System Validation Lifecycle

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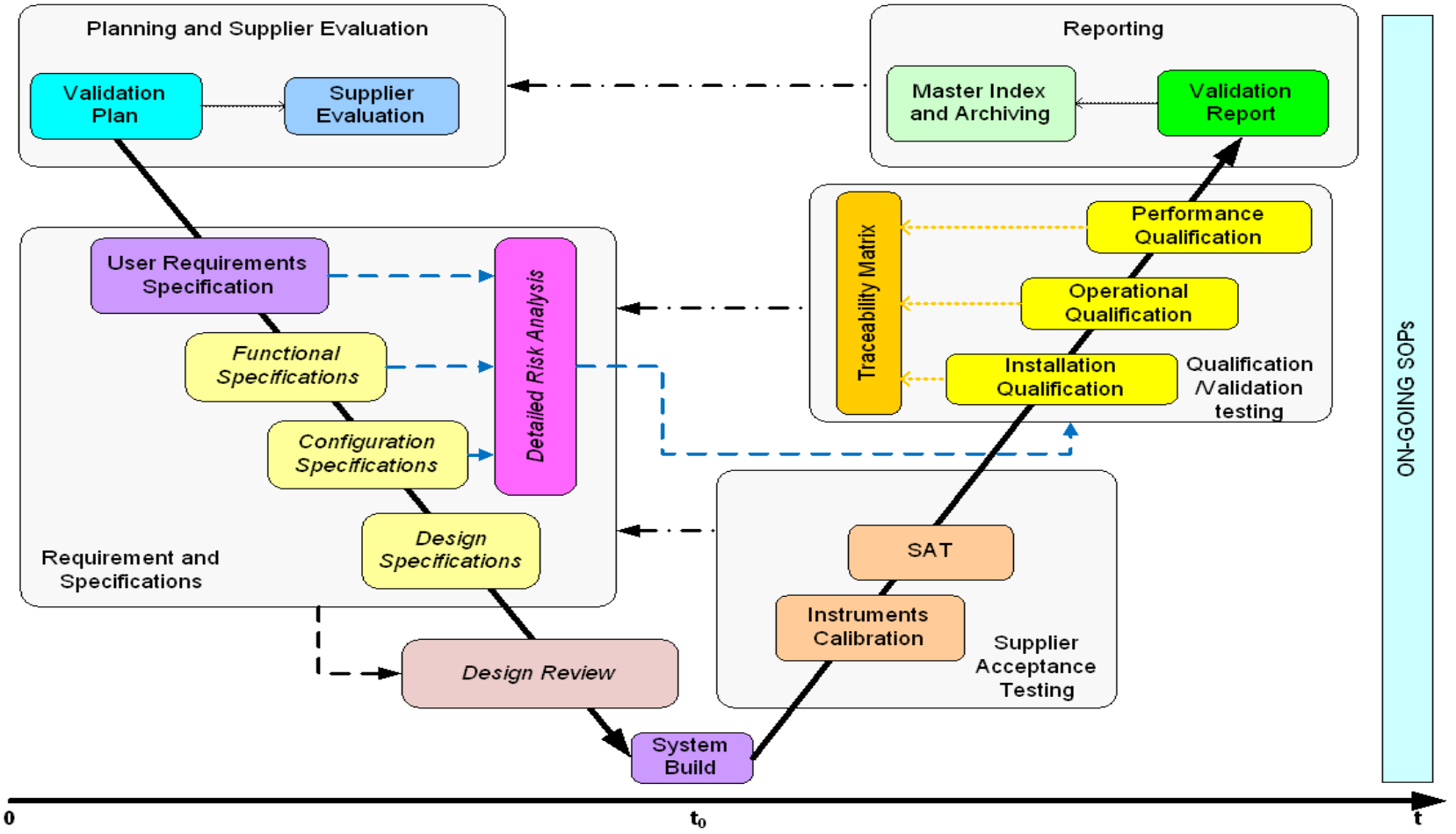
General Scheme



