



PQE

Pharma Quality Europe s.r.l.

GAMP Guideline & Validation Documentation

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GAMP Guideline & Validation Documentation

■ GAMP Guideline

- ┌ Planning documents
- ┌ Specification Documents
- ┌ Testing Documents
- ┌ Acceptance Documents

Purpose of GAMP

- ✓ To help USERS understand the requirements for prospective validation of an automated system and the level to which the validation should be performed
- ✓ To help SUPPLIERS ensure that systems are developed according to good practice, and to provide documentary evidence that their systems meet the agreed specification

History of the GAMP (1)

First Draft	<i>February 1994</i>	Distributed to UK industry for comments.
Second Draft	<i>January 1995</i>	Incorporating comments from 31 companies.
Version 1.0	<i>March 1995</i>	As Second Draft but incorporating EC GMP Annex 11.
Version 2.0	<i>May 1996</i>	Revision and new content, incorporating further comments from Europe and the USA.
Version 3.0	<i>March 1998</i>	Revision and new content. Separation into User and Supplier Guides. Addition of Volume Two.



History of the GAMP (2)

GAMP4

December 2001

Major revision and new content in line with regulatory and technological developments. Broadened scope to include regulated healthcare industries. Greater coverage of user responsibilities and detail on operational activities.



GAMP 4 Objectives

The extent and scope of Validation needs to be easily determined using simple and well-understood rules. The existing guidance on categories of software is very useful, but should be developed further. Validation life-cycles and associated documentation needs to be scaleable to take due account of the size, complexity, and criticality of the computer system.

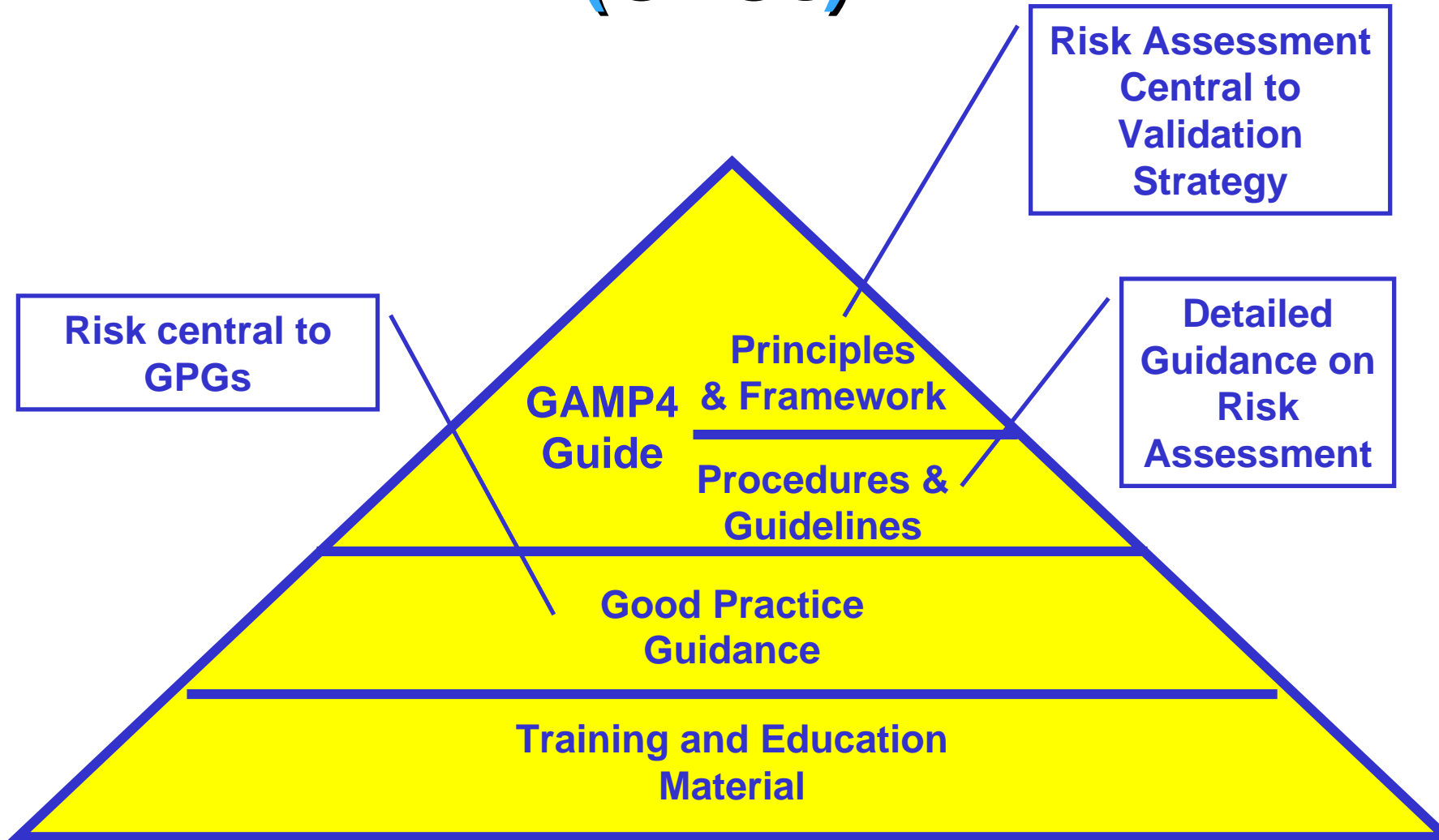


GAMP 4 Objectives

The balance of validation work required by users needs to be examined. **More use should be made of the development work performed by suppliers, so that less supplementary work is required by the users.** Greater emphasis is required on the benefit, use, and control of configuration of systems based software packages.



GAMP 4 vs Good Practice Guides (GPGs)



Good Practice Guides (GPGs)

- **A Risk-Based Approach to Compliant Electronic Records and Signatures**
- **Testing of GxP system**
- **Validation of Process Control System**
- **Global Information Systems Control and Compliance**
- **Validation of Laboratory Computerized Systems**
- **IT Infrastructure Control and Compliance**

Principles and Framework

**A strategic framework for computer validation
drawing together the key validation principles
and practices**

**How to apply these principles to determine extent
and scope of validation for different types of
systems**

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Principles and Framework

- **Introduction to GAMP**

- ✓ Including Purpose, Scope and Benefits

- **Validation Overview**

- **Validation Life Cycle**

- Including User Requirements Specification, Determining Validation Strategy, Validation Reporting, and Maintaining the Validated State

- **Management System for Suppliers of IT Systems**

- **Process Control System Validation**

- **Benefits of Validation**

- **Good Practice Definitions**

- **Glossary, Acronyms, and Source Material**

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Procedures and Guidelines

A supporting set of rationalized and revised procedures and guidelines for computer system validation and compliant operation, classified into:

- Management**
- Development**
- Operation**

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Management Appendices M1÷M10

Validation Planning
Supplier Audit
Risk Assessment
Categories of software and hardware
Design Review and Traceability Matrix
Quality and Project Planning
Validation Reporting
Project Change Control
Configuration Management
Document Management

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Development Appendices D1÷D6

User Requirement Specification
Functional Specification
Hardware Design Specification
Software Design and Software Module Design
Specification
Production, Control, and Review of Software
Testing of an Automated System

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Operation Appendices 01÷09

Periodic Review
Service Level Agreement
Automated System Security
Operational Change Control
Performance Monitoring
Record Retention, Archive and Retrieval
Backup and Recovery of Software and Data
Business Continuity Planning
EU Annex 11 – APV Interpretation

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GAMP 4 Themes

**Defined Development Lifecycle
Planning
Risk And Impact Assessment
User and Supplier Partnership
Specifications
Traceability
Design Review
Formal Testing and Verification
Documented Evidence**

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Validation approach through GAMP

Category	Name	Description
I	Operating Systems	Established, commercially available software
II	Firmware	Software already contained in equipment that cannot be manipulated by the user
III	Standard Software Packages	These are commercial off the shelf COTS configurable software
IV	Configurable Software Packages	These are custom configurable packages. They permit users to develop their own application by configuring predefined SW modules and developing new application SW modules
V	Custom (Bespoke) Systems	Unique application developed to meet specific needs of a user company

**GAMP
categories**



Validation Approach

Validation Approach (1)

CATEGORY

VALIDATION APPROACH

1 Operating Systems

Record version (including Service Pack). The Operating System will be challenged indirectly by the functional testing of the application

2 Firmware

For non-configurable firmware record version. Calibrate instrument as necessary. Verify operation against user requirements.
For configurable firmware record version and configuration. Calibrate instrument as necessary and verify operation against user requirements

3 Standard Packages

Record version (and configuration of environment) and verify operation against user requirements. Consider auditing the supplier for critical and complex application



Validation Approach (1)

