Data integrity – Case study:

Data vulnerability assessment and KNEAT (Paperless validation software) implementation

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PDA Parenteral Drug Association

PDA Aseptic Processing of Biopharmaceuticals Conference 2024

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Data Vulnerability Assessment

Hannah Lee (Sr. Quality System Specialist)

Objectives

Lessons learned from a year-long data vulnerability assessment at a manufacturing site with hybrid data flows involving multiple human interfaces and stand-alone equipment

Background

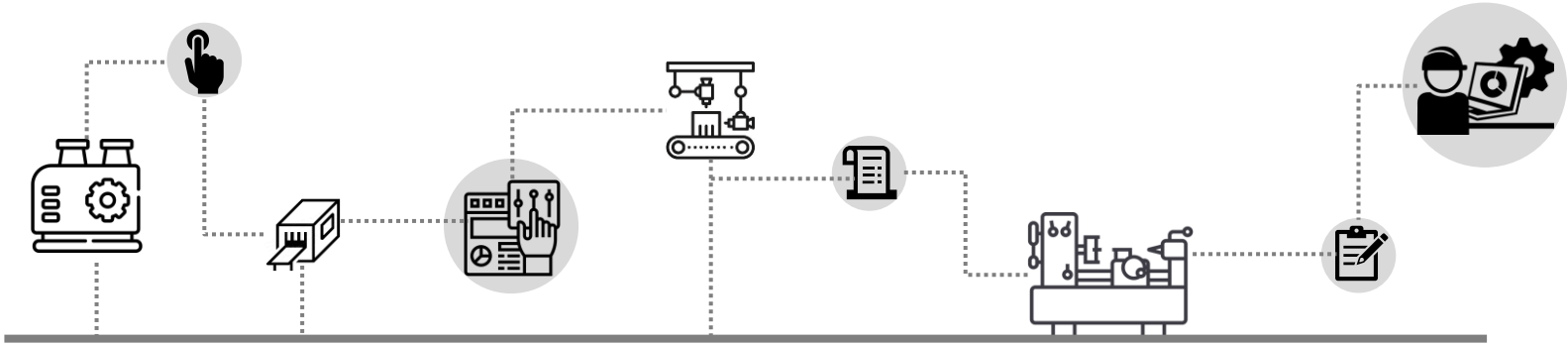
Data Integrity harmonization program

Assessment and remediation of all our electronic systems in Lab and Manufacturing to compliance.

shift

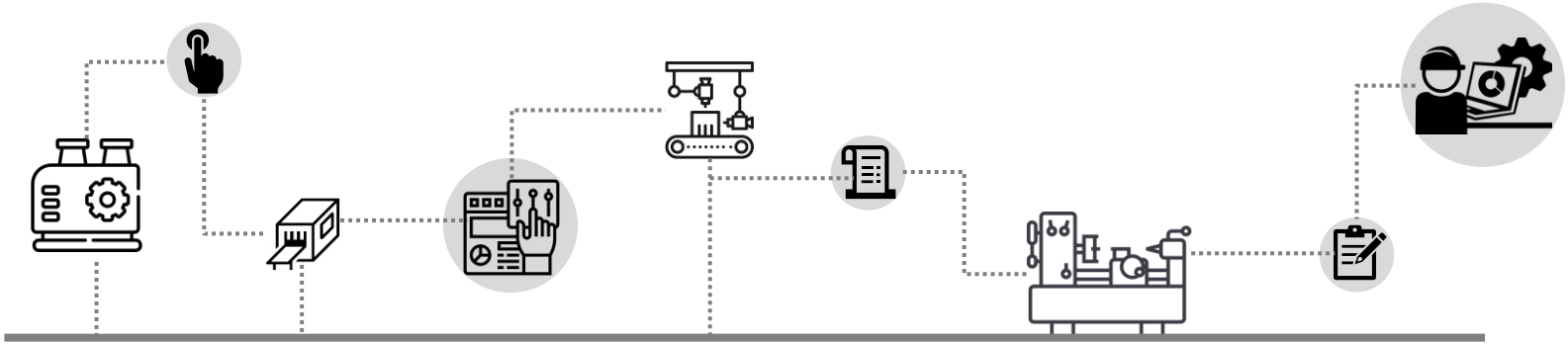
How we define ‘data vulnerability’

Data Criticality	**High**	H/L (Green)	H/M (Orange)	H/H (Red)
	Medium	M/L (Green)	M/M (Green)	M/H (Orange)
	Low	L/L (Green)	L/M (Green)	L/H (Green)
		Low	**Medium**	**High**
	Data Control Risk			



Assessment tool

Process Area								
Sub-process	Step	Data Name	Data format	Data criticality	Hazardous situation	Current technical & procedural controls to minimize the hazard	Data control risk	Vulnerability level



