運銷系統之軟體確效準備

ZUELLIG PHARMA

making healthcare more accessible

Objectives

At the end of the session, the participants will:

- Know what is Computerized System Validation (CSV, 電腦化系統確效)
- Understand why do you need CSV
- Recognize when CSV is required
- Understand the requirements of CSV
- Determine the validation requirement based on the level of risk of a system

What is Computerized System Validation (CSV, 電腦化系統確效)

Q1: 什麼是電腦化系統 (Computerized System)?

電腦化系統是指電腦系統及其相關之受控功能，包括硬體、軟體、週邊設備、控制對象、操作人員、文件 (手冊和SOP)，均為電腦化系統確效的範圍

Q2: 什麼是確效 (Validation)?

係指有文件證明的行動，能證實程序、製程、機械設備、原材料或系統確實能持續穩定的導致預期之效果

Q3: 什麼是驗證 (Qualification)?

對於設施及設備本身之性能確認有關事宜

Q4: CSV 主要交付文件有哪些?

- 確效計畫 (Validation Plan)
- 風險評估 (Risk Assessment)
- 使用者需求規格 (User Requirement Specification)
- 功能需求規格 (Functional Requirement Specification)
- 安裝驗證 (Installation Qualification)
- 操作驗證 (Operational Qualification)
- 性能驗證 (Performance Qualification)
- 需求追溯矩陣 (Requirements Traceability Matrix)
- 確效總結報告 (Validation Summary Report)

What is Computerized System Validation (CSV, 電腦化系統確效)

Q5: 哪些監管法規重點要求了 CSV?

- FDA 21 CFR Part 11 Electronic Records; Electronic Signatures
- EU GMP Annex 11
- 西藥藥品優良製造規範
- 電腦化系統確效作業指導手冊
- 藥品優良製造確效作業基準
- 醫療器材軟體確效指引

Q6: CSV 相關國際標準有哪些?

- ISPE GAMP 5 Guide: Compliant GxP Computerized Systems
- PIC/S GMP Annex 11
- PIC/S Good Practices for Computerized Systems in Regulated "GXP" Environments
- ISO 13485 Medical devices – Quality management systems (醫療器材品質管理系統標準)
- IEC 62304 Medical device software – Software life cycle processes (醫療器材軟體生命週期)

電腦化系統確效的時機為何?

(1) When introducing a NEW computer system that will support GxP operation, processes or functions

(2) When a major change is being applied on an existing GxP regulated computer system

1. Records of computerized system validation (CSV)

- Documented and signed validation activities

2. ER ES Compliant (if applicable)

- Controls to maintain data accuracy, data integrity, confidentiality and availability
- Authorized access to system and data
- Secured, computer generated time-stamped audit trail
- User training
- Signed electronic records
- Electronic signature controls
- Uniqueness of combined id and password, ageing password

3. SOPs to support and maintain the system

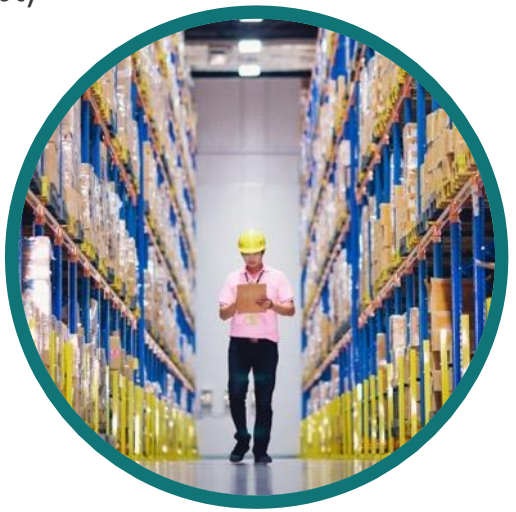
- Change Management
- Incident Management
- Configuration Management
- Backup and Restore
- Disaster Recovery
- Data Retention
- Archiving