CATEGORY

VALIDATION APPROACH

- | | |
|--------------------------------|--|
| 4 Configurable Packages | Record version and configuration, and verify operation against user requirements
Normally audit the supplier for critical and complex application
Manage any custom (bespoke) programming as Category 5 |
| 5 Custom or Bespoke | Audit supplier and validate complete system |

e.g. ERP System components vs GAMP Categories

Category	Name	System Component	Description
I	Infrastructure	Network	Communication reliability verified through PQ
		Database Server	Document OS version and configuration and check it in the IQ phase.
		Application Server	
		Workstations	
III	Standard Software Packages	Pervasive SQL database	Document Package version and check it in the IQ phase.
		Crystal Reports application	Verify Package functionality through the testing of MAX & MQM systems.
IV	Configurable Software Packages	ERP	Record version and Configuration, and verify operation against user requirements within PQ
V	Custom (Bespoke) Systems	Interface ERP-MES	Full Validation Life Cycle



What's new: Hardware Categories in GAMP 4 Appendix M4

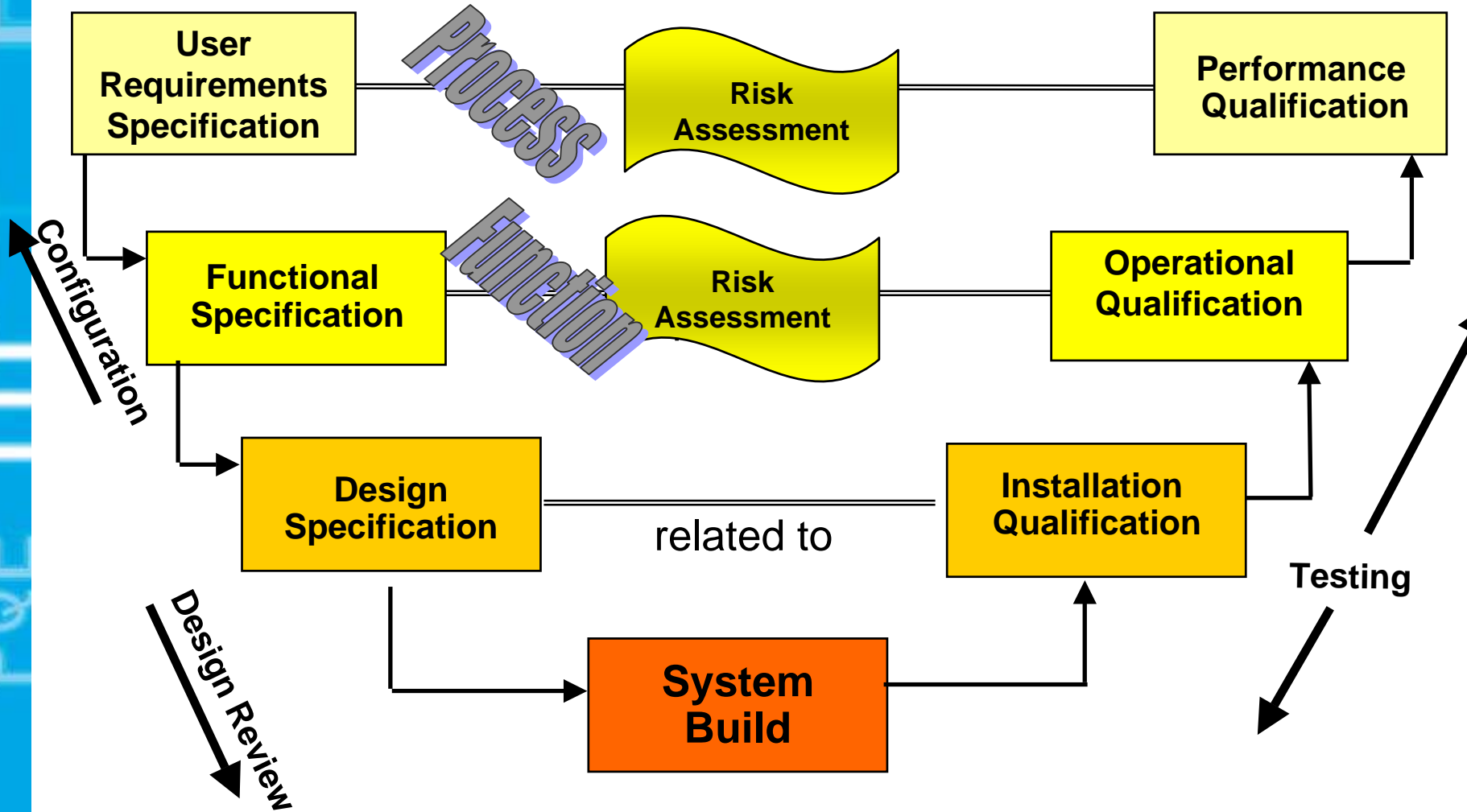
•Cat. 1 - Standard Hardware Components

- Should be documented including manufacturer or supplier details and version number
- Verify installations and connections through IQ
- Record Model, version, serial number of pre-assembled hardware
- Use hardware data sheet or other specification if necessary
- Change Control and Configuration Management apply

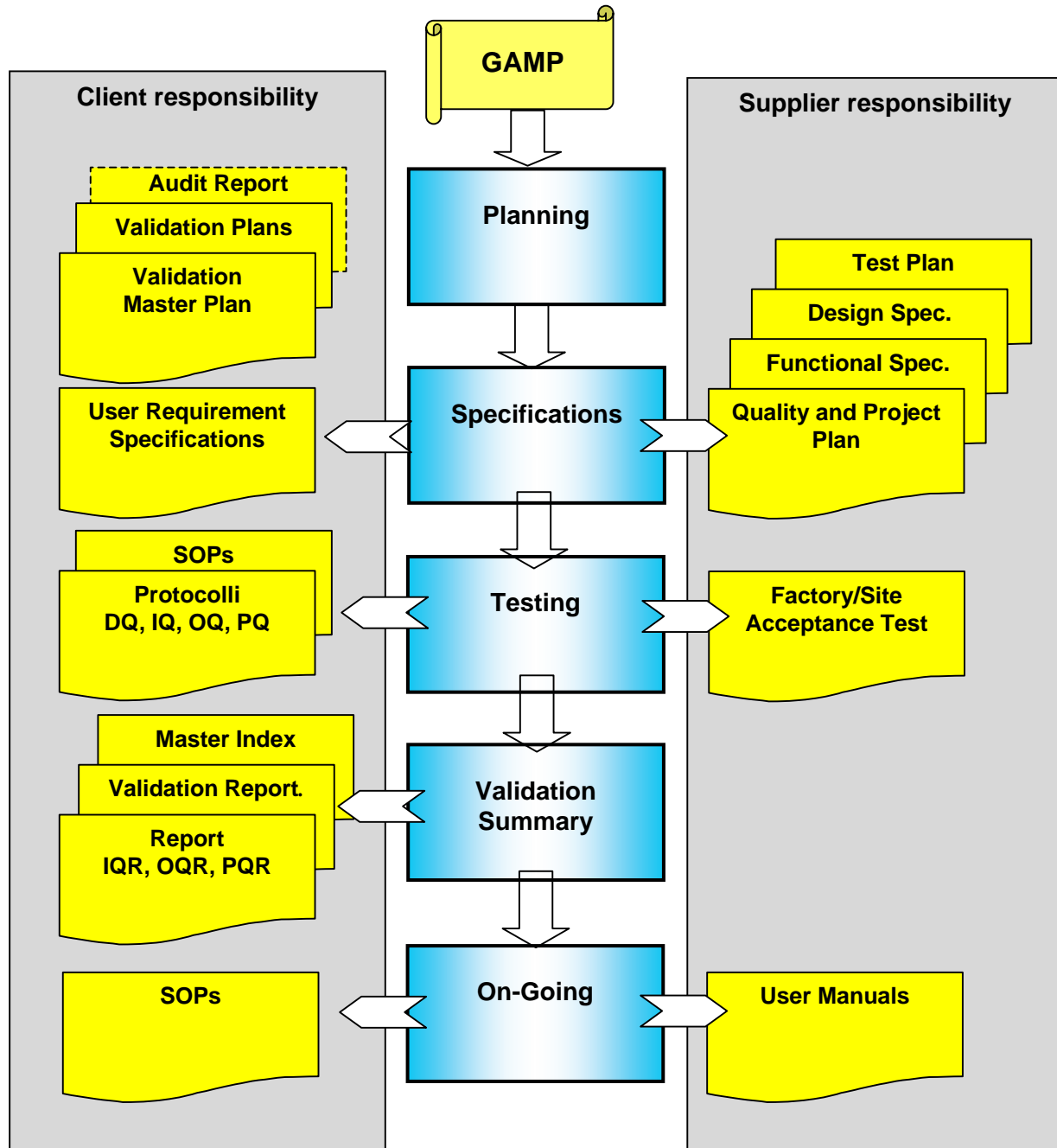
•Cat. 2 - Custom Built (Bespoke) Hardware Components

- As category 1 plus...
- Design Specification and Acceptance Testing
- Supplier Audit for bespoke hardware required
- Configuration defined in Design Documentation
- Verify through IQ
- Change Control and Configuration Management apply