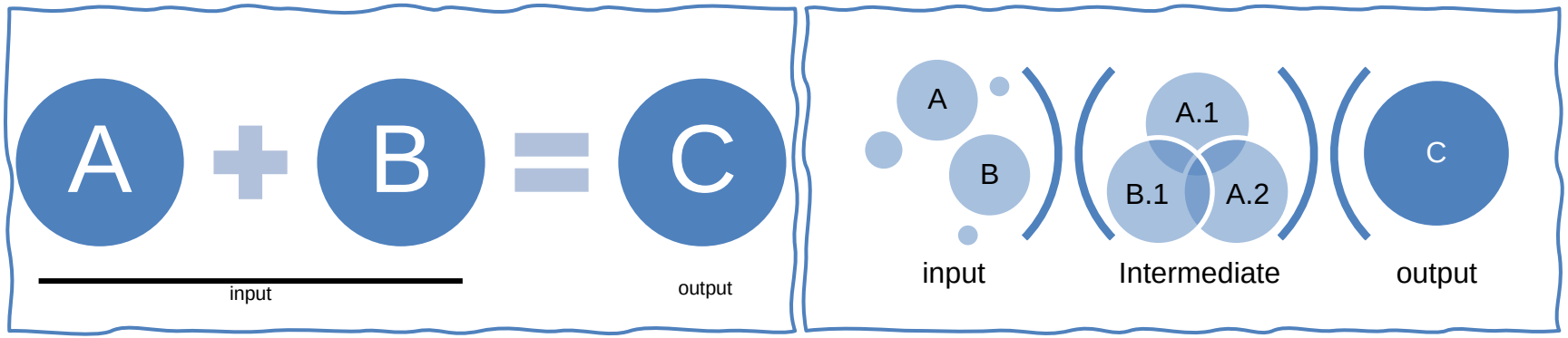
Data criticality examples

Level	Description
High (CQA, CPP)	CQA, CP (Critical Process), CPP (Impacts quality and safety)
Medium (Non-CPP)	Noncritical processes and process parameters
Low (Others)	Monitoring noncritical environmental conditions, utilities, noncritical equipment calibration and maintenance

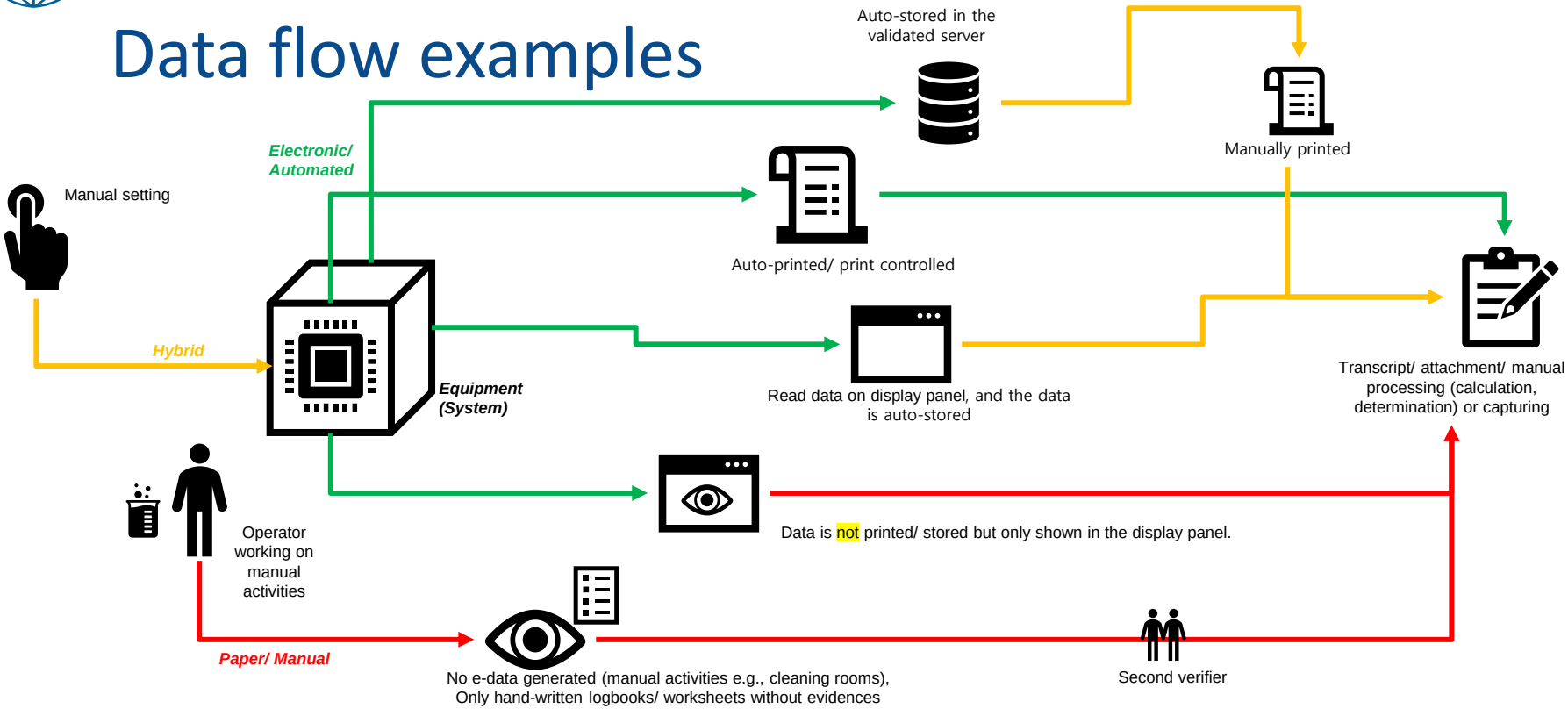
Process Area			Filling					
Sub-process	Step	Data Name	Data format	Data criticality	Hazardous situation	Current technical & procedural controls to minimize the hazard	Data control risk	Vulnerability level
Vial washer and Depyrogenation Tunnel	Tunnel preparation	Heating Zone 2 temp. (℃)	Hybrid	High (Critical Material Attribute control)	Operator mis transcribe the data	1. The data is verified by second person in real time 2. The alarm is triggered, and the machine is halted if the minimum criteria is exceeded and adjust the temperature automatically if the maximum criteria is exceeded 3. Process data is saved and printed and attached	Medium	H/M (Orange)
Preparation of filling process	Filling equipment autoclave	filling equipment clean hold time check	Paper	Medium (Noncritical parameter, process monitoring)	Operator mis check the checkbox	1. The data is not saved to check the accuracy afterward. (Cleaning start date/time of filling equipment) 2. Calculation formula is specified in BR 3. The data is verified by second person in real time.	High	M/H (Orange)
Preparation of filling process	Pre-FIT	Redundant filter(1) wetting volume	Hybrid	Low (Readiness check of noncritical equipment)	Operator mis transcribe the data	1. The data is not saved to check the accuracy afterward. 2. Calibrated equipment is used, and the data is showed by the digital format.	High	L/H (Green)
Filling	Filling and Stoppering	Fill volume check (pass/fail)	Hybrid	High (Critical Process Parameter)	Operator mis check the check box	1. The data is verified by second person 2. The alarm is triggered, and the machine is halted if fill volume criteria is exceeded. 3. The data is automatically recorded in the batch report by the validated system 4. Filling report is saved and printed and attached	Medium	H/M (Orange)