4. Reviews

- Audit Trail Review
- System Periodic Review

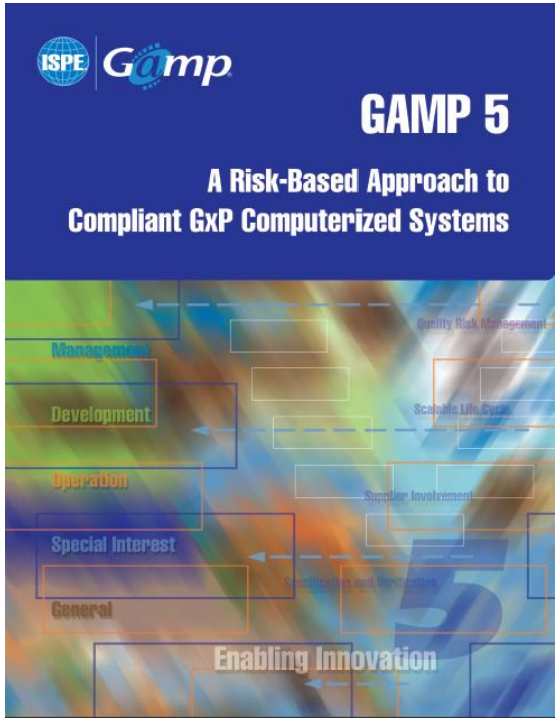
醫藥運銷之主要流程

1. **Incoming Goods Receipt (進貨管理)**
   - Identity (product name, dosage form, strength, lot number, batch number, expiry)
   - Traceability (storage location, manufacturer lot number, date receipt)
2. **Material Status Management (物料管理)**
   - Quality inspection, release or disposition
   - Product return management and disposition
3. **Storage of Product (倉儲管理)**
   - Storage conditions
   - Storage location assignment vs label storage requirements
   - Traceability within the warehouse (stock movement)
4. **Stock Control (庫存管理)**
   - Inventory Management (actual vs system)
5. **Shipping (運輸管理)**
   - Transport condition
   - Traceability (customer name, address, date of dispatch, etc.)
6. **Records and Reports (文件與記錄管理)**
   - Production, control and distribution records – original and true copies
   - Review of production records, inspections, complaints
   - Records retention period



GAMP 5

A Risk-Based Approach to Compliant GxP Computerized Systems



- GAMP stands for “Good Automated Manufacturing Practice”
- GAMP 5 is a guideline for developing, qualifying, validating and maintaining computer systems in a Pharmaceutical/ healthcare environment
- Published by the ISPE (International Society of Pharmaceutical Engineering)

GAMP 5 軟體分級 (Software Categories)

Category	Description	Typical Examples
1 – Infrastructure Software	• Layered software (upon which applications are built) • Used to manage the operating environment	• Operating Systems • Anti-virus Software • Database Software (SQL / Oracle) • Server and Network Hardware • Firewalls, including configuration • Backup Systems
3 – Non-Configured	• Run-time parameters may be entered and kept but the software cannot be configured to suit business process	• COTS (Commercial-Off-The-Shelf) • Instrument-based application
4 – Configured	• Software, often very complex, that can be configured by the user to meet the specific needs of the user's business process. Software code is not altered	• LIMS • SCADA • ERP • DCS • Building Management Systems • CRM
5 – Custom	• Software custom designed and coded to suit the business process	Varies, but includes: • Internally and externally developed IT applications • Internally and externally developed process control applications

GAMP 5 風險評估 (Risk Assessment)

GxP Impact/Implication

No GxP implication	None of the functional areas identified is regulated <e.g. printing of sales invoice>
GxP with direct impact	If there's at least one functional area that has direct impact to patient safety, product qualityor GxP data integrity (e.g. medical kitting, temperature control management)
GxP with indirect impact	If no functional area has direct impact to patient safety, product quality or GxP data integrity and has at least one functional with indirect impact (e.g. Delivery/Transport)
GxP with no direct/indirect impact	Normally is on quality sytem supporting a GxP system and has no direct nor indirect impact to patient safety, product quality or GxP data integrity

RISK & COMPLEXITY HEAT MAP			
Impact	GAMP		
	Out of the Box (3)	Configured (4)	Custom (5)
GxP-Direct	2	3	3
GxP-Indirect	2	2	2
GxP-None	1	1	2
Non-GxP System	1	1	1