Validation Strategy: Validation Plan

- The Validation Plan is a strategic document defining
  - Validation strategy to be applied based on Risk Assessment and activit
  - Deliverables to be produced for each activity
  - Validation team along and related responsibility for the completion of each activity

- The Validation Plan shall identify the validation documentation to be created with the relevant responsibilities and the general acceptance criteria for the validation process

- Validation Strategy and effort depend on:
  - Complexity (Architecture and SW Category)
  - Criticality (Managed process and Record)

Basic vs. Evolved systems

Reduced Validation Life Cycle

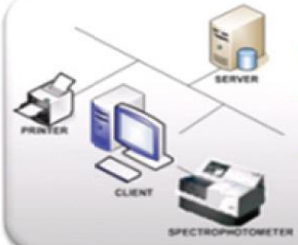
BASIC SPECTROPHOTOMETER

- This system is not interfaced to a computer and it is controlled through the embedded firmware
- Some system allows to save last instrumental run-time parameters for data acquisition
- The data are directly printed by a printer connected to the instrument.

- NO Regulated Electronic Records
- NO Configuration needs
- NO User Profiles
- NO Security Configuration
- NO Methods Management

GAMP CATEGORY 3

EVOLVED SPECTROPHOTOMETER



- Application SW installed on a Server.
- Equipment controlled by a Client to connected to the instrument
- All information among Server and Clients are transferred through the Company LAN.

- Regulated Electronic Records (Analysis parameters. Analytical Method, Results, Template Report)
- Configuration Required
- Security Configuration
- Methods Management

GAMP CATEGORY 4

Full Validation Life Cycle required

User Requirements Specifications

- The User Requirements Specification document defines the **Intended Use** of the System and what it is expected to do, written from user's point of view

- Describe compliance, business and technical requirements, as well as non-functional needs (such as performance, design constraints and availability)

- Describes in details what the computer system is expected (NOT how it will do it) in specific, measurable and testable/verifiable terms. Each requirement should be uniquely identified

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

- The user requirements should be developed independently of a specific solution prior of selection of a supplier solution. A preliminary version of the URS may be sent to suppliers as part of the vendor selection process.

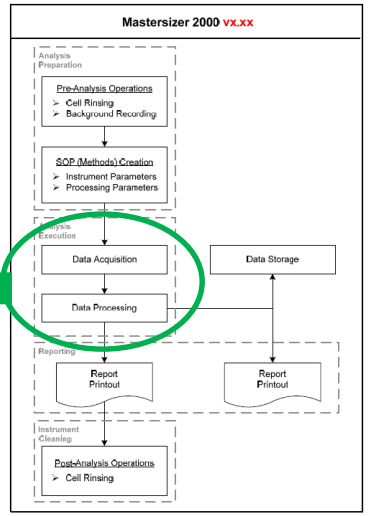
From Process Flow To Process Requirements

- Electronic Records and Signatures (if any) and applicable requirements for Data Integrity compliance should be identified
- Process Requirements shall be developed starting from the system process flow

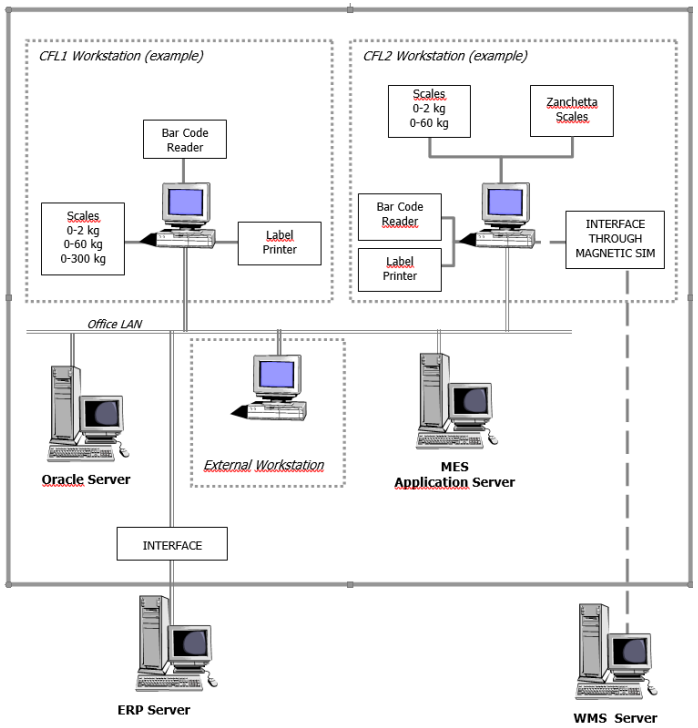
Uniquely identified
Unambiguous
Not repeated