Data criticality in data flow

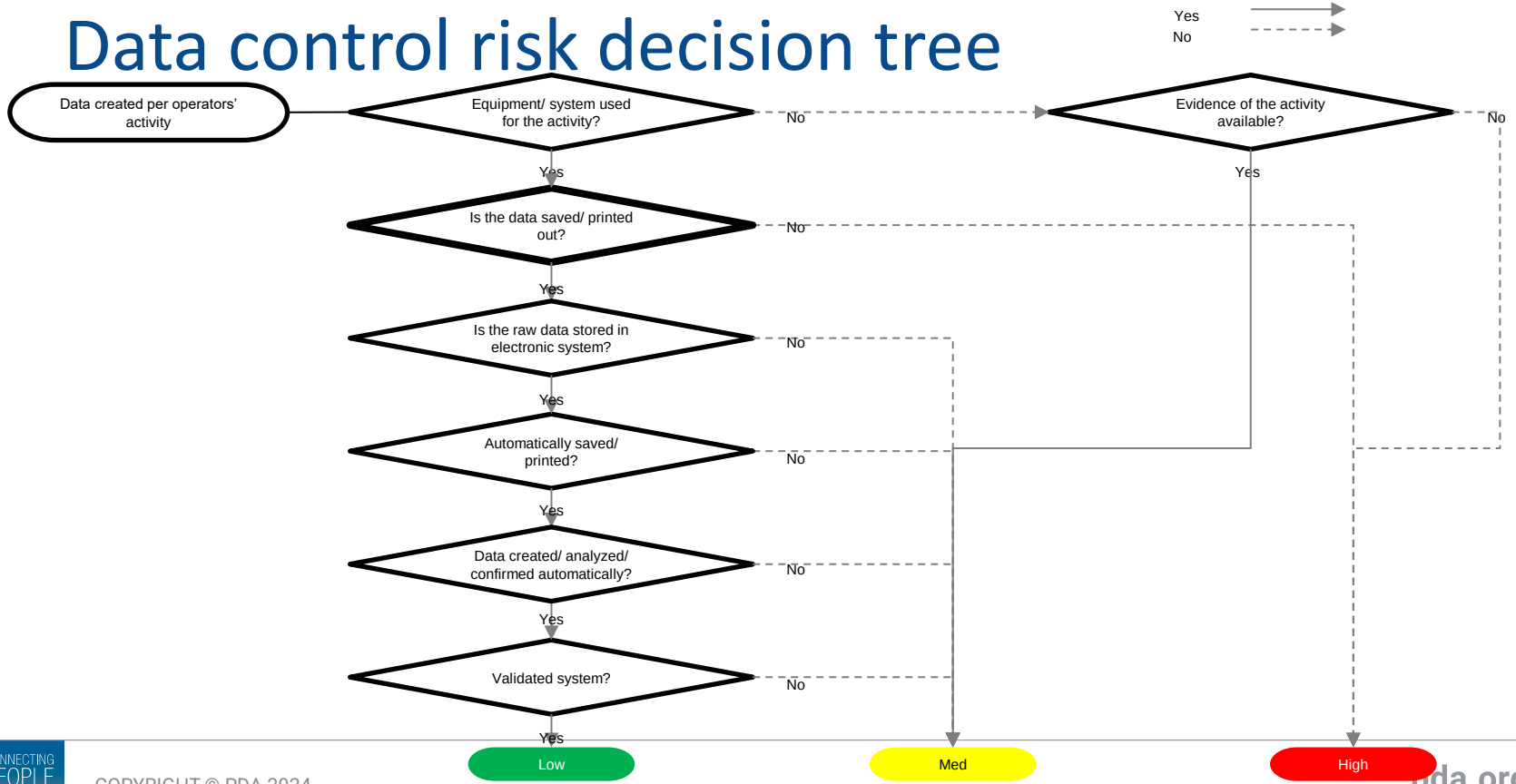
If
C = High criticality
AND
A and B are not (n)CPP/CQA,
THEN
A and B = High?