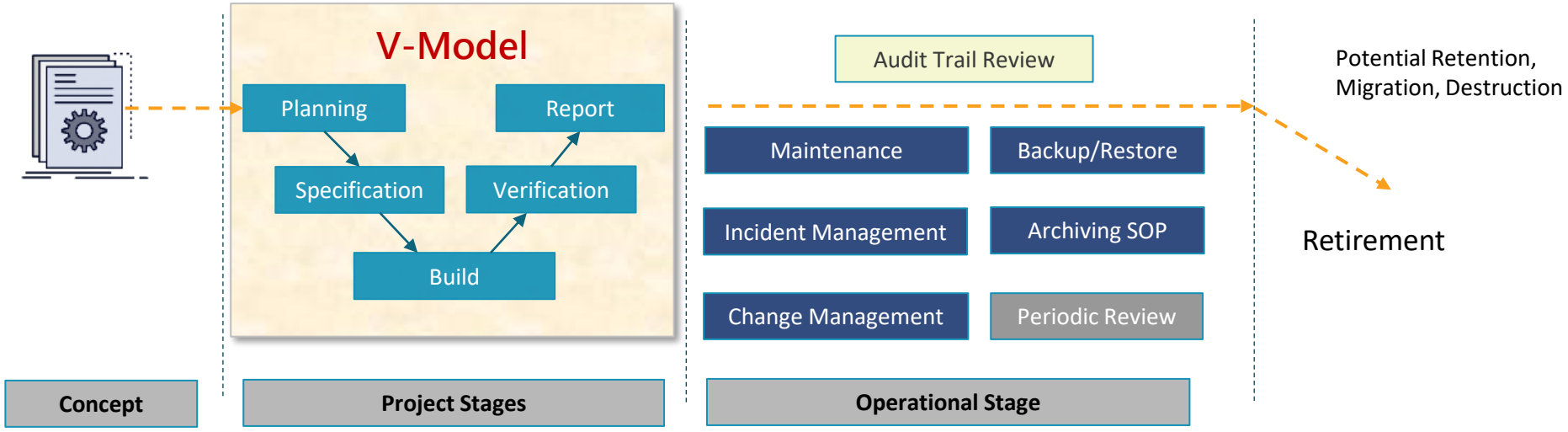
Legend:

1 Low

2 Medium

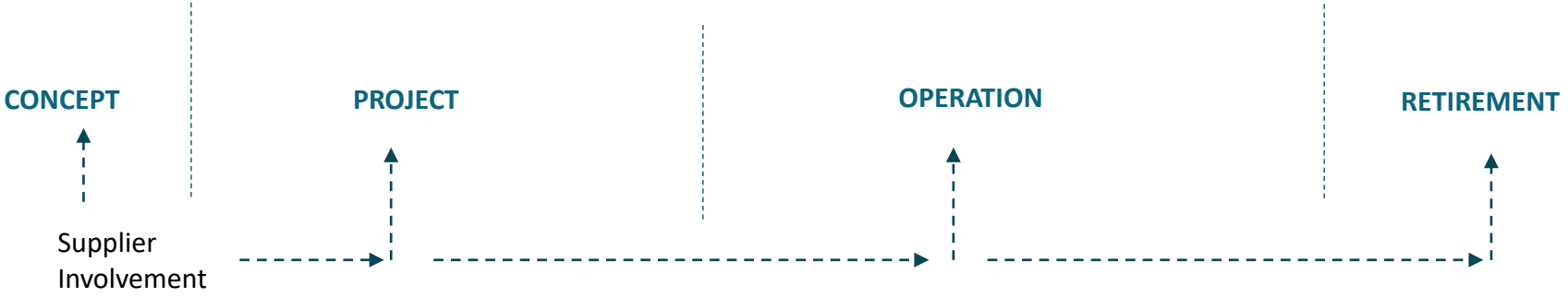
3 High

Project Stages and Supporting Processes within the Computerized System Life Cycle

