsibilities

The associations between the URS and FS as described in this article provide clear distinction as to the roles and responsibilities of the external contractors/suppliers and end user. The importance of various project controls aimed at regulating the effects end user "wish lists" and contractor "extras" have on project budgets and schedules is paramount.

6. Evolution of URS/FS

The evolution of the URS/FS helps to ensure continuity from one execution phase to the next, and may, depending on the nature of the documents prepared, assist in interdisciplinary coordination - often a complex "web to untangle."

7. Management Of Change (MOC)

The URS/FS can be viable tools during their evolution to help manage change requests by both the end user and contractors associated with a particular project. The value of the Trace-

ability Matrix can be felt by ensuring the FS is updated, reviewed, and approved accordingly. The URS/FS should not replace existing MOC procedures on either the end user or contractor side, but be structured to work with these (often existing) sets of vital policies and procedures. Note that it is not uncommon for an entity's MOC processes to have strict CFR implications due to their potential impacts on the environment and safety (i.e., 29 CFR, Part 1910.119).

8. Work Scope Boundaries

Some end users desire turnkey installations with little internal employee involvement, others desire absolute control. In either case, the URS, through an element of enforcement, and the FS, as a formal interpretation of user requirements, may better define the lines between designer creativity and user expectations, helping to minimize the occurrence of stray tasks.

9. Establishing Positive Relationships

Using the URS as a "scope of design" and the FS as an "acknowledgement of design," their transformations to comprehensive and formal validation documents for use by external validation consultants is greatly facilitated (and may even be greatly appreciated by both auditors and end user alike, thereby leading to additional opportunities for relationship building).

10. Standardization through GAMP

The URS, FS, along with other key life-cycle documents, are established validation deliverables described in the GAMP guidance to provide an element of standardization throughout the industry. This standardization effort provides a common language, terminology, and procedural task flow essential to accurate, comprehensive, and competitive project implementation and maintenance - it simply makes sense.

Significance of 21 CFR Part 11

With the increasing availability of highly sophisticated computer systems capable of processing and centrally registering enormous quantities of information, the advantages of full-scale automation had become evident. However, with the increased power and capacity of computer systems, coupled with the desire to electronically register, process, and file production data in the form of batch records, security likewise had become an area of considerable concern. For this reason, the FDA (in association with other regulatory agencies, standards organizations, manufacturing facilities, and contractors) have compiled a set of rules that the end user, and those in association with the end user, must comply with in order to maintain, manage, and preserve the integrity of historical electronic records. This set of rules are collectively presented and organized in the 21 Code of Federal Regulations (CFR) Part 11 (or Part 11).

The Part 11 structure consists of two key components: 1) Electronic Records and 2) Electronic Signatures. Per code, the concept of Electronic Records (or Erecs) "applies to those in electronic form that are created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth in Agency regulations." Therefore, for example, it is not in the best interests of the end user to assume all data in electronic form are subject to Part 11. Therefore, the URS should be the key component precisely differentiating what information collected (by the end user) is vital for maintaining and ensuring the safety and efficacy of their human-consumable product offerings from data to be used for academic and internal purposes.

To ensure continued compliance to Part 11, the Electronic Signatures (or Esigs) component links the electronic record (and any data contained within the record) to an individual or group that can verify the information is derived from reliable validated sources.