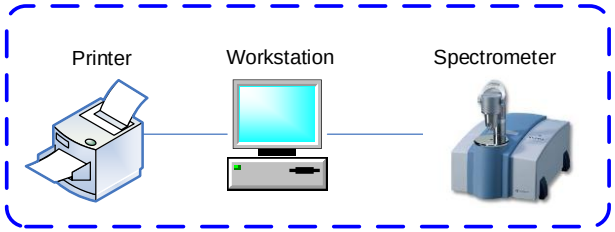
Testable

MASTER2.FPR.003	*Analysis Execution and Data Processing*	Data Acquisition	The system shall be able to acquire data according to the method configured/selected
MASTER2.FPR.004		Data Visualization	The system shall be able to display the curve on-line during the acquisition
MASTER2.FPR.005		Data Processing and Storage	The system shall be able to automatically process the acquired data during acquisition and to save them processed in the specified folder



URS for a Complex vs Simple System





Complex Configurable System (e.g MES)

- URS Package Content -> 300 pages
- Process Reqs -> 260 pages

Simple System (e.g. Stand-Alone Lab System)

- FRS Content -> ca 30 pages
- Process Reqs -> 4 pages

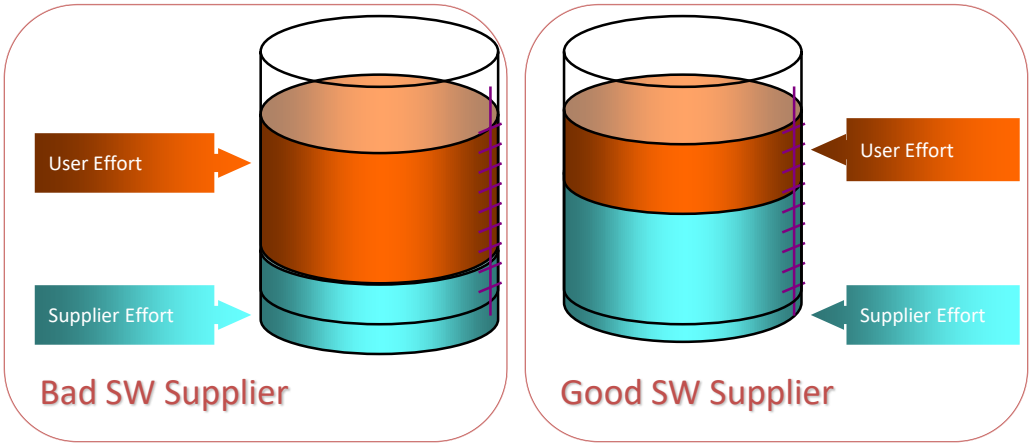
Supplier Selection Benefits

The target of the Supplier Evaluation is to determine if system providers:

- can provide a high quality product or service
- can meet regulatory requirements
- have Quality processes in place and if they are the adequate

Depending on System Risk Level, a Postal or On-Site Supplier Audit should be performed

Validation testing can be greatly decreased if the supplier provides a reliable set of verified functional testing

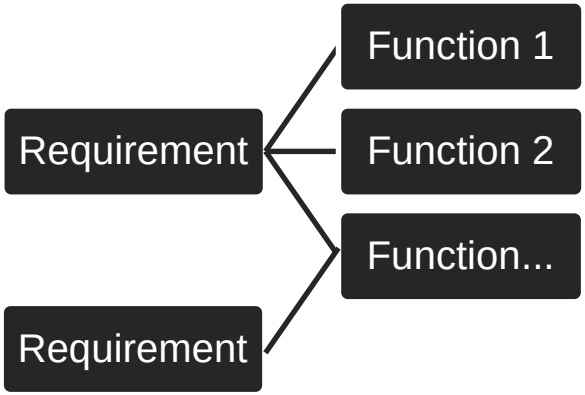


Functional specifications

- Functional Specifications describe how the selected solution will be able to meet the intended business needs identified in the User Requirements