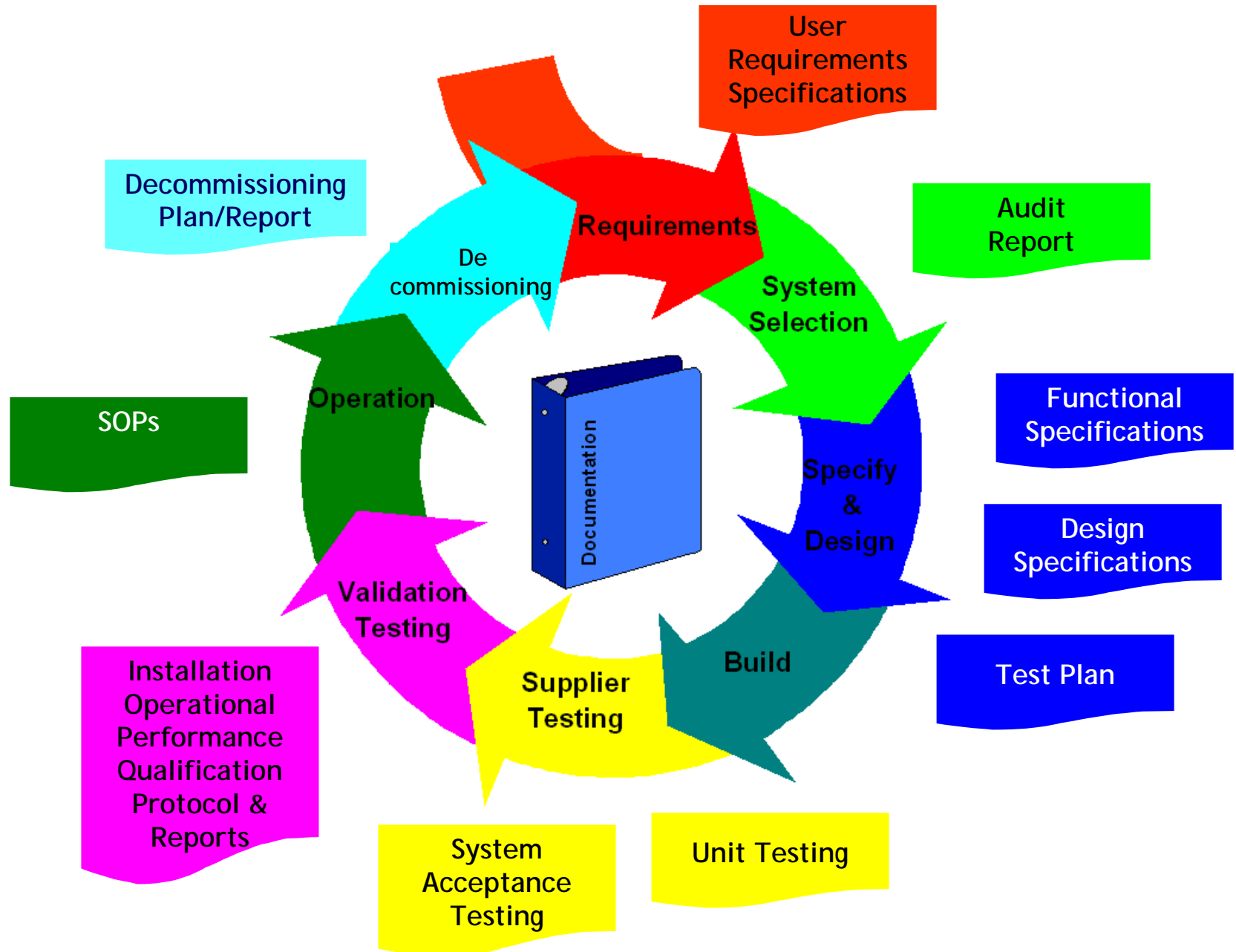
GAMP Validation Lifecycle



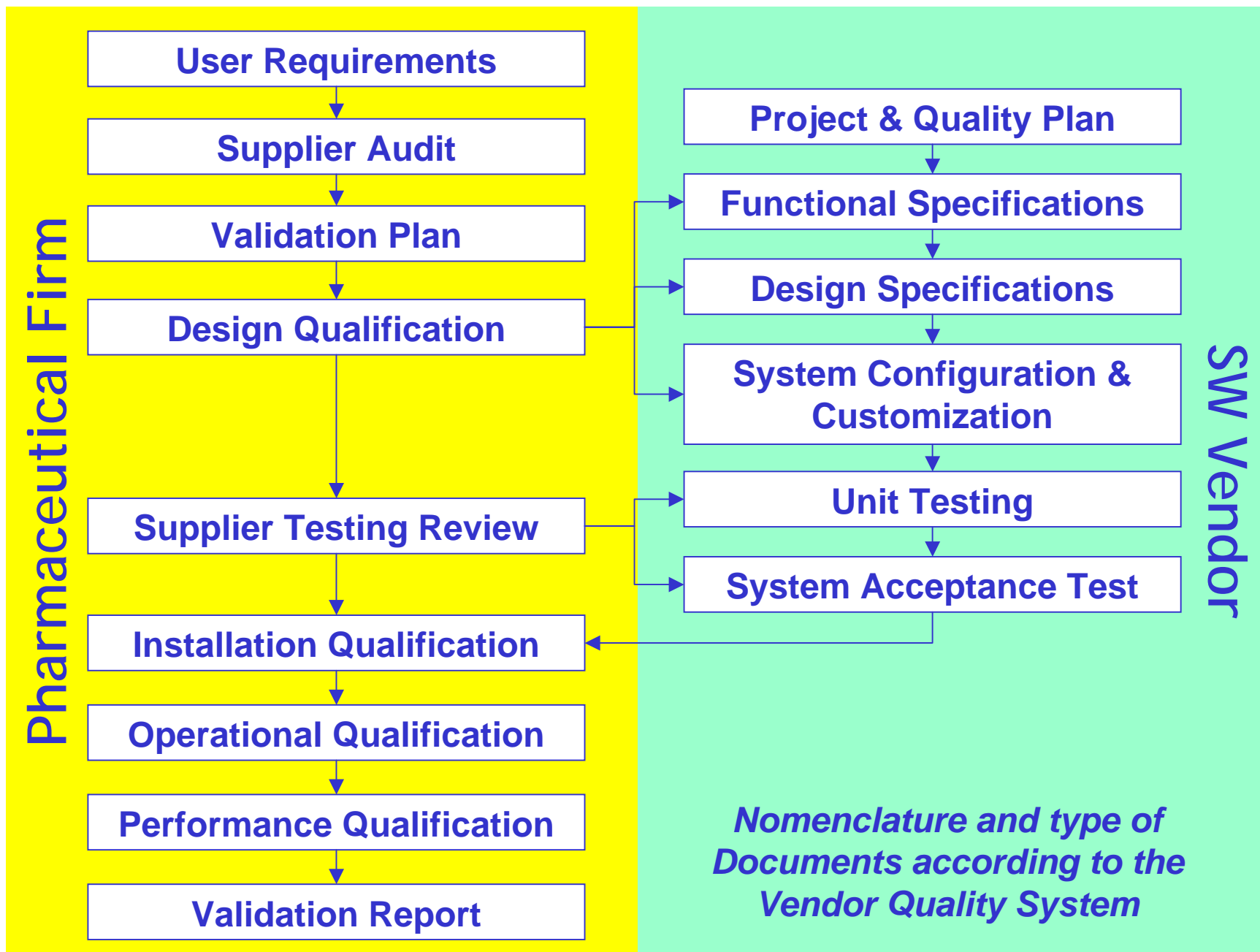
CS Validation Documents



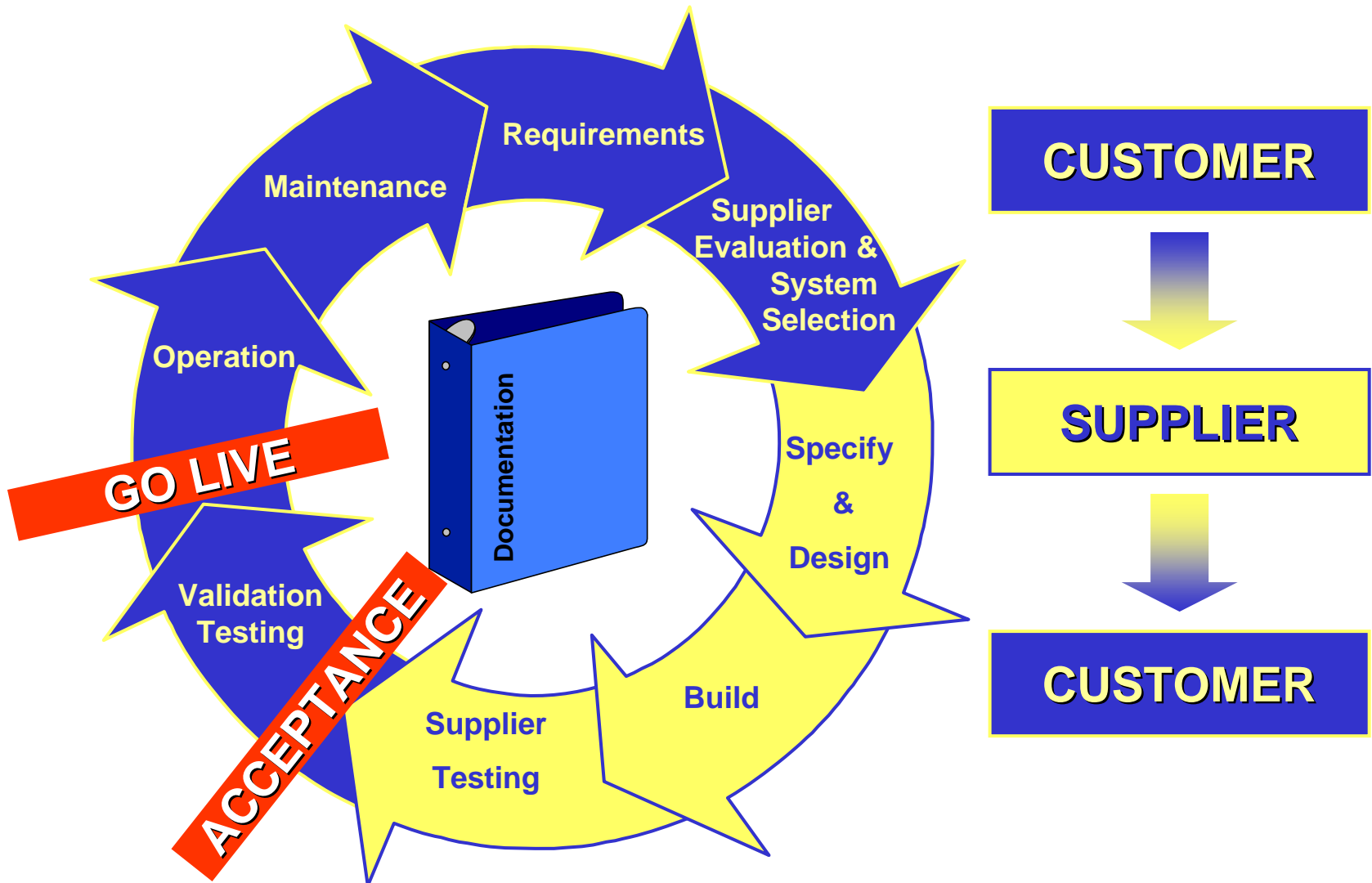
Validation Deliverables



Validation Process



Responsibilities



GAMP Guideline & Validation Documentation

└ GAMP Guideline

■ Planning documents

└ Specification Documents

└ Testing Documents

└ Acceptance Documents

Validation Plan (1.3)

It is the formal documentation of the comprehensive validation activity plan (according to system life cycle).

It describes the planned validation activities, responsibilities and approval authorities.

Validation Plan (2.3)

Each validation effort must have a Computer Validation plan that includes the following:

- System name and version**
- System description**
- System owner/responsible**
- Scope of validation (System Boundaries)**
- Reference to SOPs or standards used to perform the validation**
- For automated equipment, the plan should be combined and/or integrated with the equipment validation plan and not performed separately**

Validation Plan (3.3)

The Validation plan shall define the deliverables, responsibilities and SOPs that define the quality and validation requirements for the System in order to be agreed upon among the project team.

A rationale shall be determined for any deviation from the standards

The Validation plan shall define the Validation approach based upon

- Criticality
- Complexity
- SW Category

GAMP Guideline & Validation Documentation

- ┌ GAMP Guideline
- ┌ Planning documents
- **Specification Documents**
- ┌ Testing Documents
- ┌ Acceptance Documents