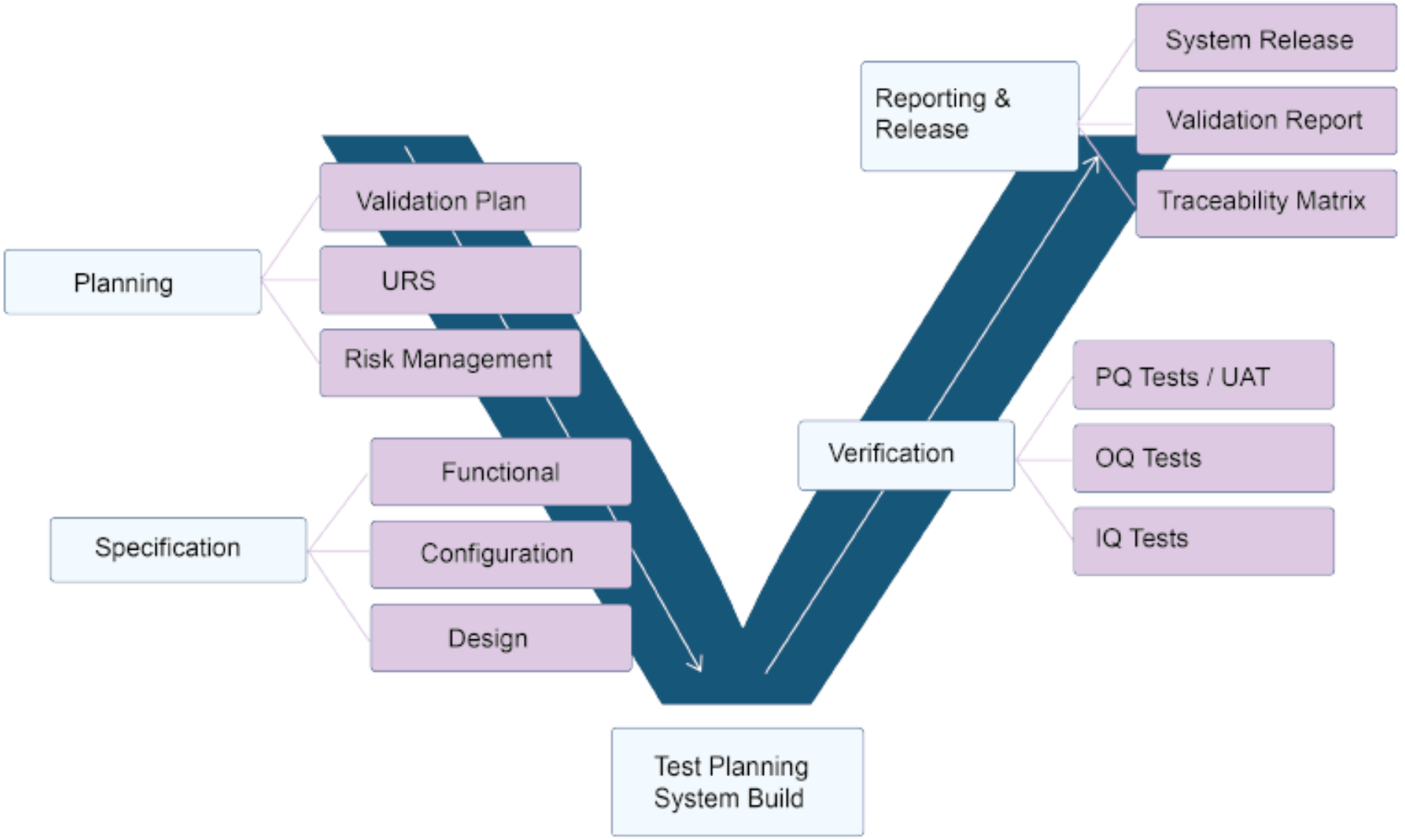


Risk Management, Design Review, Change and Configuration Management, Document Management; Traceability, Revalidation

Supporting Processes



CSV according to the V-Model



軟體開發專案各階段 CSV 交付文件

CONCEPT
- HL User Requirements Specification
- Initial GxP Risk Assessment
- ER ES Assessment
- Supplier Assessment, if applicable

PLANNING
- Validation Plan
- Supplier Documentation, if applicable
- Data Migration, if applicable

SPECIFICATION
- System/Network Architectural Design (On premise only)
- Functional Specification
- Functional Risk Assessment
- Configuration Specification
- Technical Specification

BUILD
- Configuration/Code Review
- Unit Testing Documentation

QUALIFICATION
- Installation Qualification
- Operational Qualification
- Performance Qualification

REPORTS
- Validation Summary Report
- Annex 11 Compliance Report
- Data Migration Report
- System Release Notice

Supporting Processes
- Computerized Systems Inventory
- Traceability Matrix
- User Training Record

SOPs
- Change Management SOP
- Configuration Management SOP
- Incident Management SOP
- Backup & Restore SOP
- Disaster Recovery Plan
- Data Retention Period
- Archiving

