

Data integrity – Case study:

Data vulnerability assessment and KNEAT (Paperless validation software) implementation

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PDA Aseptic Processing of Biopharmaceuticals Conference 2024

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

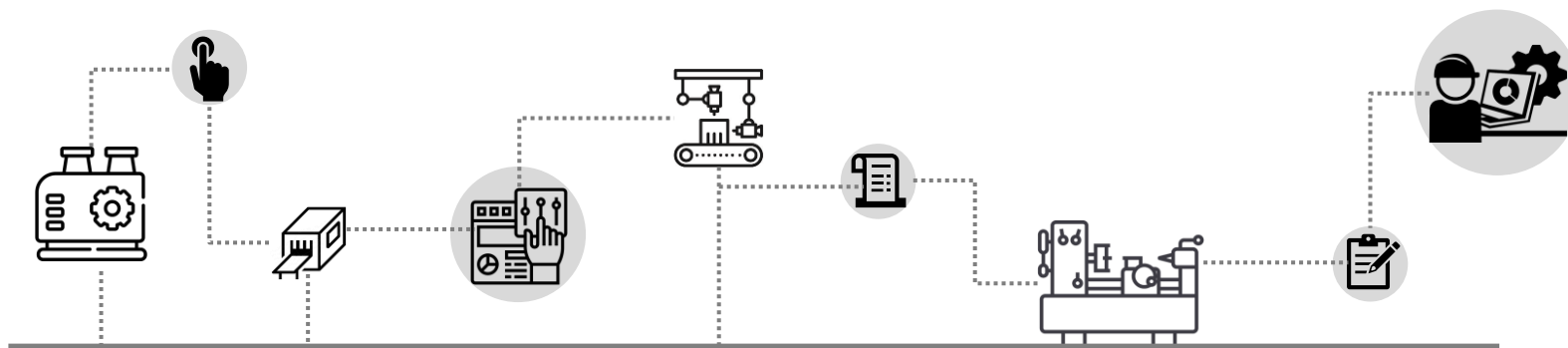
Data Integrity harmonization program

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



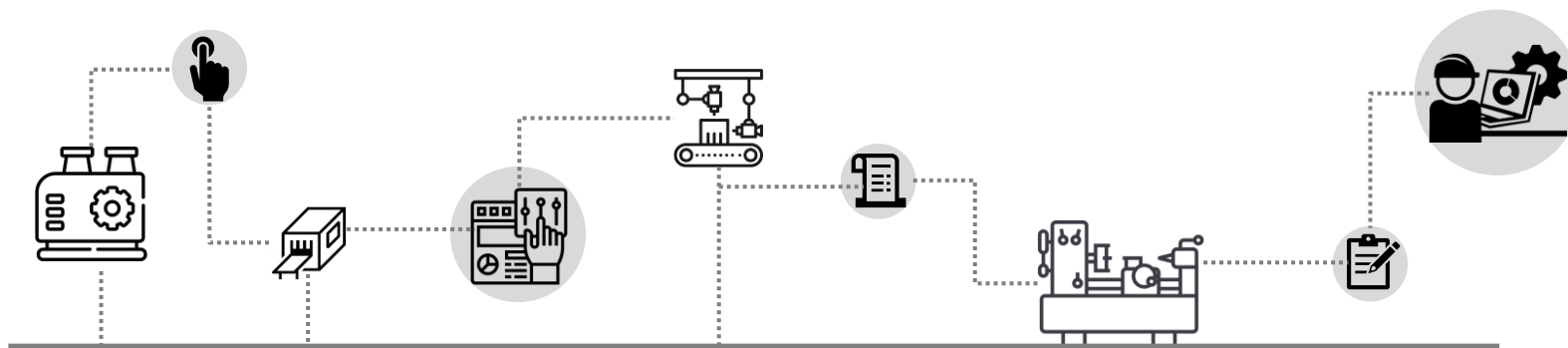
How we define ‘data vulnerability’