User Requirements Specification (1.5)

Without requirement specification well defined and translated into measurable parameters, no validation is possible.

Requirements specification shall describe in details **what the computer system will do**
BUT NOT
how it will do it

Most of CS defects are due to incorrect requirements specification

User Requirements Specification (2.5)

URS must address:

- Regulatory Requirements
- Process Requirements
- What e-Records are managed by the system
- Where e-Signatures are employed
- Necessary audits trails (who, what, when)
- Data retention
- Security / authorization
- Business continuity plan
- Unused system functions
- Operating environment and the computer's role

User Requirements Specification (3.5)

Each Requirement shall be:

- Uniquely identified**
- Unambiguous**
- Testable**
- Not repeated**
- Prioritized (if any)**

Quality attributes of Requirement:

- Accurate**
- Clear**
- Consistent**
- Complete**

User Requirements Specification (4.5)

The fundamental question for Requirement:
Which the adequate level of detail ???

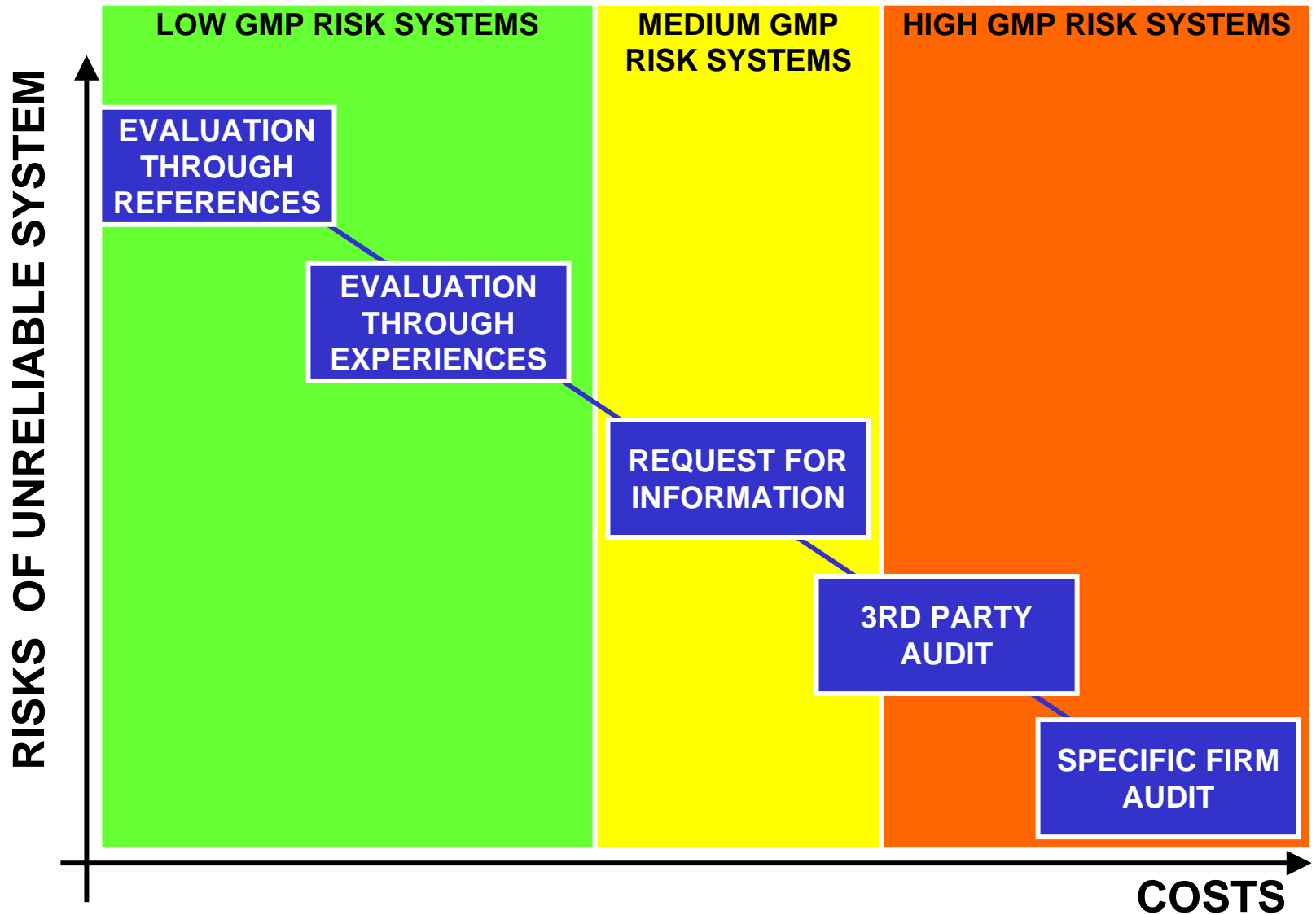
The requirements shall be written with enough details **to provide guidance for the design specifications and functional testing** and may reference other documents

User Requirements Specification (5.5)

Use of diagrams to help describe interfaces and complex processes:

- Business process (in Requirements)**
showing work flow and parts automated by system
- Interfaces (in Requirements)**
showing links to other systems
- System process (in Requirements)**
showing the internal system processes