Data flow examples



Data control risk decision tree

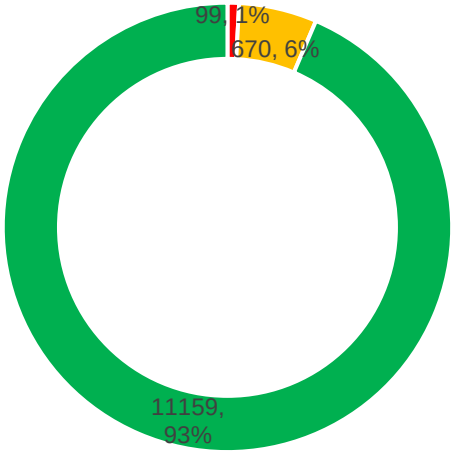


Data control risk examples

Level	Description
High (Manual entry)	Manual data capture, No automated data analysis, Manual data transcription, Heavy reliance on second person witnessing of data entries
Medium (Hybrid)	Hybrid systems or manual data capture, limited automated data analysis, manual data transcription
Low (Auto transfer)	Validated and effective automated or hybrid data capture and analysis system in place

Process Area			Filling					
Sub-process	Step	Data Name	Data format	Data criticality	Hazardous situation	Current technical & procedural controls to minimize the hazard	Data control risk	Vulnerability level
Vial washer and Depyrogenation Tunnel	Tunnel preparation	Heating Zone 2 temp. (℃)	Hybrid	High (Critical Material Attribute control)	Operator mis transcribe the data	1. The data is verified by second person in real time 2. The alarm is triggered, and the machine is halted if the minimum criteria is exceeded and adjust the temperature automatically if the maximum criteria is exceeded 3. Process data is saved and printed and attached	Medium	H/M (Orange)
Preparation of filling process	Filling equipment autoclave	filling equipment clean hold time check	Paper	Medium (Noncritical parameter, process monitoring)	Operator mis check the checkbox	1. The data is not saved to check the accuracy afterward. (Cleaning start date/time of filling equipment) 2. Calculation formula is specified in BR 3. The data is verified by second person in real time.	High	M/H (Orange)
Preparation of filling process	Pre-FIT	Redundant filter(1) wetting volume	Hybrid	Low (Readiness check of noncritical equipment)	Operator mis transcribe the data	1. The data is not saved to check the accuracy afterward. 2. Calibrated equipment is used, and the data is showed by the digital format.	High	L/H (Green)
Filling	Filling and Stoppering	Fill volume check (pass/fail)	Hybrid	High (Critical Process Parameter)	Operator mis check the check box	1. The data is verified by second person 2. The alarm is triggered, and the machine is halted if fill volume criteria is exceeded. 3. The data is automatically recorded in the batch report by the validated system 4. Filling report is saved and printed and attached	Medium	H/M (Orange)

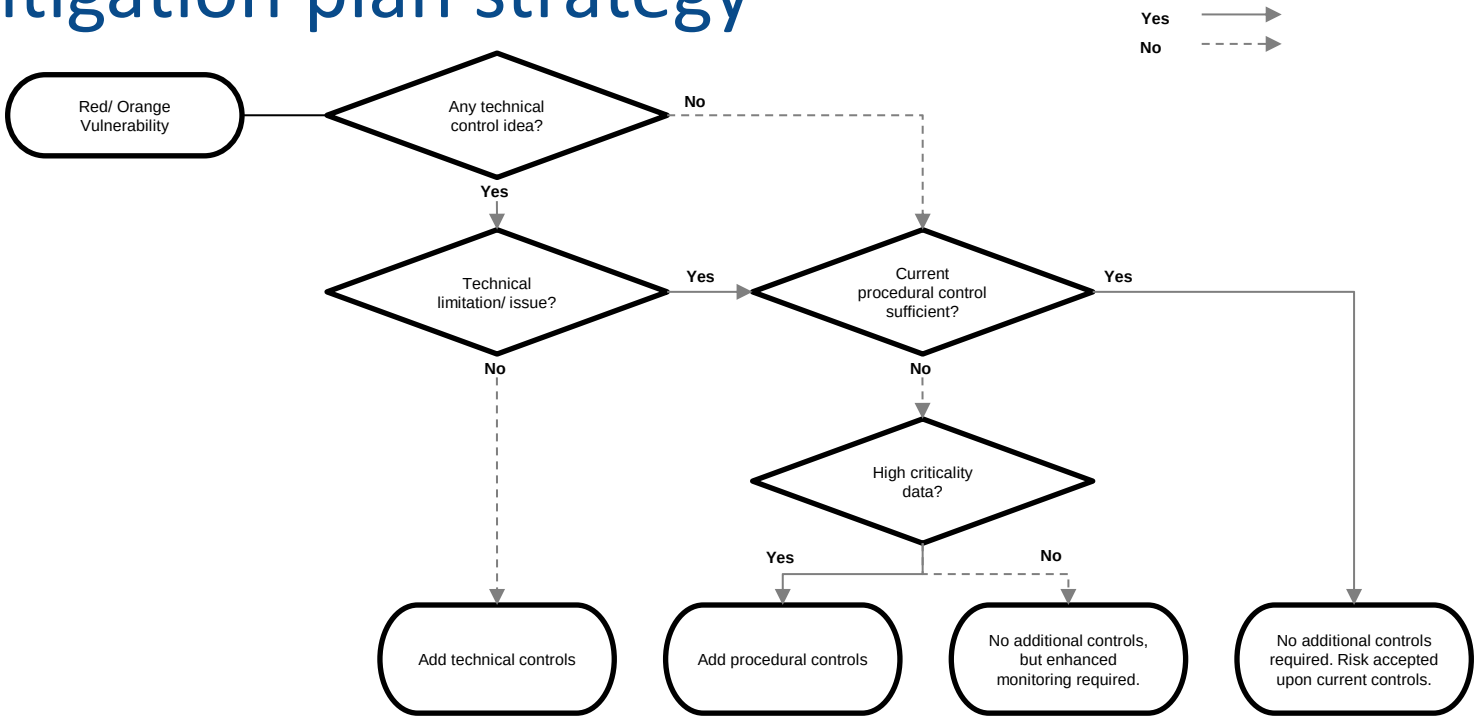
Result



Unit: # of data points

Control Risk / Data Criticality	Low	Medium	High	Total
High	27	76	99	202 (1.69%)
Medium	164	1,544	594	2,302 (19.30%)
Low	456	3,662	5,306	9,424 (79.01%
Total	647 (5.42%)	5,282 (44.28%)	5,999 (50.29%)	**11,928**