Risk-Based CSV Deliverables Matrix

Example

Phase	Stage	1.1 Document	Category 1	Category 3			Category 4			Category 5		
				Low	Med	High	Low	Med	High	Low	Med	High
Concept		CSV-003 User Requirements Specification			✓	✓		✓	✓		✓	✓
		CSV-003_01 User Requirements/Functional Specification		✓			✓			✓		
		CSV-001_01 Initial Risk Assessment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
		CSV-001_02 ERES Assessment		✓	✓	✓	✓	✓	✓	✓	✓	✓
		CSV-004 Supplier Assessment		✓	✓	✓	✓	✓	✓	✓	✓	✓
		ZPAP-QA-CKL-005 Supplier Quality Checklist				✓			✓			✓
Project	Planning	CSV-002 Validation Plan			✓	✓		✓	✓		✓	✓
		CSV-002_01 Validation Plan and Report (Retrospective Validat	✓		✓	✓		✓	✓		✓	✓
		CSV-004 Supplier Documentation		✓	✓	✓	✓	✓	✓	✓	✓	✓
		CSV-004_02 Supplier Quality Agreement										
		CSV-004_03 Purchase Orders and/or Contracts of Supply										
		CSV-005 Data Migration Plan & Report		✓	✓	✓	✓	✓	✓	✓	✓	✓
	Specification	CSV-006 System/Network Architectural Design (On premise only)		✓	✓	✓	✓	✓	✓	✓	✓	✓
		CSV-007 Functional Specification			✓	✓		✓	✓		✓	✓
		CSV-001_03 Functional Risk Assessment		✓	✓	✓	✓	✓	✓	✓	✓	✓
		CSV-008 Configuration Specifications					✓	✓	✓	✓	✓	✓
		CSV-009 Technical Specification								✓	✓	✓
	Build	CSV-010 Code Review									✓	✓
		CSV-011 Unit Testing documentation						✓	✓		✓	✓
	Qualification	CSV-012 Installation Qualification							✓			✓
		Operational Qualification (OQ)							✓			✓
		▪ CSV-013-01 OQ Test Protocol				✓	✓	✓	✓	✓	✓	✓
		▪ CSV-013-02 OQ Test Data				✓	✓	✓	✓	✓	✓	✓
		▪ CSV-013-03 OQ Test Report				✓	✓	✓	✓	✓	✓	✓
		Performance Qualification (PQ)	✓			✓	✓	✓	✓	✓	✓	✓
		▪ CSV-014-01 PQTest Protocol				✓	✓	✓	✓	✓	✓	✓
		▪ CSV-014-02 PQ Test Data				✓	✓	✓	✓	✓	✓	✓
		▪ CSV-014-03 PQ Test Report				✓	✓	✓	✓	✓	✓	✓
		▪ CSV-014-04 Performance Monitoring Report during Hypercare				✓	✓	✓	✓	✓	✓	✓
	Report	CSV-016 Validation Summary Report			✓	✓		✓	✓		✓	✓
		CSV-017 Annex 11 compliance report (only if applicable)		✓	✓	✓	✓	✓	✓	✓	✓	✓

Q & A

Verification Protocols: IQ / OQ / PQ

- **Installation Qualification (IQ, 安裝驗證)**

為一種確認作業，旨在確認設施或設備於既訂條件下安裝，並能於限制條件與耐受範圍內呈現恆定性能之措施

- **Operational Qualification (OQ, 操作驗證)**

為一種確認作業，旨在確驗設施或設備於其操作極限範圍與正常範圍內能適當運轉

- **Performance Qualification (PQ, 性能驗證)**

為一種確認作業，旨在確認設備或設施能持續穩定的表現其應有之性能

Who are the players during CSV?

BUSINESS PROCESS OWNER

- Ensures that the computerized system and its operation comply with the CSV Policy, Guidelines, Procedures
- Facilitates the validation planning
- Reviews and confirms the user requirements

SYSTEM OWNER

- Is responsible for the availability, support and maintenance of the system and the security of the data residing in the system
- Ensures that the computerized system is supported and maintained is accordance to CSV policies and applicable SOPs

IT OPERATIONS

- Provides the infrastructure, hardware and software required to operate the system
- Protects the system against risks of failure and improper use of the infrastructure
- Responsible for the Installation Qualification of the system
- Ensures backup are regularly performed and restoration of backup is regularly tested

QUALITY ASSURANCE

- Set policies and standards related to CSV
- Determines if system requires CSV
- Clarifies the regulatory requirements that must be met by the system
- Performs audit for compliance
- Review effectiveness of Quality Systems and processes

DEVELOPMENT TEAMS

- Design the solution with consideration on the requirements of the regulation
- Perform and document validation activities required from the team (Specifications, Coding/Configuration, Unit Testing and Code/Configuration review

PROJECT MANAGER

- Schedules and manages planned validation activities and deliverable
- Manage the expectation of stakeholders