Supplier Selection



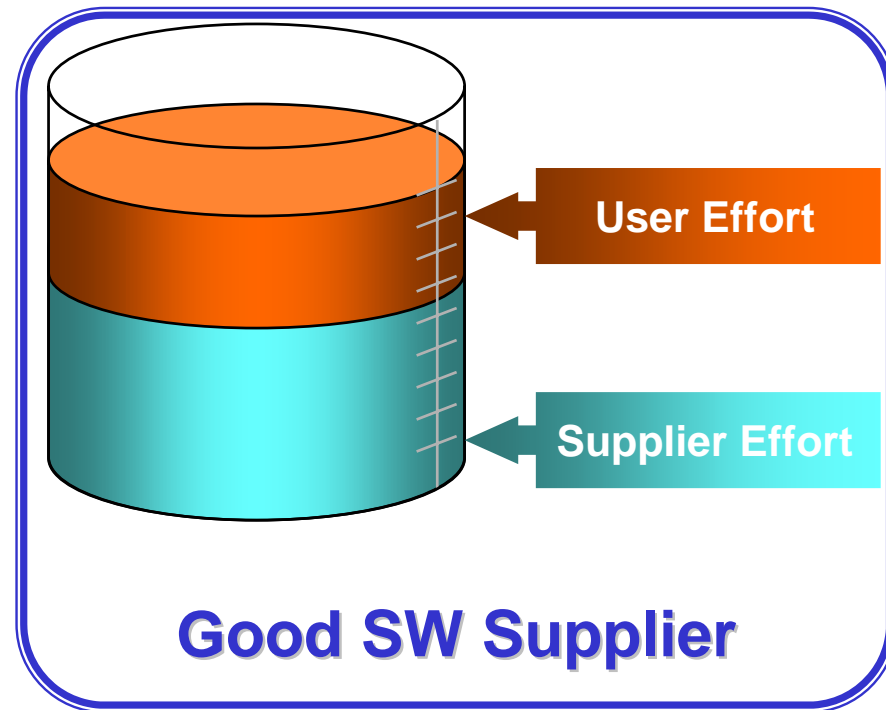
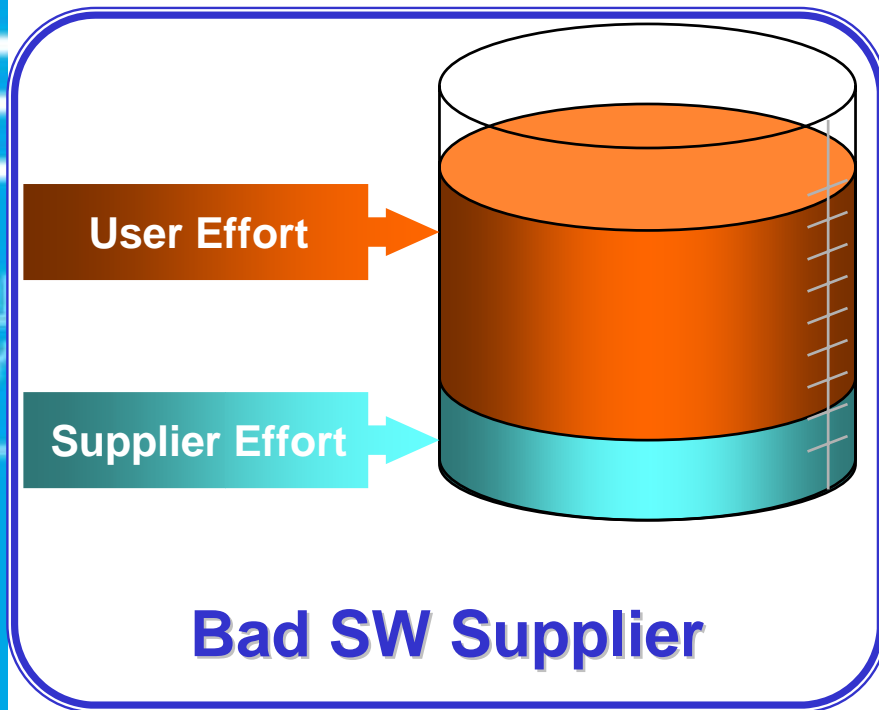
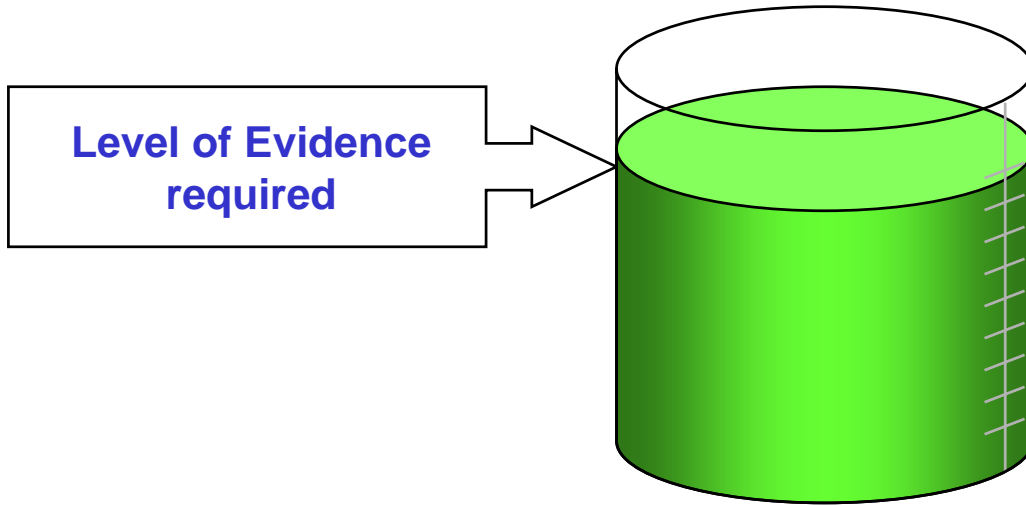
**HIGH GMP RISK SYSTEMS:
1st screening**

**HIGH GMP RISK SYSTEMS:
Evaluation**

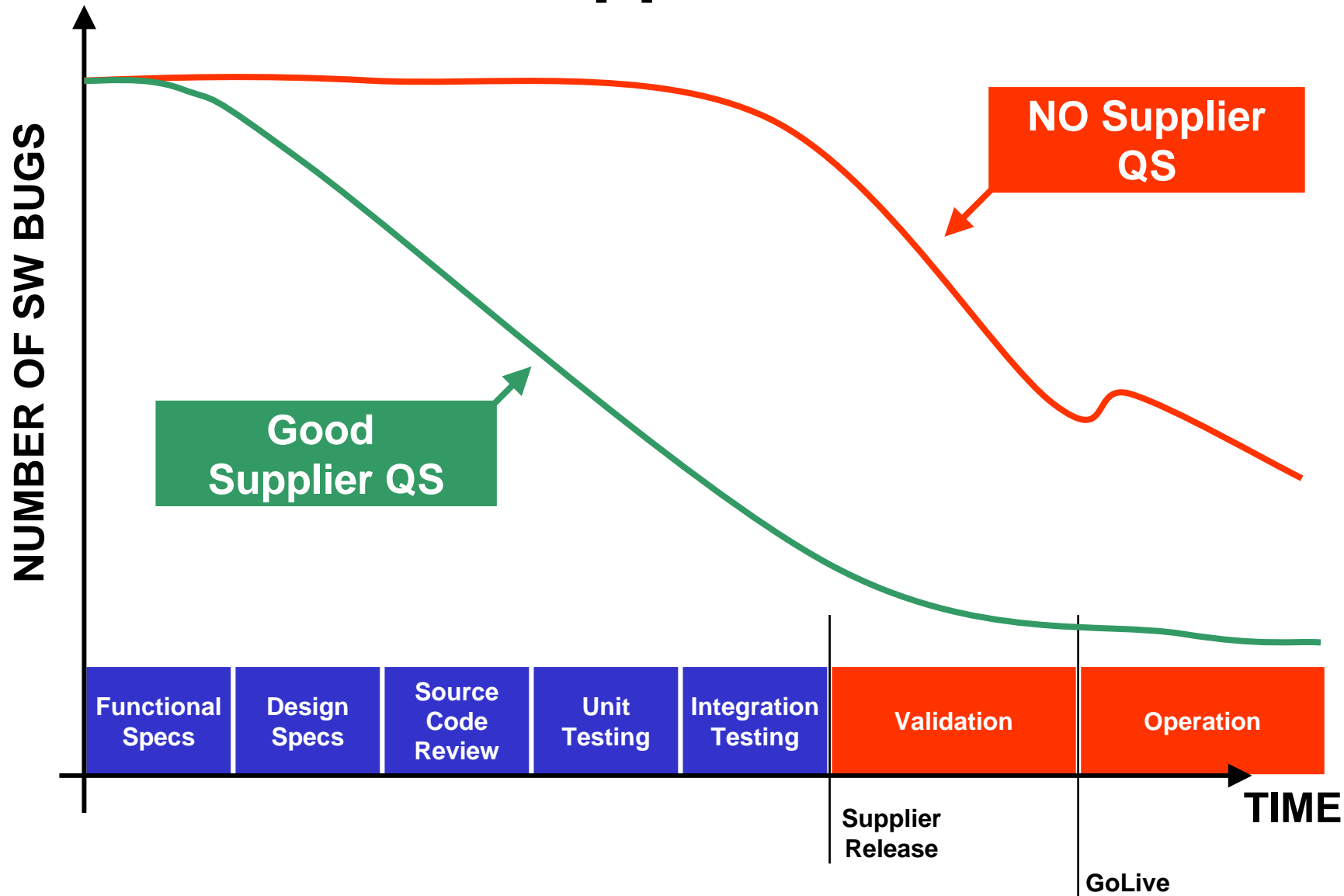
**HIGH GMP RISK SYSTEMS:
Final Selection**



Beker's rule



Why should I choose a Good SW supplier?