Mitigation plan strategy



Mitigation examples

Phase	Action Item
Phase 1	Form improvement to check the data directly through electronic systems
	Double verification/ witnessing
Phase 2	Remove the duplicated, transcribed data of low risk data
	Software upgrade to utilize the storage functionality
Phase 3	Add alarm functionality to the process system
	Replace with a balance that has storage functionality
Phase 4	Introduce barcode system to load date/ time data & feed the data into the warehouse management system

Less paper/ manual record, more electronic/ automated record

Key takeaways

- Strong alignment on data criticality
- Clear understanding of data flow and format
- Early agreement on action ownership

Communication does matter at all assessment steps

A Case Study: Implementation of Digital Validation Software for Analytical Instrument Lifecycle Management

Haneul (Sky) Jie (QC Analyst)

Analytical Instrument Qualification

Analytical Instrument Qualification

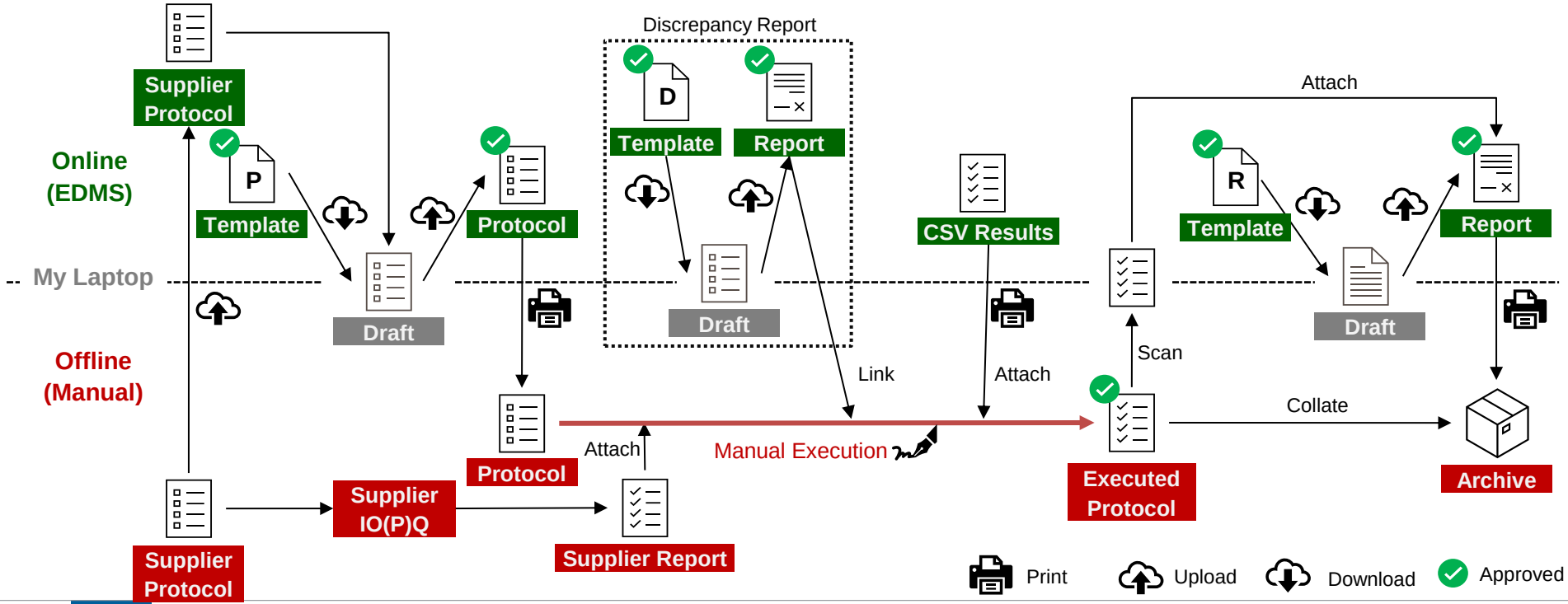
AIQ is the collection of documented evidence that an instrument performs suitably for its intended purpose. Use of a qualified instrument in analyses contributes to confidence in the validity of generated data.

ANALYTICAL INSTRUMENT QUALIFICATION DOCUMENTATION

Documents obtained during qualification activities should be retained in an accessible manner. Where multiple instruments of one kind exist, documents common to all instruments and documents specific to an instrument may be stored separately. During change control, additional documents may supplement those obtained during the qualification process, and both sets of documents should be retained and maintained in a suitable manner that allows for appropriate protection and access.