- Provided by the System Supplier according to its Quality System. reviewed and approved by the regulated company

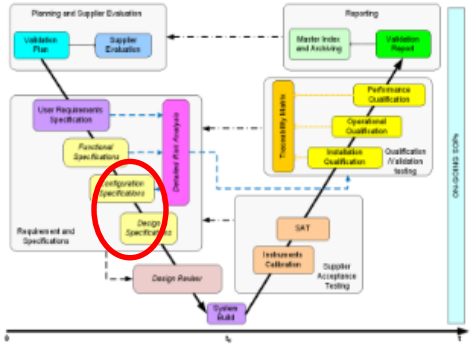
- Traceable vs User Requirements



- Standard System → User Manual
- Configurable/Custom System → Functional Specs

Configuration amd Design Specifications

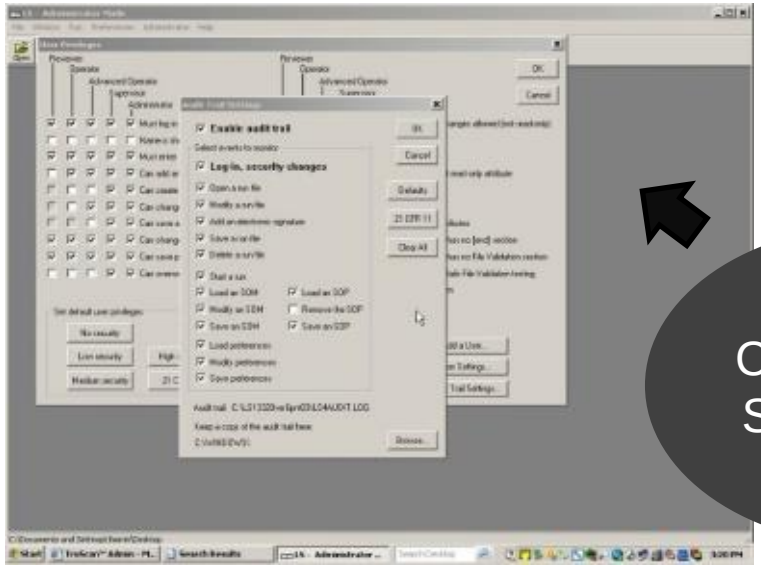
- The Configuration Specifications document describes how the system configuration parameters have been set to meet the user requirements
- CS address:
  - the list of HW/SW components included in the Computerized System
  - Security settings
  - Process related parameters which may impact one or more GMP functionality



- The SW Design Specifications are required for the customized components in order to provide a detailed, technical explanation of how the custom functionality has been developed and works
- It can be written in pseudo-code language
- Intended recipient of DS include IT personnel (SW analysts and developers)

