"Good traceability yields benefits" – guidance from the GAMP® Forum on achieving the correct level of traceability between requirements, design, and testing documents for regulated GxP applications.

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GAMP® Traceability for GxP Regulated Applications

The purpose of this document is to provide guidance on how to achieve an appropriate level of traceability between requirements, design, and testing documents for regulated GxP applications. Although the expectation for traceability by regulatory authorities has been clearly stated,[1,2] there is little definitive guidance on the practicalities of achieving and sustaining traceability.[3]

This guidance addresses this gap and should be treated as a supplement to GAMP® 4, GAMP® Guide for Validation of Automation Systems.[4]

Principles

Processes and supporting documentation should be established and maintained to link requirements, design, and testing. In addition, it should be possible to trace back from testing to both design and requirements - *Figure 1*. This traceability provides a means to ensure that all elements of design, as well as all requirements, have been tested. It also enables the identification and flow of documentation in the event of requests during an audit.

The linkage between requirements, design, and testing is not necessarily limited to a 1:1:1 relationship:

- Multiple requirements may be covered by a single design specification and tested by a single test.
- Multiple design specifications may be linked to a single requirement.
- Multiple tests may be required to address one requirement or one design specification.

Whatever process is used to achieve traceability, it should be:

- appropriate to the system size, complexity, impact, and risk
- documented and approved in the validation planning stage
- an integrated part of the overall life cycle of the project and beyond into the support and maintenance of the system

Benefits of Traceability

Good traceability yields a number of tangible and intangible benefits. Examples include:

- Traceability will assist risk management. Focus should be placed on any critical requirements as part of the risk assessment. Traceability will help to identify critical design elements and necessary testing. There should be increased testing rigor applied to the critical aspects of a system, compared to the non-critical aspects of the system.
- Traceability will improve test coverage. Traceability should make it possible to demonstrate which requirements and design elements are tested. Therefore, duplicate or redundant testing may be avoided.
- Traceability can help demonstrate that validation is complete. All requirements should be functionally tested, covered by an audit, handled through a user operating procedure, or accepted as not requiring testing, and monitored in the live environment.

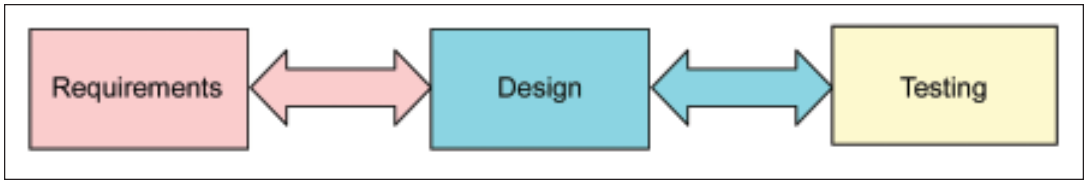

Figure 1. Principles of Traceability.

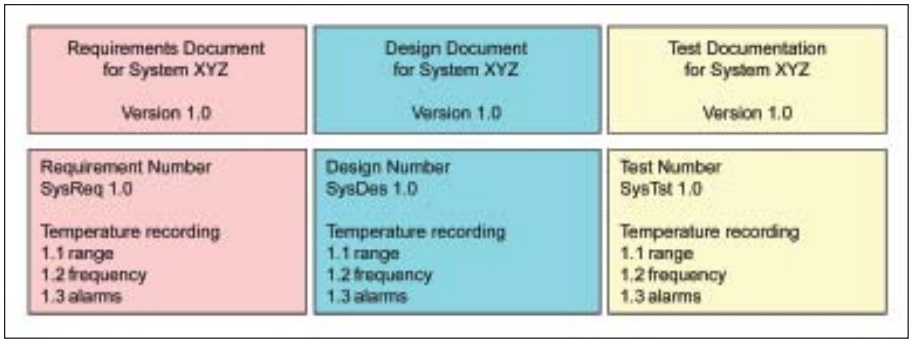

Figure 2. Example of embedded traceability for simple systems.