USP <1058>

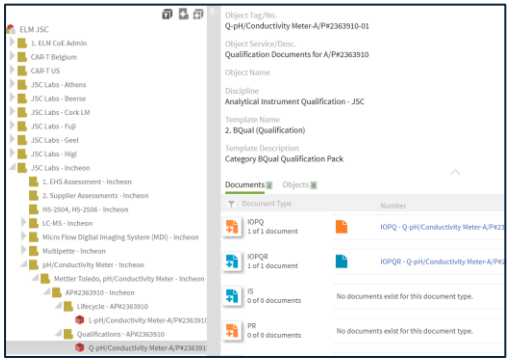
AIQ Process Map in J&J Incheon Site



Inherent DI Risks of Hybrid Documentation

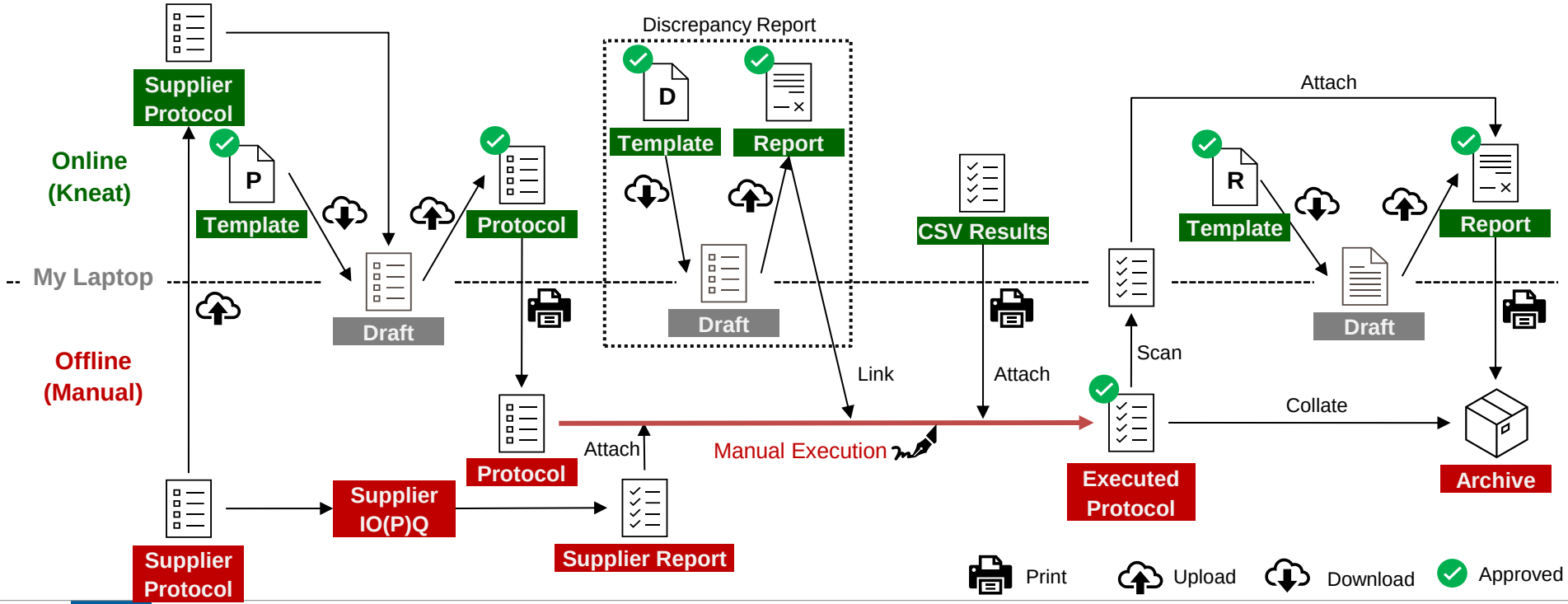
Solution: Digital Validation System

- 21 CFR 11, Annex 11 Compliance
- End-to-End Execution Online
- Requirement Traceability Matrix (RTM)
- Efficient & Resource Saving

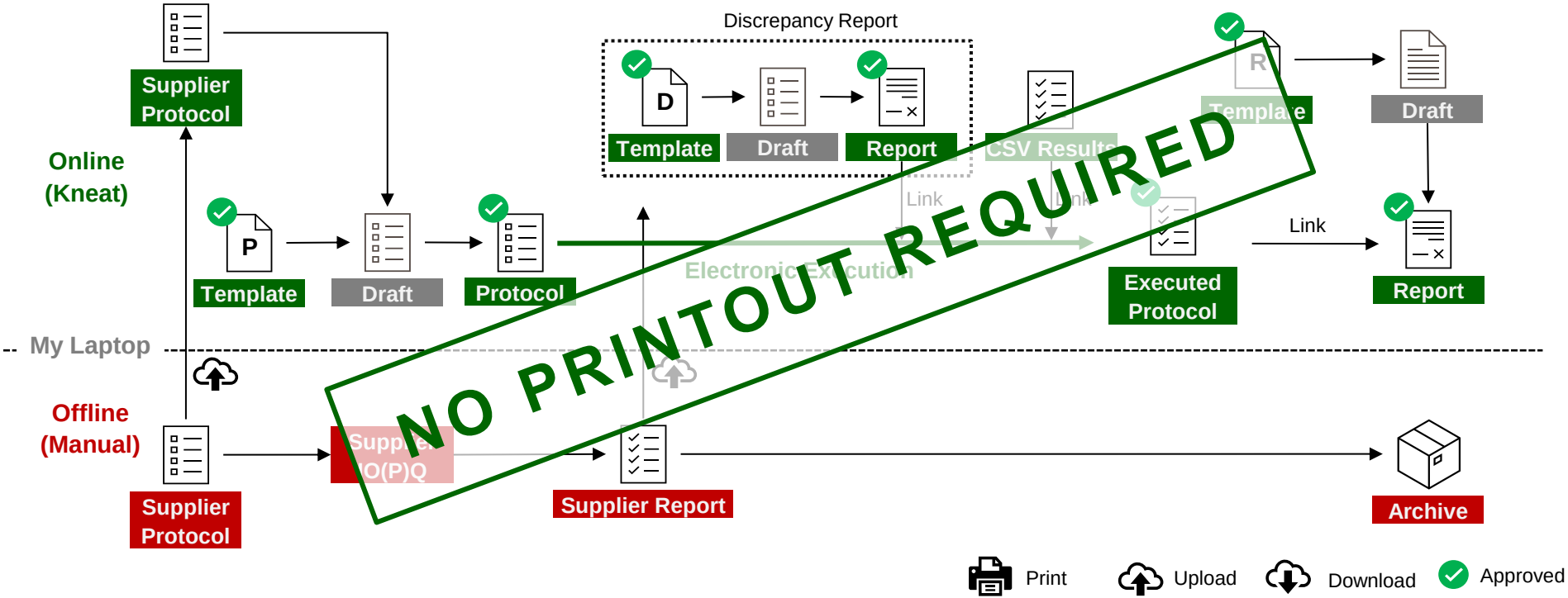


All qualification documents created during the lifecycle of an analytical instrument are accumulated under the same folder, allowing users to easily locate them and provide a clear view of lifecycle events that resulted in requalification activities.