Configuration Specifications - Regulatory impact

Security Settings

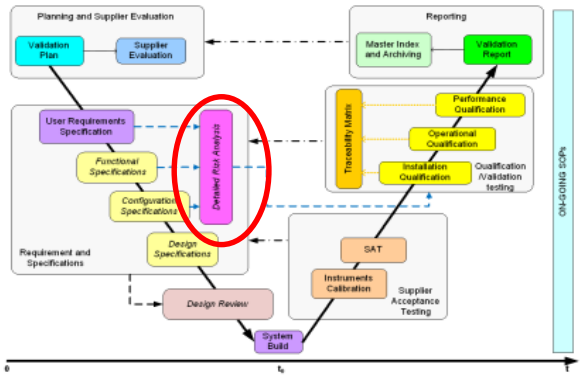


Configuration Specification

OPTIONAL SETTINGS			
Table/position	**Allowed Values**	**Ascoli Value**	**Description of Optional Setting**
ET 101, 'Allow prorating soft BOM for SFG' field	Blank		Does not allow prorating of U-factors in the Soft BOM of Semi finished goods belonging to the specified plant
	1	✓	Allow prorating of U-factors in Soft BOM of Semi finished goods belonging to the specified plant. Only the U-factor for components defined as variable are recalculated. This function is only available in the soft BOM for version controlled items.
ET 301, Position 66	Blank	✓	Invoice three-way matching for units will not be performed
	1		Invoice three-way matching for units will be done by the system
ET 301, Position 71	Blank		The system will not automatically set the receipt complete even if the receipt quantity falls within the receipt tolerance percent
	1	✓	The system will automatically set the receipt complete flag when the actual receipt quantity is within the receipt tolerance range for the item
ET 301, Position 40	Blank	✓	A warning message is displayed during receipts if the quantity received is greater than the quantity ordered
	1		A hard error is displayed if the quantity received is greater than the quantity ordered
T 301, Position 55	Blank	✓	Requisition functionality is enabled – Standard MAPS
	1		Requisitions cannot be accessed or approved through Requisition Maintenance or approval. MRP details from planning are automatically updated in the work area. Purchase orders can be created from this point.
ET 301, Position 60	Blank	✓	Actual Hours will not be created
	1		Automatically create actual hours for non-manufacturing routings. The Flag is system wide and applies to all materials/products. The non-manufacturing routing used will be from the 'current' costing time frame.
ET 301, Position 70	Blank	✓	Use purchase order vendor code
	1		Use Global vendor code associated to purchase order vendor
ET 301, Position 76	Blank	✓	ASL's will be checked during excess quantity approval.
	1		ASL's will not be checked during excess quantity approval.
ET 304, Code 02, 'Inter-Company tolling flag' field	Blank	✓	Normal Order Type
	1		Inter-Company tolling Type
ET 301, Key VMI, Position 26	Blank	✓	Multiple line Purchase Orders are created
	1		Only single line VMI orders will be created
ET 401, Position 36	Blank	✓	Pharmasyst Not Active