Quality & Project Plan (1.3)

Quality Plan

Agreed between user and supplier, and defining actions, deliverables, responsibilities, and procedures satisfying the user quality and validation requirements.

Project Plan

Agreed between user and supplier detailing project phases, activities, and milestones

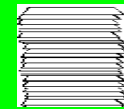
BAD DOCS



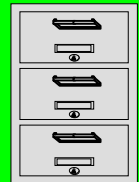
Customer docs



GOOD DOCS



Customer docs



Supplier docs (Reference)

Quality & Project Plan (2.3)

The Quality Plan shall include

- Who produced the document, under which authority, and for what purpose**
- The contractual status of the document**
- Relationship with, and reference to, relevant policies, procedures, standards and guidelines (such as GAMP)**
- Relationship with, and reference to, the Validation Plan if appropriate**

The Quality Plan shall describe how the user company quality requirements are to be met by the supplier. The activities to be undertaken, the procedures to be followed, and responsibilities should be defined.

All user company quality requirements should be listed here. User quality requirements take precedence over the supplier's Quality Management System.

Quality & Project Plan (3.3)

Activities addressed by the QPP

- **Specification**
- **Design Reviews**
- **Programming standards and code reviews**
- **Testing**
- **Installation**
- **Data migration**
- **Acceptance (both supplier factory and user site acceptance testing)**
- **Document Management**
- **Change Control**
- **Configuration Management**
- **Issue and risk management**
- **Project training**
- **Handover to support organization**

System Specification

Functional Specifications is normally written by the supplier and describes in detail the functions of the system, i.e., what the system will do. The user should review and approve Functional Specifications. It is normally considered a contractual document.

Design Specifications should contain sufficient detail to enable system build and maintenance

Functional Specification (1.3)

Functional Specification shall describe how the system performs the function required

Quality attributes of Functional Specifications:

- Traceable to the requirement**
- Uniquely identified**
- Unambiguous**
- Detailed**
- Testable**
- Not repeated**

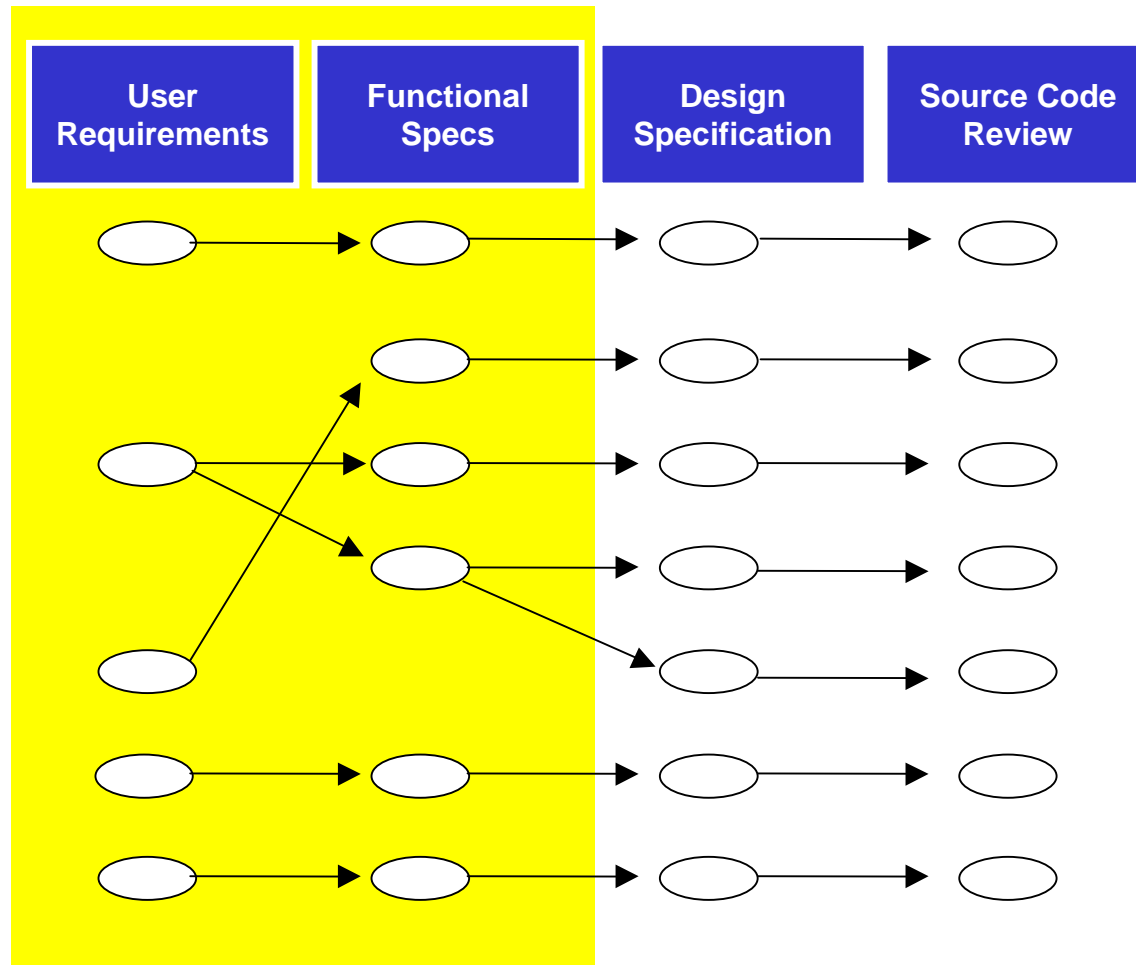
Functional Specification (2.3)

WHO	WHEN
SUPPLIER	ACCORDING TO URS DURING NEGOTIATION PHASE
SUPPLIER + USER	AFTER ANALYSIS IN CASE OF CUSTOMIZATIONS

Functional Specification (3.3)

must initiate:

Requirements Traceability



Design Specifications

Design Specification shall describe how the system has been developed in order to perform the functions required

Design Specifications shall include:

- Standard model used in developing the application**
- Information flows**
- Software elements of the system**
- Configuration (in case of configurable systems)**

Design Specification shall

- ⇒ provide sufficient detail to build or buy a computer system or components**
 - ⇒ Be the basis for additional activities such as module and subsystem development, test planning, subsequent maintenance and enhancement.**



Design Specifications

Design Specifications maintained by the firm shall document the part of the system under user's (ie firm) control

Design Specification maintained by the firm shall include the following (but not limited to):

- ⇒ HW/SW Specifications (GAMP category 3)**
- ⇒ Package Configuration Specifications (GAMP category 4)**
- ⇒ SW Design Specifications (GAMP category 5)**

Package Configuration Specifications

This document describes the required configuration of standard components to be provided as all or part of the solution.

It should address:

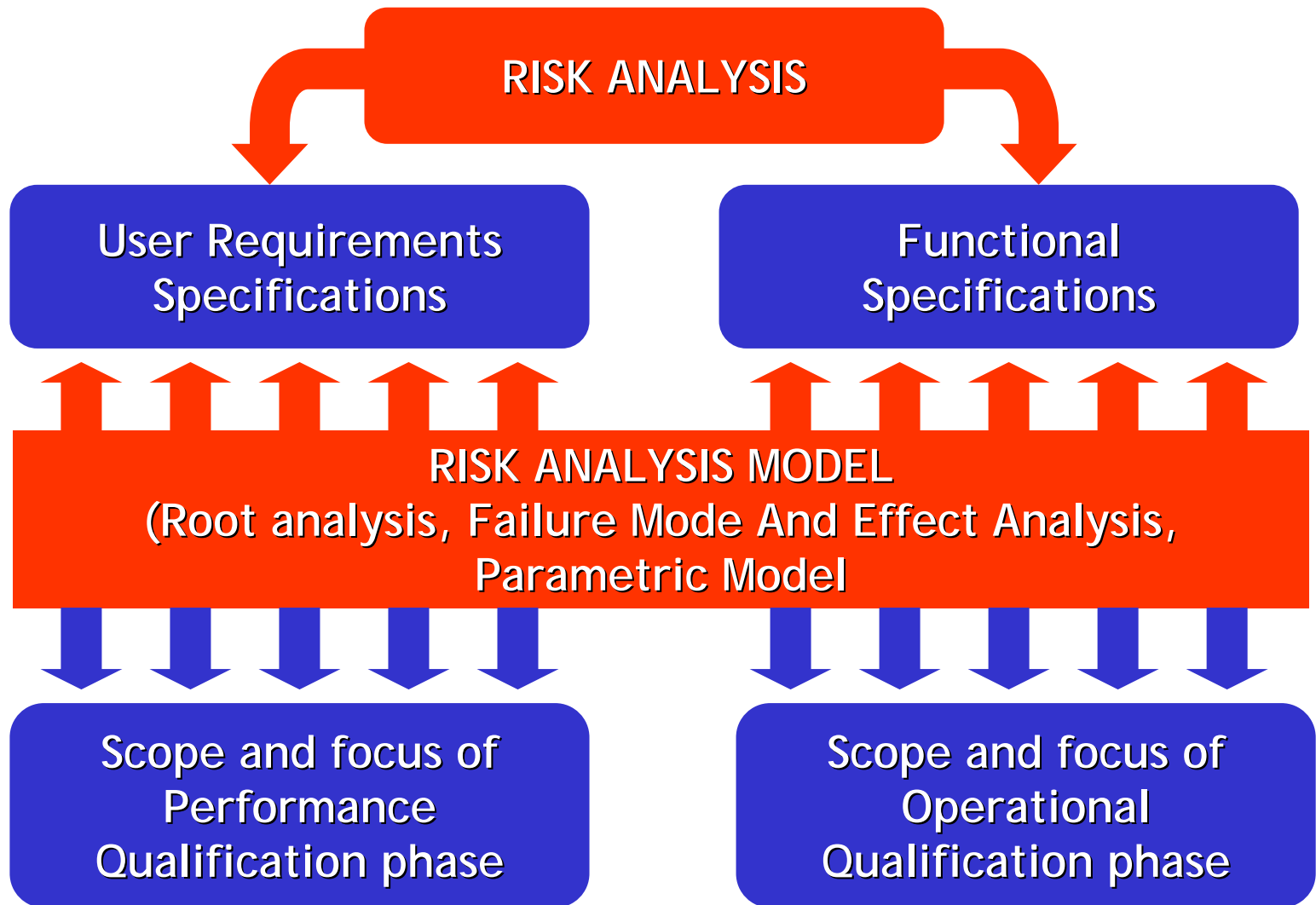
- Required configuration settings or parameters**
- Reason for setting, with reference to controlling specification**
- Tools or methods that will be used to set the required options**
- Dependencies and impacts on other modules or systems**
- Security of settings**