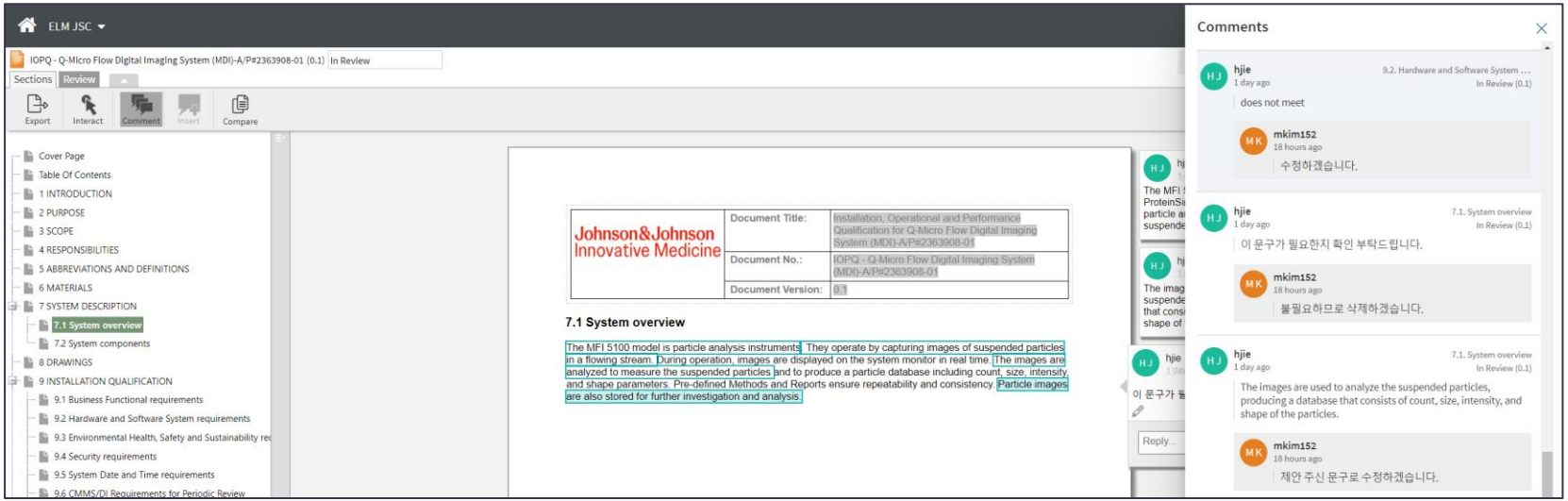
Streamlined Process Flow with Kneat DVS



Streamlined Process Flow with Kneat DVS

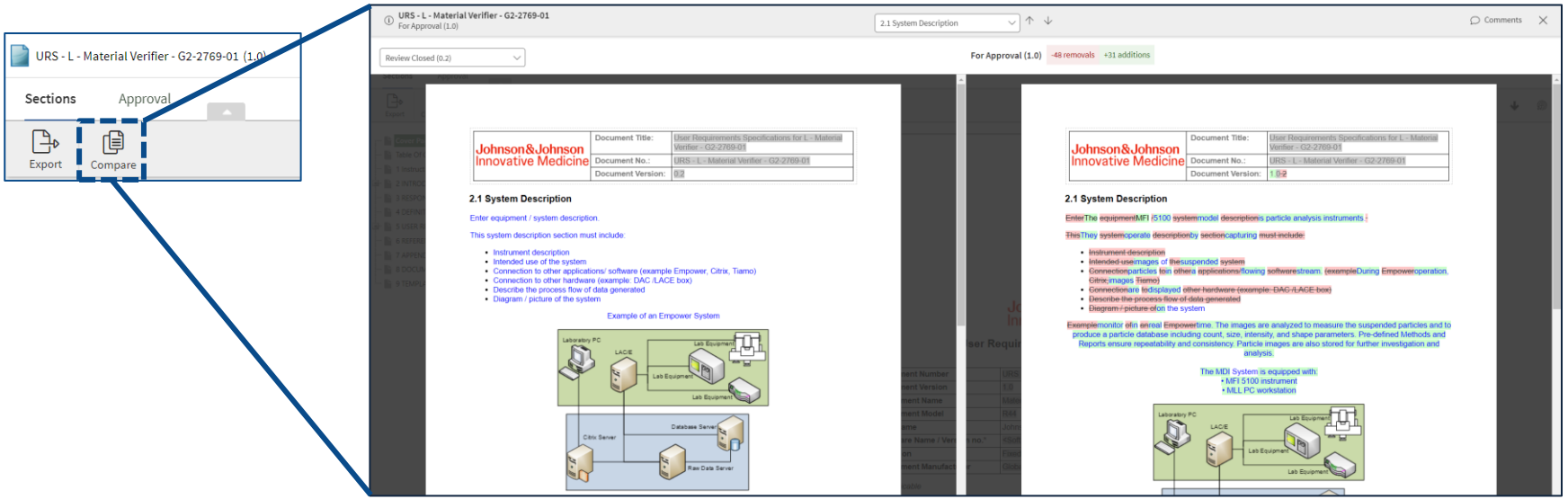


Key Features



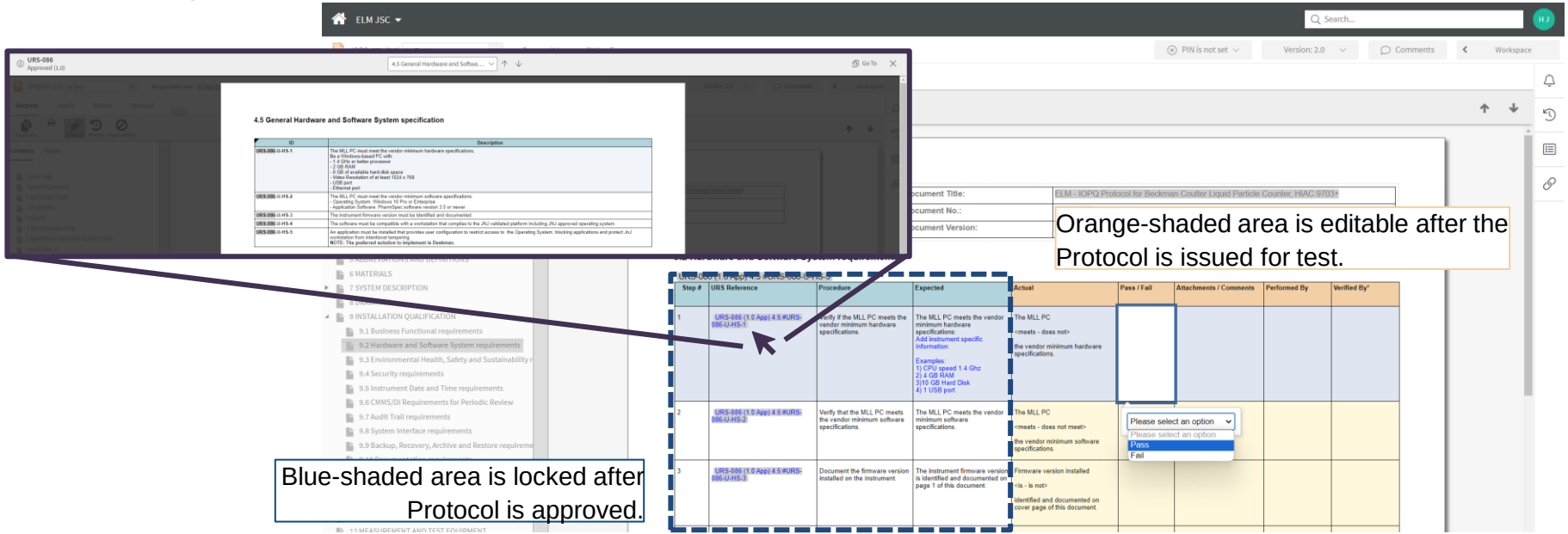
Reviewer can leave comments and the Author can reply.

Key Features



[Compare] button allows easy tracking of changed elements.

Key Features



Each test item can be executed digitally, and linked documents are opened in a pop-up.

Key Features

Traceability Matrix Report

Report: KGX-REP-0005 Version: 8.5
Run Date Time:26-Sep-2024 2:53 am
All Times in UTC

Owning Document Number:	URS - L-OSMOMETER-A/P#2305065-01 (1.0)
Document Version:	1.0
Reference Folder:	No References Exist
Risk Assessment Document Number:	

Report data last updated: 25-Sep-2024 9:05 pm

Table Legend
Approved Documents
Non Approved Documents

			Design	Test
Document Number	**Identifier**	**Description**	**URS**	**IOPQ**
URS - L-Osmometer-A/P#2305065-01	URS - L-Osmometer-A/P#2305065-01-U-BF-1	The instrument must pass the initial vendor Installation & Operational qualification.	URS - L-Osmometer-A/P#2305065-01(1.0)5.1#Business Functional RequirementsURS - L-Osmometer-A/P#2305065-01-U-BF-1	NA
	URS - L-Osmometer-A/P#2305065-01-U-BF-2	Appropriate test methods and test scenarios can be performed by the system *and the correct steps are performed in the correct sequence.*	URS - L-Osmometer-A/P#2305065-01(1.0)5.1#Business Functional RequirementsURS - L-Osmometer-A/P#2305065-01-U-BF-2	NA