Process Related Settings

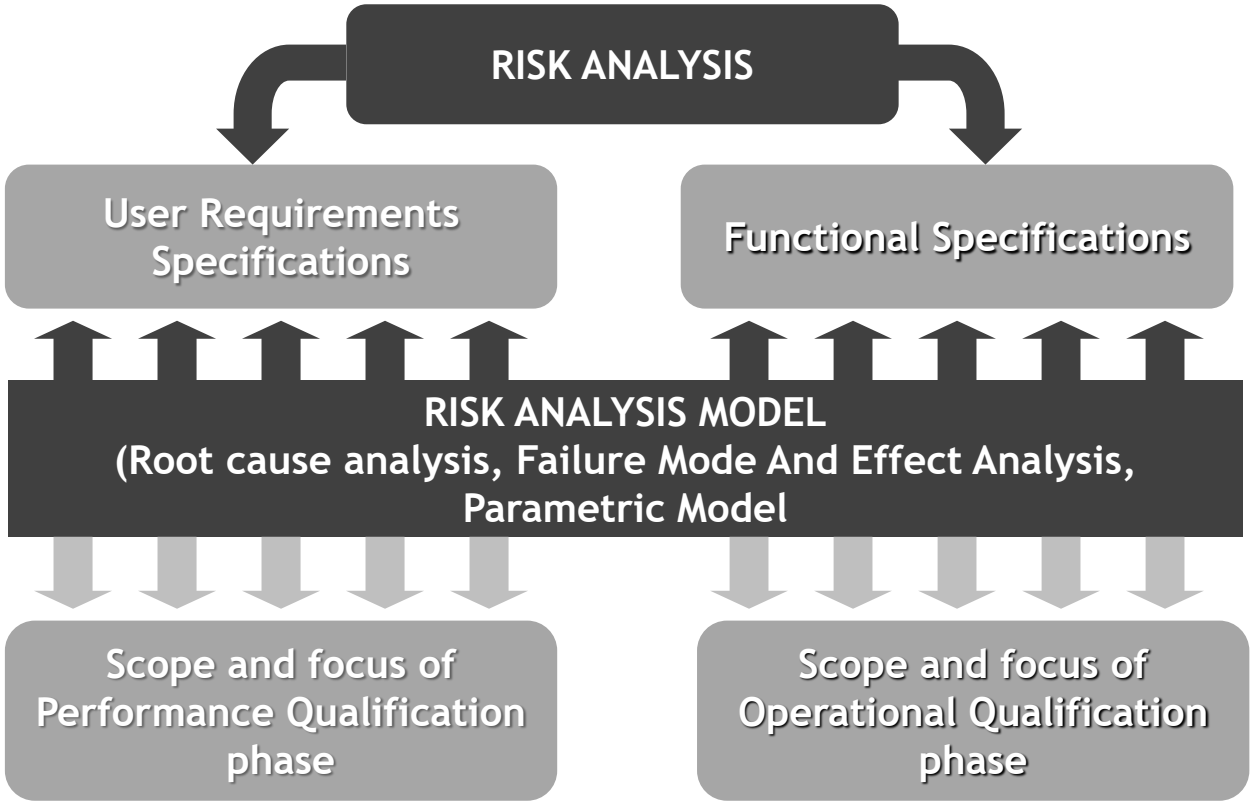
Risk Analysis



- Quality Risk Management is a systematic process for the assessment, control communication and review of risks
- The evaluation of the risk to quality should be based on scientific knowledge and ultimately linked to the protection of the patient

- The level of effort, formality, and documentation of the quality risk management process should be commensurate with the general System Risk level

Risk analysis approach



Risk analysis focused on processes

To outline possible **Risks** associated with the implementation of business **Processes** and **Functions**

PROCESS RISK ANALYSIS (FMEA)

Risk Scenario Description	Consequence	Risk Root Cause	1 (I) Risk Impact (Severity)	2 (L) Risk Likelihood (Customize)	4 (D) Detectability (H, M, L)	5 Risk Priority	Comments (C)/ Mitigation (M)
The system allows the access to unauthorized user	Unauthorized use of the system and application software	Wrong Configuration	L	M	L	M	- Configure and document individual User Accounts for application SW (if managed) or - Implement a paper based user management process based on dedicated security and utilization SOPs
	Unauthorized use of data acquired	Wrong Configuration	M	M	L	H	- Configure and document individual User Accounts for application SW (if managed) or - Implement a paper based user management process based on dedicated security and utilization SOPs
Wrong user profiles / privileges assignment	Wrong system use and application software	Wrong Configuration	L	M	L	M	- Configure and document individual User Access level for SW application (if managed) or - Implement a paper based user management process based on dedicated security and utilization SOPs
Wrong username / password assignment	Incorrect workflow traceability	Wrong Configuration	L	L	M	L	- Configure and document individual User Access level for SW application (if managed) or - Implement a paper based user management process based on dedicated security and utilization SOPs

Mitigation Actions identification (i.e. configuration, SOPs update, double check)

Risk analysis focused on functions
Functional risk assessment

To outline possible **Risks** associated with the selected solution

FUNCTIONAL RISK ANALYSIS (PARMOD)