Design Qualification

Design Qualification (also termed Design Review) is a planned and systematic review of specifications, design, and development throughout the life cycle.

Design Reviews evaluate deliverables against standards and requirements, identify problems, and propose required corrective actions.

Risk Analysis Methods



GAMP Guideline & Validation Documentation

- ┌ GAMP Guideline
- ┌ Planning documents
- ┌ Specification Documents
- **Testing Documents**
- ┌ Acceptance Documents

Testing

“The process of exercising or evaluating a system or a system component by manual or automatic means to verify that it satisfies specified requirements or to identify differences between expected and actual results”

IEEE Std. 729

Testing is the keystone of the validation process...



**INDEPENDENCE FROM
DEVELOPMENT**

Tests should include not only “normal or “expected” values, but also stress conditions. Test conditions should extend to boundary values, unexpected data entries, error conditions, reasonable challenges, branches, and combinations of inputs.

Testing

- Testing based on Test Procedure (Protocols)
- Testing performed in dedicated environment
- Attention to produced documentation
- Production of the testing final report

Testing shall be based upon:

- system documents, which describe the characteristics of systems that will be the subject of tests
- test procedures, which describe how to perform the test
- test results, which report results of system tests
- anomaly reports, which describe errors and bad workings found by tests

Test Procedures

Test Procedure shall describe **in details** how to perform test

- Uniquely Identified
- Traceable to the specification
- Unambiguous
- Accurate
- Specify expected results

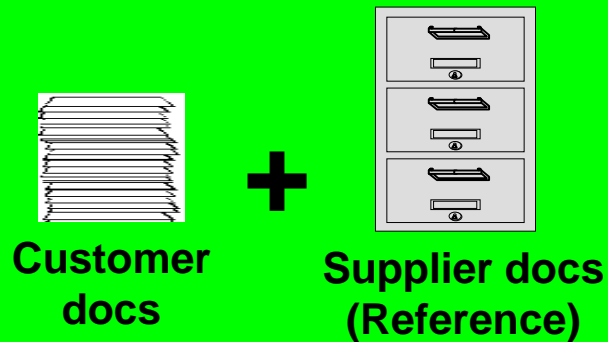
Testing Focus

- Specify expected and actual results
 - Evidence of test results generated during testing must be recorded (e.g., printouts, screen dumps, display of alarm color, event observation)
 - If evidence cannot be generated, a second person (verifier) may need to verify critical events (when specified by test plan)
- Deviations and unexpected results are investigated, resolved and documented

Supplier Testing Benefits

- Validation testing can be greatly decreased or not executed if the supplier has a reliable set of **verified functional testing**.
- **Vendor documentation** for technical support may reduce or eliminate the need to recreate such documentation.

GOOD AUDIT



BAD (or NON EXISTING) AUDIT



Supplier Testing

- ❑ **Supplier Testing** shall be executed through following approaches:
 - ❑ **White Box:** Examining the internal structure of the source code. Includes low level and high level code review, path analysis, auditing of programming procedures and standards actually used, inspection for extraneous “dead code”, boundary analysis and other techniques.
 - ❑ **Black Box:** Testing that ignores the internal mechanism of a system software or a software component and focuses solely on the outputs generated in response to selected inputs and execution conditions.
- ❑ **Independence of Review** shall be ensured by the Vendor, i.e. at least a testing stage shall not be executed by the persons who developed the code



Supplier Testing

Unit Testing activities will be performed in order to test each single software object against its Unit Design Specification and verify the correct implementation of each single process management functions.

Integration Test Specification Defines those tests that demonstrate that all software modules communicate with each other correctly and that the software system meets its design specification. For solutions based on configurable software it may be necessary at this point to integrate the configuration previously tested using Package Configuration Test Specifications

Site Acceptance Testing is performed by the Supplier in order to verify:

- system correct functionality
- system coverage of User Requirements
- interface suitability between systems and instruments (if any)



User Qualification

- Criticality and complexity of the computer system will impact the extent and focus of testing**
- Results of the Software Supplier Evaluation may impact the quantity of formal user testing required, especially OQ (unit) testing**
 - Testing may be greatly reduced if the supplier has a reliable set of functional testing**
 - Vendor testing weaknesses may need to be addressed with additional testing**

Installation Qualification (1.4)

Installation Qualification is in practice performed to assure that the CS has been installed as specified and documented evidence exists to demonstrate this.

IQ shall confirm that:

- Software has been loaded correctly
- Specific site hardware items have been assembled and installed correctly
- Power supplier, earth connections, data connections and field connections are correct and enable the system to be powered up
- Control and monitoring instrumentation have been calibrated and installed correctly
- Basic system functions operate on power up and any built in diagnostics are satisfactorily

Installation Qualification (2.4)

Documented verification that a system is installed according to written and pre-approved specifications.

- Characteristics of PC HW and SW**
- Configuration/parameterization files print (if any)**
- Quality SW Supplier Certification (if any)**
- Software Certification (if any)**
- Reference to specifications (Design Specification)**
- Base tests to verify correct installation**

Installation Qualification (3.4)

Documentation must exist for installation of the application software in the production environment, including:

- Name and version of the software
- Who performed the installation
- Date/time of installation
- Installation instructions (listed or referenced)
- Special set-up parameters
- Verification that the installation was successfully completed

Installation Qualification (4.4)

- If testing is not performed in the production environment, include documented evidence that:
 - Test environment is essentially the same as production environment
 - Test installation meets the same criteria as production installation

Operational Qualification (1.2)

Assuring that the installed system works as specified in the Functional Specification and/or **Requirements** throughout the **intended operating ranges** and sufficient documentary evidence exists to demonstrate this. The Functional tests should be **traceable** through the OQ Test Protocols to the Functional Specification.

The Operational procedures, Critical algorithms and parameters should be tested as well as Data integrity, security, accuracy and reliability. **Stress test would normally be a part of OQ.**

Operational Qualification (2.2)

- ❑ Tests must challenge normal and abnormal conditions including:
 - ❑ Security controls
 - ❑ Range checking for data entry
 - ❑ Sequences of operations
 - ❑ Alarm conditions

- ❑ Additional testing should focus on portions of the system which are most critical and complex

Performance Qualification (1.2)

As part of the PQ it is necessary to prove that the system works correctly and consistently in the intended operational environment at the Client as part of the process for which it has been designed, using all procedures, equipment, utilities.

The equipment IQ & OQ and the Automation system IQ and OQ must be completed and approved before the PQ protocol is executed.

The Process SOP's needs to be tested during the PQ, and the PQ should verify that the CS will work accordingly to the Requirements.