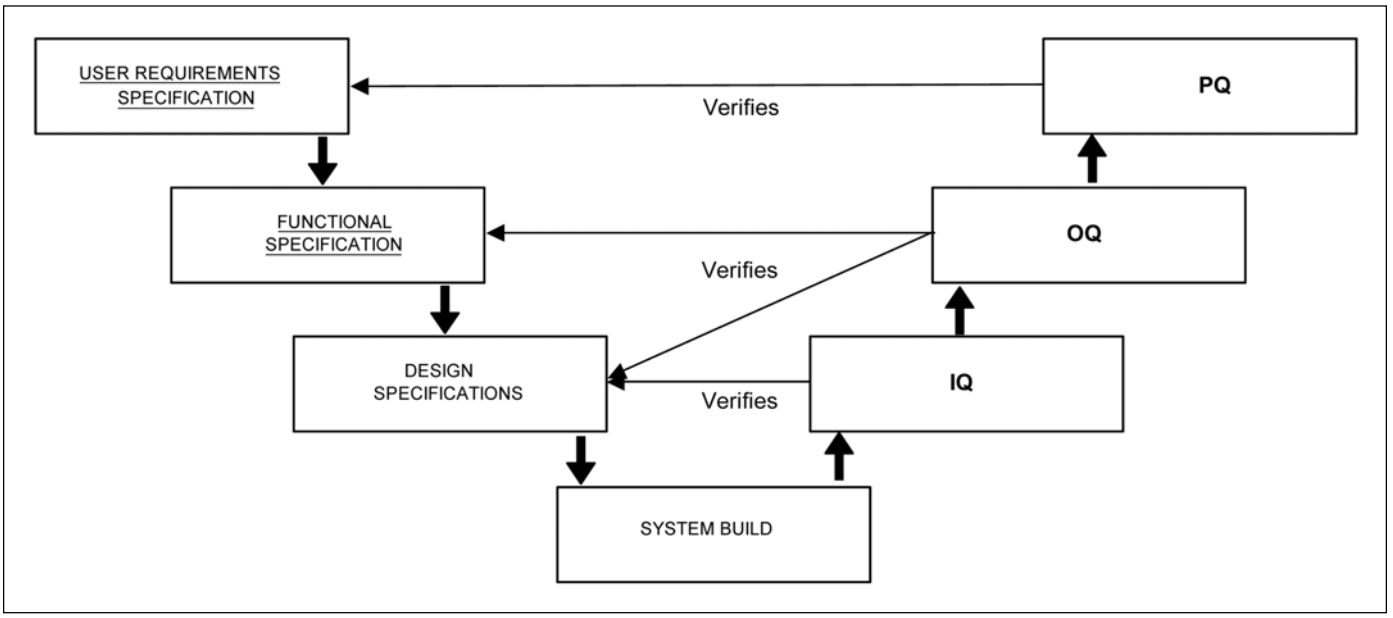

Figure 1. A basic framework for specification and qualification.

In addition to the identification of data subject to Part 11 policy, the URS (and subsequently the FS) should contain references and/or statements regarding specific procedures detailing the handling, security, and authentication of such information (via username/password prompts, audit trails, and other metrics). The overall objective of the URS/FS combination is to ensure end user compliance to Part 11 and the total elimination of "483" violation letters issued by FDA auditors.

This article is not intended to cover all the details of Part 11 policy or its implementation. However, the importance of the URS/FS as vital communications tools among those parties involved in Part 11 interpretation, implementation, and compliance is stressed. Note that Part 11 is a subcomponent of validation and is not intended to replace any components of the validation process.

Conclusion

Until the next revolutionary communications processes emerge, and more viable tools are identified, GAMP philosophy can be readily applied in validated projects such as those with an automation scope. Starting with the URS/FS combination of life cycle documents, the GAMP methodology may be employed to help manage dialog between the contractors and associated parties (including the end user), establish enforcement protocols, and cover bases of inconsistencies and deviations. As the URS and subsequently the FS evolve throughout the detailed design phases, for example, the compromise between flexibility and rigidity can lead to stronger and more profitable end user-contractor relationships well into the future…and of course, a positive reputation breeds a persistent flow of opportunities (not only for the end user through increased profitability, but for the contractor's continued contributions to the bottom line of the customer).

References

1. *GAMP Guide for Validation of Automated Systems*, GAMP 4 (ISPE (GAMP Forum), 2001).

2. Code of Federal Regulations 21, Parts 11 (August, 1997), 210, and 211.

3. CRB Reference Library on GAMP-related Policies and Procedures. CRB Consulting Engineers, Plymouth Meeting, PA. Various applications and releases.

About the Author

Matt Bothe is a licensed Professional Engineer in four states (NY, CT, PA, and TX) and serves as Senior Automation Engineer for CRB Consulting Engineers, Inc. at their Plymouth Meeting, PA office. He is responsible for the specification and selection of instrumentation and process control methodologies (for both continuous and batch operations), and provides comprehensive services in the areas of FAT/SAT/IQ/OQ/PQ, 21 CFR Part 11, and general validation support. He possesses BS degrees in both chemical and electrical engineering from NC State University, Raleigh, NC, a Certificate of Graduate Completion in hybrid circuit design from National Technological University, Fort Collins, CO, and an MBA from Texas A&M-Corpus Christi. He is currently an active member of ISPE and ISA, and former Key Person Chairman for the IMC. His experiences are primarily centered on Instrumentation and Process Controls (including Advanced Control) in a variety of industries that include automotive, power, commodity and bulk chemicals, and biopharmaceuticals. Some of his major accomplishments include the design and installation of a comprehensive 17-node Power Quality Monitoring System, design and installation of redundant model-based PLC-resident Rectifier Control systems for a Chorine-Caustic production facility, advanced custom controller based on Iterative Convergence Control Technology for a major chemicals manufacturer, and participated in and supervised numerous large and small DCS/PCS installations in large scale chemical facilities. In support of his areas of responsibilities, he has created numerous database and software applications using VBA, SQL, and Visual C++. He can be contacted at: matt.bothe@crbusa.com.

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