		SEVERITY Key decision							OCCURRENCE Key decision								DETECTABILITY Key decision					
Function code	Function description	Does the function create or maintain Regulated Electronic Records such as analytical methods, raw data and results?	Does the function generate report or data to be included in the Batch Record?	Is the function utilized to drive an analytical equipment?	Can the improper use of the function generate failures in the analysis execution?	Can a failure to the function be detected by operational checks or downstream controls?	Does the function manage system security and access?	Criticality (H, M, L)	Does the function include customized software?	Can the function be configured to meet the user requirements?	Does the function manage interfaces with external critical Systems?	Does the function execute complex algorithms which updates data?	Does the function execute an operational check of the outputs of another function?	Does the function execute data input validation (Invalid Record)?	Complexity (H, M, L)	Risk Level	Manual controls, Alternative systems or Paper equivalent processes are available for the function	The data managed by the function are under Audit Trail	Detectability (H, M, L)	Risk Priority	Testing Effort
GCS.FS.001	Analytical raw data can be stored in multiple locations determined by users with the appropriate privilege.	Yes	Yes	Yes	No	Yes	Yes	H	No	Yes	No	No	No	No	L	M	Y	Y	H	L	_User Training _Security SOP
GCS.FS.002	One or more results may be backed up at once time. Results backup will take all analytical information and place them in a specific location.	Yes	No	No	Yes	Yes	No	M	No	No	Yes	Yes	No	Yes	M	M	Y	N	M	M	_User Training _Security SOP _Testing activities in normal conditions (OQ)
GCS.FS.003	One or more results may be restored at one time. Results restore will take all information from a backup set and restore the results to the state at which it was at the time of backup.	Yes	No	No	Yes	Yes	No	M	No	No	Yes	Yes	No	Yes	M	M	Y	N	M	M	_User Training _Security SOP _Testing activities in normal conditions (OQ)
GCS.FS.004	Use a method template to copy the specified information in one zone. It is possible to select single method and create multiple copies.	Yes	Yes	Yes	Yes	No	No	M	No	No	Yes	Yes	No	No	L	L	Y	Y	H	L	_User Training _Security SOP

Testing Effort determination

Testing & Acceptance

The system testing is performed to ensure that computerized systems meet their predefined requirements, prior to system release.

The testing includes:

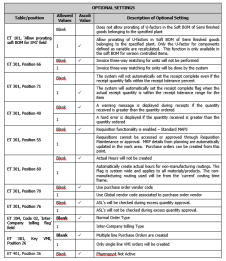
- Vendor Testing (e.g. Commissioning Testing, Unit and Integration testing, FAT/SAT), executed by the SW Supplier according to its Quality System or to a predefined Quality & Project Plan

- Validation Testing, executed in the qualification and/or production environment according to pre-defined protocols for the following Validation Testing phases:
  - Installation Qualification (Configuration Verification)
  - Operational Qualification (Functional Verification)
  - Performance Qualification (Requirements Verification)

- Tests shall be performed in an appropriately qualified environment according to a predetermined Test Plan and Test Specifications including predefined expected results.

Installation Qualification (Configuration Verification)

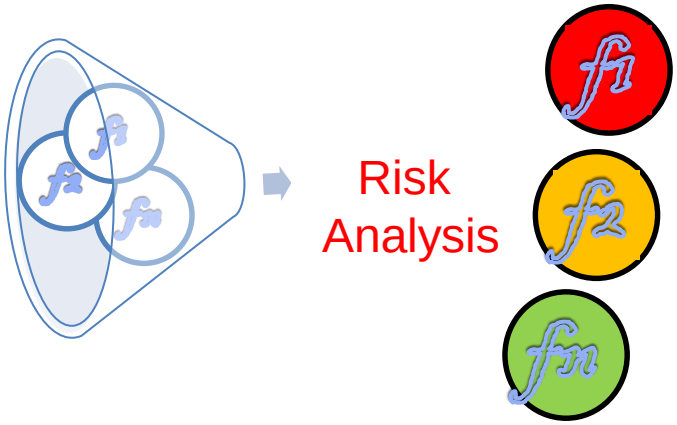
- Installation Qualification is performed to assure that the Configuration and Design have been installed as specified and documented evidence exists to demonstrate this



MASTER2.IQT.006					
No	Test Action	Expected Result	Actual Result		Remarks / Attachment ID
			PASS	FAIL	
1.	Verify that the application SW assigns for each user a unique set of: • User ID • Password	The configuration is compliant with CDS document			
2.	Verify that Password policy settings are configured according to Best Practices and relevant CLN Security of Computerized Systems SOP [Code] as defined in the CDS document	The Password policy settings configuration is compliant with the CDS document			

Operational Qualification (Functional Testing)

- Assuring that the installed system works as specified in the **Functional Specification** throughout the **intended (regular and exceptional) 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