	URS - L-Osmometer-A/P#2305065-01-U-BF-3	Inputs (numbers and letters) and their outputs (on the display) are consistent.	URS - L-Osmometer-A/P#2305065-01(1.0)5.1#Business Functional RequirementsURS - L-Osmometer-A/P#2305065-01-U-BF-3	NA
	URS - L-Osmometer-A/P#2305065-01-U-BF-4	The data on the display and the output on the printout must be equivalent.	URS - L-Osmometer-A/P#2305065-01(1.0)5.1#Business Functional RequirementsURS - L-Osmometer-A/P#2305065-01-U-BF-4	NA
	URS - L-Osmometer-	All settings selected during the setup must be recorded.	URS - L-Osmometer-A/P#2305065-01(1.0)5.1#Business Functional	NA

Traceability Matrix Report links requirements and documents in a dynamic manner.

Conclusion

- Alignment between regulatory requirements and internal procedures is critical to seamless deployment of digital validation solution.
- The suppliers/partners we work with are still heavily dependent on paper-based documentations, which prevents the complete transition into a paper-less way of working.
- Continued efforts to minimize data vulnerability points through lab digitalization in J&J Incheon, including instrument interfacing with LIMS, electronic worksheets, expansion of scope for DVS application, etc.

Thank You!

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