- Traceability will improve change management. When a change control is raised, traceability enables an accurate assessment of its impact by identifying related requirements, design elements, and test scripts. Regression testing can thereby be clearly scoped.

- Traceability will help root cause analysis of software malfunctions. It should be possible to more easily track and trace design element interdependencies when conducting root cause analysis of incidents attributable to software malfunction.

- Traceability will help audits and inspections. It should be relatively easy to identify any and all supporting documentation for any given operation. It should be much easier to provide timely responses to requests for information.

Methods of Achieving Traceability

Traceability may be achieved in a number of ways, including:

- a Requirements Traceability Matrix (RTM)

- automated software tools

- excel spreadsheets

- embedding references directly within documents

If an RTM is chosen, it may be generated as a separate deliverable or as part of an existing deliverable, such as the requirement document: the choice will be dependant upon maintainability of the deliverable.

Traceability for simpler systems may be achieved through common or consistent numbering of requirements, design statements, and testing - *Figure 2*. The numbering for "temperature recording" in this example is the same in the requirements, design, and test documentation; thereby enabling traceability without creating a separate traceability matrix. This approach works well with smaller systems in low risk situations.

For purely Commercial Off-the-Shelf (COTS) software products, the traceability may be reduced to that of requirements to testing (or qualification) only. However, this will depend upon the user's knowledge of the supplier and their processes, the system usage within the company, and the level of acceptable risk. In most cases, the design column in Figure 2 could be replaced with a link to configuration items, providing traceability between requirements, configuration, and testing (or qualification).

The user of the COTS software products will need to be able to demonstrate an intimate knowledge of the supplier's quality process, as a mitigation of risk to the user processes when using the COTS system. This may necessitate multiple visits to the supplier during the project phase, as risks are identified at points throughout the project, and during the ongoing contact of the support and maintenance phases of the system life cycle.

The depth or granularity of the requirements will be influenced by the size and complexity of the system, along with its potential to impact drug product:

- Safety

- Identity

- Strength

- Purity

- Quality

This granularity will influence the need for the traceability matrix and its contents; the greater the granularity the larger the matrix, and therefore, the greater the need for a tool to maintain the matrix.

An example Requirements Traceability Matrix (RTM) is shown in - *Figure 3*. Each reference within the traceability matrix, e.g., U1.1.2, F3.1, D1.2, T8.2, could be a reference to a section or subsection within the relevant document, or to a totally separate document. The method used and the process should have been declared and approved within the validation plan.

Level of Detail Practicalities

It can be difficult to determine the level of detail required for traceability. The following information is intended to help pitch the detail at a level which satisfies regulatory expectations for traceability, while remaining practical to maintain.

A strategy for traceability should be established during validation planning. User requirements should be developed with traceability in mind.

The level of traceability could stop with a reference to vendor documentation; if documentation needs are met by the vendor documentation when supported by in-depth supplier assessment and a vendor management plan.

The supplier should have their own traceability for the documentation and testing under their control. This should be verified during Supplier Assessments, where appropriate.

Requirements need not trace to technical controls in all circumstances. Requirements may trace to procedural controls, in which case cross-references to identified SOPs is appropriate.

- For simple systems, an RTM is not recommended, as sufficient trace-

ability may be incorporated within document cross-references.

For global systems, planning for traceability in the validation plan is imperative since the control of local and global requirements needs to be resolved at this point for tracking the combination of local and global requirements.

Extending RTMs

There are other features that may be added to a basic traceability matrix that can assist with the overall effectiveness and efficiency of validation activities. Examples include:

- A column to include a brief written description of each requirement, which may assist in the verification that matrix contents are referenced correctly.
- A column to include change control numbers to enable tracking the system history and change impact. Reference also may be made to other documentation and processes which impact the system, such as deviations or SOP changes.
- A column to indicate the criticality of the requirements to assist levels of testing applied to any given requirement. High criticality requirements may have greater testing applied; therefore, may reference multiple tests, whereas low critical requirements may have a reference to a single test. There may be a need to reference the executed tests and the supporting test result documentation along with any failed tests.
- A column to indicate where a requirement has been met by procedural controls, along with the reference to the procedure and its version number. In this case, the requirement and design columns should be blank, but the testing column may not, as the use of the procedure may be tested at the system test level.
- The test column may be expanded to indicate at what level the testing occurs: unit, integration, acceptance (hardware or system) or where and when the testing occurs, development, qualification, production, or global, local. In this case, the level of effort in testing should relate to the criticality of the requirement and the level of acceptable risk. For example, a high-risk requirement may be tested many times and at many levels, whereas a medium risk requirement may be tested just once, and a low risk may not be tested at all, only verified through system use.
- A column linking a test to a maintenance or calibration record for the instrument required for a test and requirement. For process automation documents such as installation records, loop checks and tuning, cable integrity checks may be linked, enabling traceability from the calibration certification on an instrument all the way through to the use of that measurement in the business process and system testing.

The above additions increase the difficulty of navigating and maintaining the traceability matrix. Therefore there needs to be a balance between what is expected of the traceability matrix and the maintainability of the method chosen. Where large projects are being installed, such as ERP/MRP II, LIMS/CDS, or large process control systems, it may be prudent to seek out a document management system which has the capability to both maintain the links between documents within the document management system and references to documents generated and stored outside.

Documentation and Maintenance of Traceability

The chosen process and method which any given system will use for traceability should be documented and understood. It is recommended that this be achieved within the validation plan for smaller systems, or perhaps proceduralized for larger and more complex systems. All members of a system development team should be acquainted with the process and method to ensure that it is adopted and maintained throughout the system development life cycle.

Once a system has been accepted into use, the maintenance of traceability is required to preserve its usefulness. The method of maintenance will always be linked to whatever process is used to maintain the requirements, design, and test documentation, all of which must be updated to reflect the current system. In addition, the version control may be linked to enable system configuration controls, e.g., version 1.0 of the requirements, design, test, and traceability are in use at go-live of any system, then all versions may be increased at the same time to maintain this configuration control periodically throughout the system life cycle.

Whatever changes are made to the documentation they will be controlled through the control of a change process. Within this process, the method by which the documents will be updated should be documented, for example:

- at every change
- with a number of changes batched together
- on a chronological basis

Requirements	Design		Testing
	Functional Specification	Design Specification	
U1.1.1	F2.4.1	D2.5	T1.1
U1.1.2	F2.4.5	D2.4	T1.1
U1.2.1	F3.1	D1.1	T2.3.1
U1.2.2	F3.2	D1.2	T8.1
U1.2.3	F3.3	D3.3	T8.2

Figure 3. Example Requirements Traceability Matrix (RTM).

The method should be justified within the process and based upon documented and reasoned risk.

Conclusion

Although traceability is a valuable tool for any system, its scope, depth, granularity, and level of detail should be commensurate with the criticality and risk associated with the business process being controlled by the system. If traceability is sized correctly it may be the one tool which can influence the success of the project, support and maintenance, and 'auditability.' However, like any other tool it can achieve this success only if it is maintained throughout the system life cycle.

References

1. PIC/S Guidance on Good Practices for Computerised Systems in Regulated "GxP" Environments (PI011-2) (available at www.picscheme.org).

2. FDA, 'General Principles of Software Validation: Final Guidance to Industry and FDA Staff,' published in 2002 by the Food and Drug Administration's Center for Devices and Radiological Health (CDRH), (www.fda.gov)

3. Wingate, G.A.S. (Editor), 'Computer Systems Validation: Quality Assurance, Risk Management, and Regulatory Compliance for Pharmaceutical and Healthcare Companies,' published in 2003 by Taylor and Francis (www.crcpress.com), ISBN 0-8493-1817-8.

4. *GAMP® 4, Good Automated Manufacturing Practice (GAMP®) Guide for Validation of Automated Systems*, International Society for Pharmaceutical Engineering (ISPE), Fourth Edition, December 2001, www.ispe.org.

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