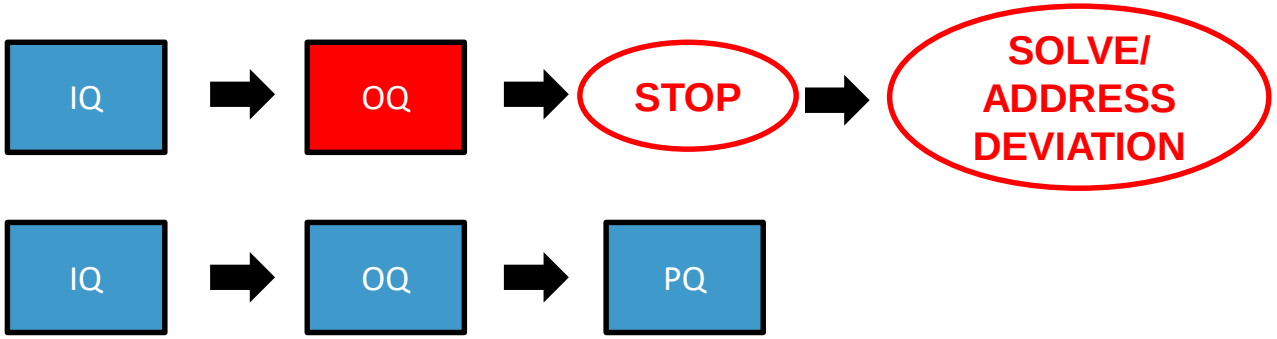


Testing effort

- Normal case (positive) testing
- Invalid case (negative) testing
- Special case (stress at the limit of permitted domain)
- Output testing
- Input combination testing

Performance Qualification (PQ)

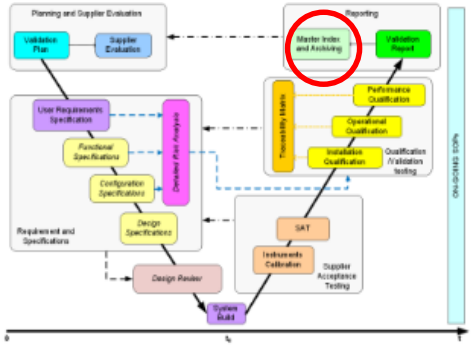
- As part of the PQ it is necessary to prove that the system **works correctly** and **consistently** in the intended operational environment at the Client as part of the process for which it has been designed, using real procedures, equipment, utilities and people
- The equipment IQ & OQ and the Automation 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 CDS will work accordingly to the Requirements.



Traceability Matrix

The Traceability Matrix:

- References the relationships between Systems User Requirements Specification versus testing (IQ/OQ/PQ)
- has to be also used during Change Control evaluation to identify the impact of changes to the system and the validation documents.



[Client Logo]

[System Name] (Id [System Code])
Traceability Matrix
Doc.ID: [SYS].VR.001_TRM
Version: 1.0

Requirements		Risk Scenario/ Potential Failure	Testing			Comments
Specification ID#	Description of requirement	ID#	Configuration Testing (IQ) ID#	Functional Testing (OQ) ID#	Requirements Testing (PQ) ID#	(Optional)
GENERAL REQUIREMENTS						
[SYS].UGR.001	Language	NA	[SYS].IQT.001	NA	[SYS].PQT.001	
[SYS].UGR.002	Instrument Control	RAS.007	[SYS].IQT.004	NA	[SYS].PQT.005	
[SYS].UGR.003	Instrument Qualification	RAS.029	[SYS].IQT.001	NA	NA	
[SYS].UGR.004	User Manuals	NA	[SYS].IQT.001	NA	NA	
[SYS].UGR.005	SOPs	NA	NA	NA	[SYS].PQT.001	
REGULATORY REQUIREMENTS						
[SYS].URR.001	Documents Change Control	NA	NA	NA	[STS].PQT.001	
[SYS].URR.002	Document Control	NA	NA	NA	[STS].PQT.001	Refer to Validation Plan, [SYS].VP.001
[SYS].URR.003	Personnel Training	NA	NA	NA	[STS].PQT.001	
[SYS].URR.004	Risk Management	NA	NA	NA	NA	Refer to Risk Analysis, [SYS].RA.001
[SYS].URR.005	Validation Standards	NA	NA	NA	NA	Refer to Validation Plan, [SYS].VP.001

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