Performance Qualification (2.2)

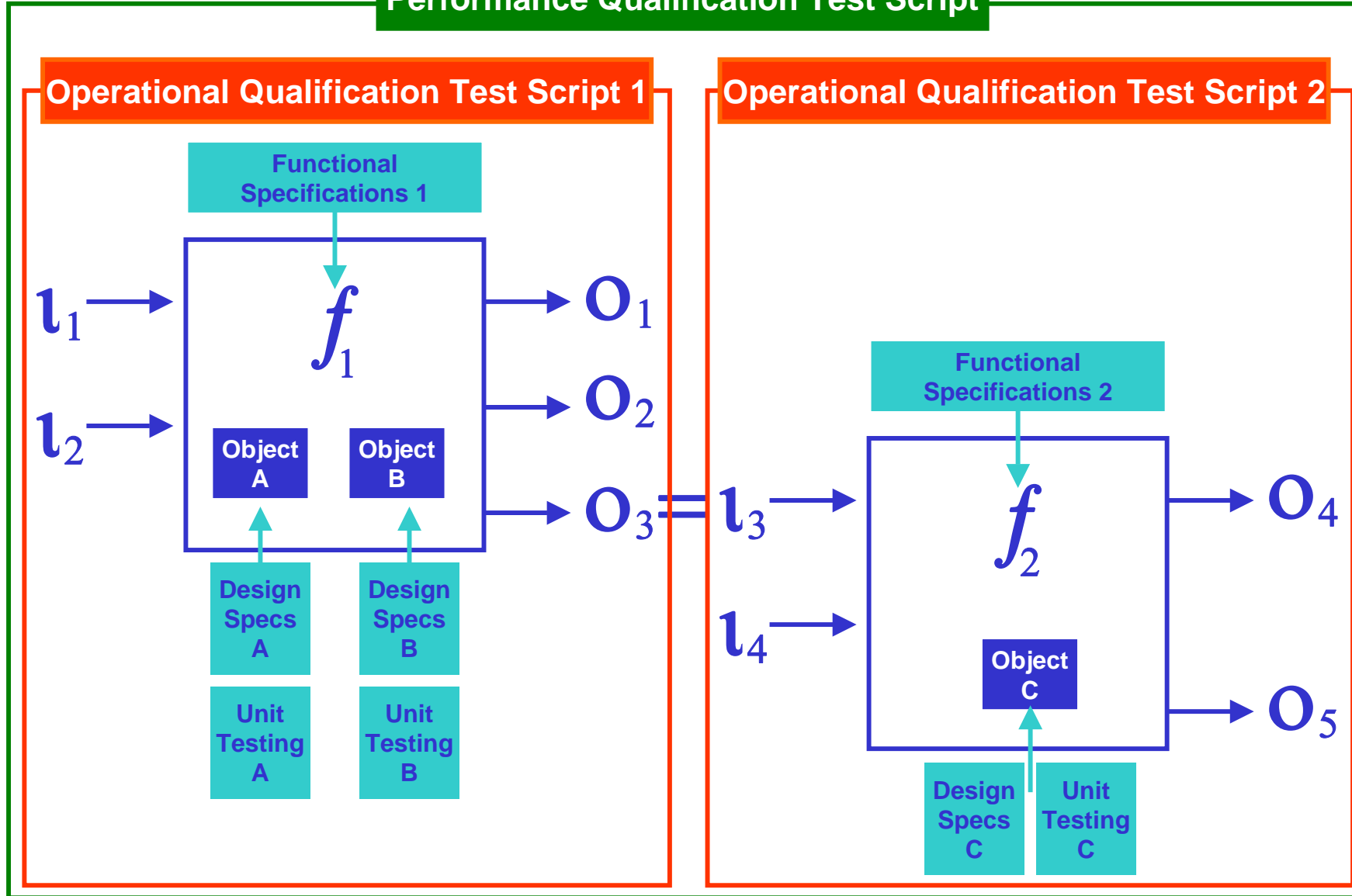
Documented verification that a system is capable of performing or controlling the activities of the processes it is required to perform or control, according to written and pre-approved specifications, while operating in its specified operating environment.

- ⇒ **Tests must be included which span the underlying business process**
- ⇒ **Tests contain most of the challenges of normal operating conditions**
- ⇒ **Each test must be traceable back to its requirement or requirements/specification**

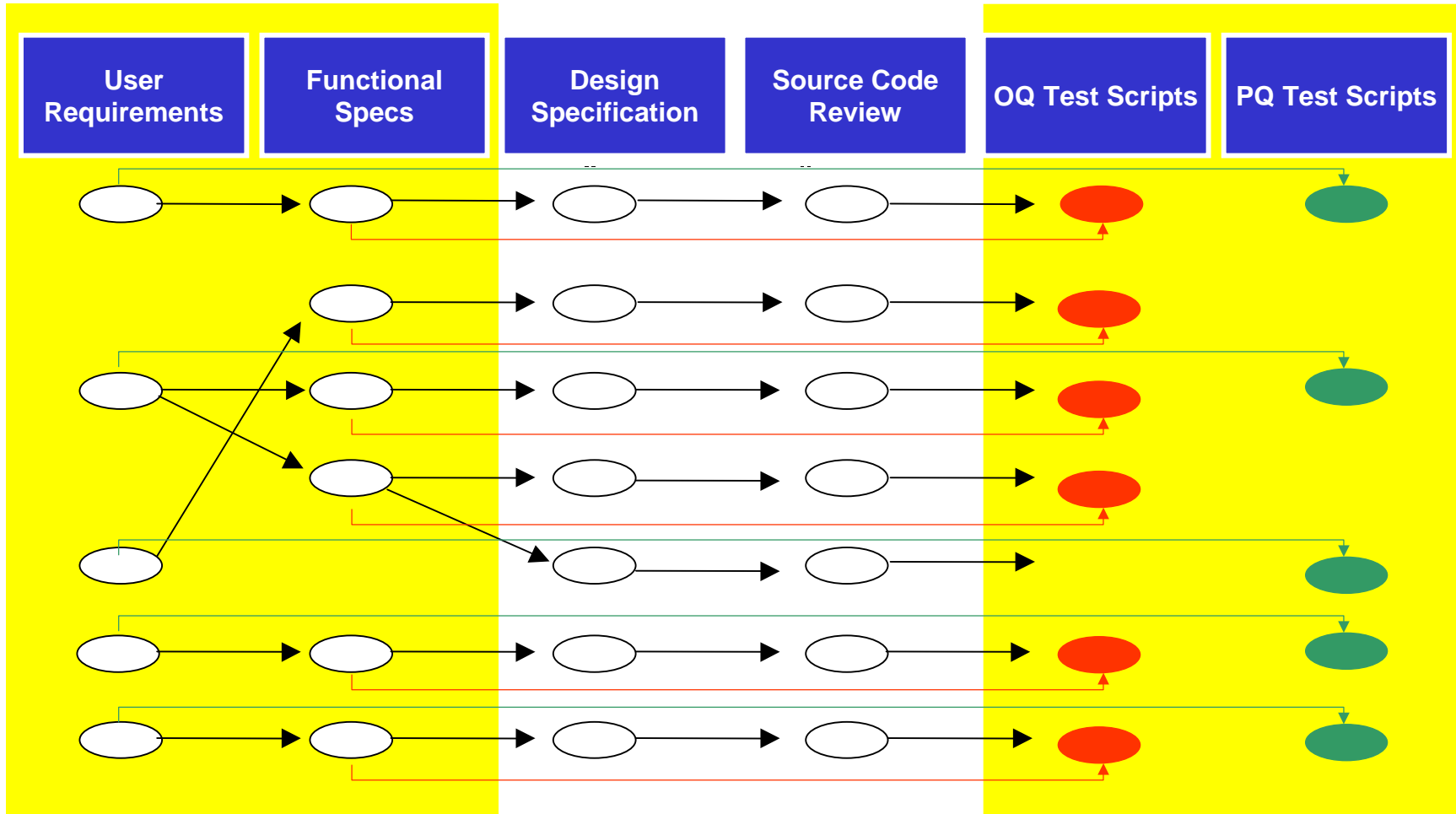


Validation Testing Scope

Performance Qualification Test Script



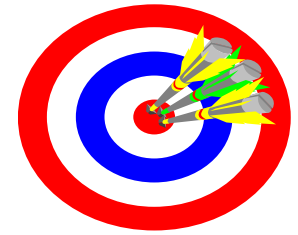
Requirements Traceability



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- ┌ Testing Documents
- **Acceptance Documents**

Validation Report



- ➔ A list of deliverables generated from the validation activities, including storage location
- ➔ Testing documentation with results
- ➔ A summary of the overall results of the validation indicating the stability of the system for use
 - ➔ For example: “This system is approved for use in production”
 - ➔ Document any limitations or restrictions on the use of the system

Documentation Archiving

Project Documentation

- User Requirements

Implementation Phase

Validation Documentation

- Validation Plan
- Validation Protocols and Records
- Validation Report

Maintenance Documentation

- Registration
- Support Agreements for HW and SW
- SOP's

Master Index

User Documentation

Maintenance Records

Change Control Documents

Periodic Review

OnGoing Phase

Training Records

Backup Log

Validation Fundamental Concepts

- ➔ **Validation is a process, not an event**
- ➔ **Planning activity should be performed as a Team**
- ➔ **Computer Validation Life Cycle provides a “road map”**
- ➔ **A solid Risk Analysis as a safe operating framework**
- ➔ **Keep the validation process under control**

Validation Keystones

To be in Compliance means:

Coordination (Policy & Standards)

Cooperation (sharing knowledge & support)

Capacity (make realistic Plans for big changes)

Competence (get trained to gain competence)

Consistency (use same measurements & tools)