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



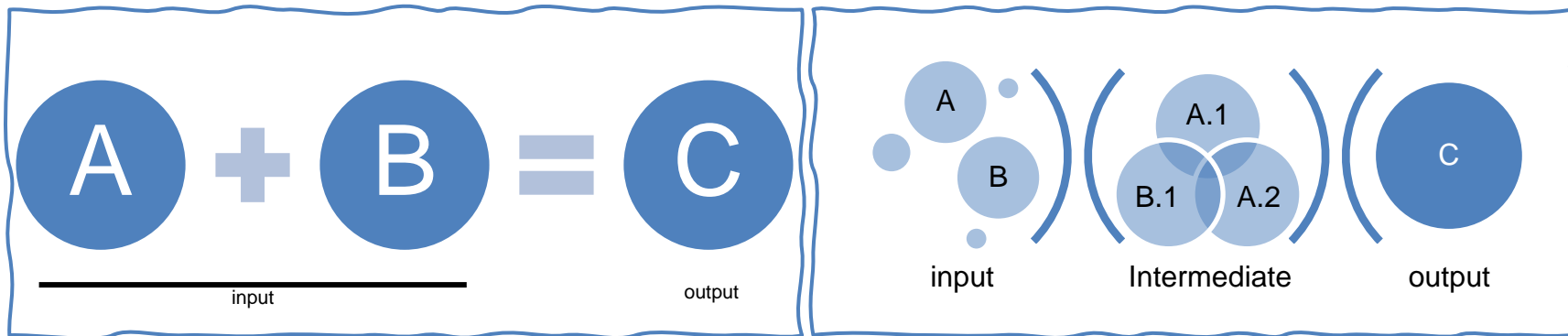
Data criticality examples

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

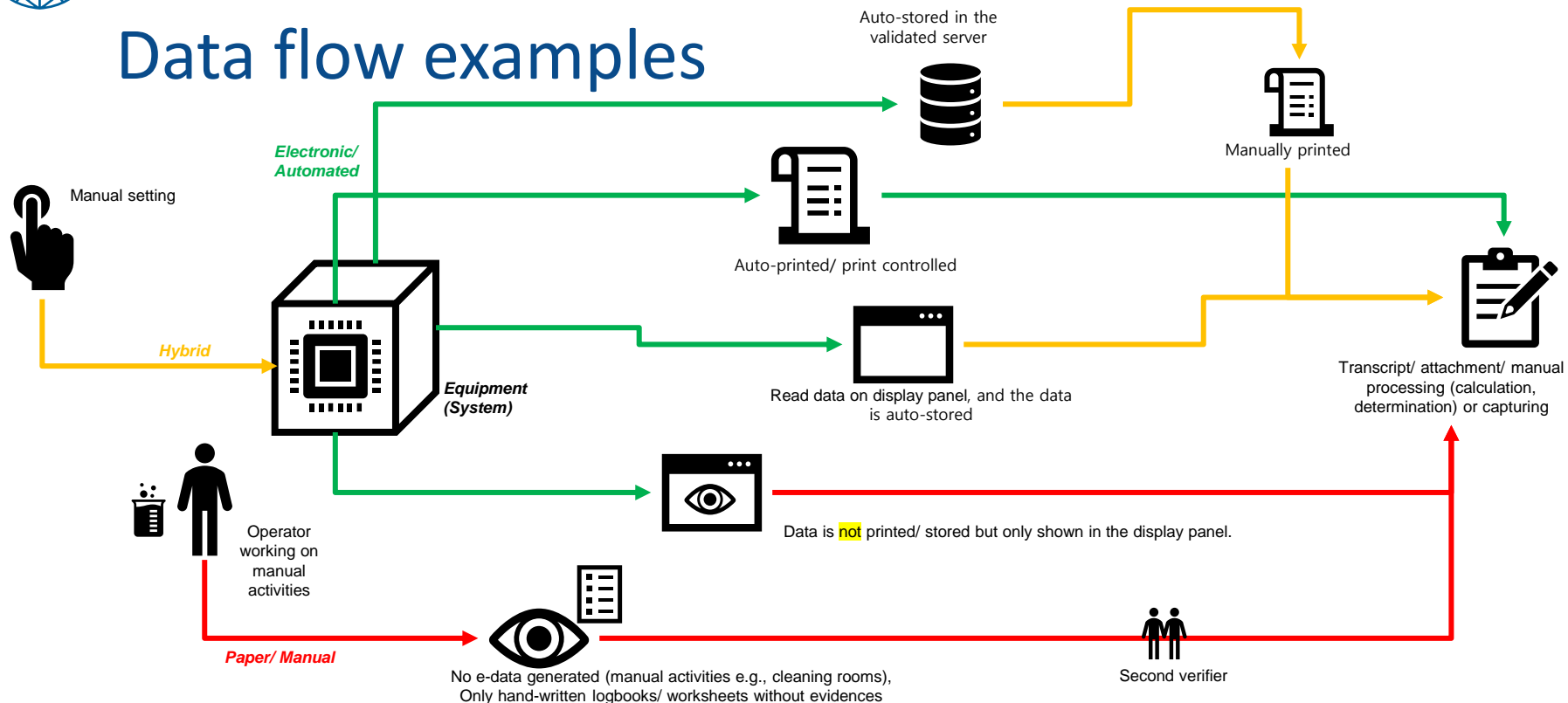
Process Area			Filling					
Sub-process	Step	Data Name	Data format	Data criticality	Hazardous situation	Current technical & procedural controls to minimize the hazard	Data control risk	Vulnerability level
Vial washer and Depyrogenation Tunnel	Tunnel preparation	Heating Zone 2 temp. (°C)	Hybrid	High (Critical Material Attribute control)	Operator mis transcribe the data	<ol style="list-style-type: none"> The data is verified by second person in real time 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 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	<ol style="list-style-type: none"> The data is not saved to check the accuracy afterward. (Cleaning start date/time of filling equipment) Calculation formula is specified in BR 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	<ol style="list-style-type: none"> The data is not saved to check the accuracy afterward. 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	<ol style="list-style-type: none"> The data is verified by second person The alarm is triggered, and the machine is halted if fill volume criteria is exceeded. The data is automatically recorded in the batch report by the validated system Filling report is saved and printed and attached 	Medium	H/M (Orange)

Data criticality in data flow

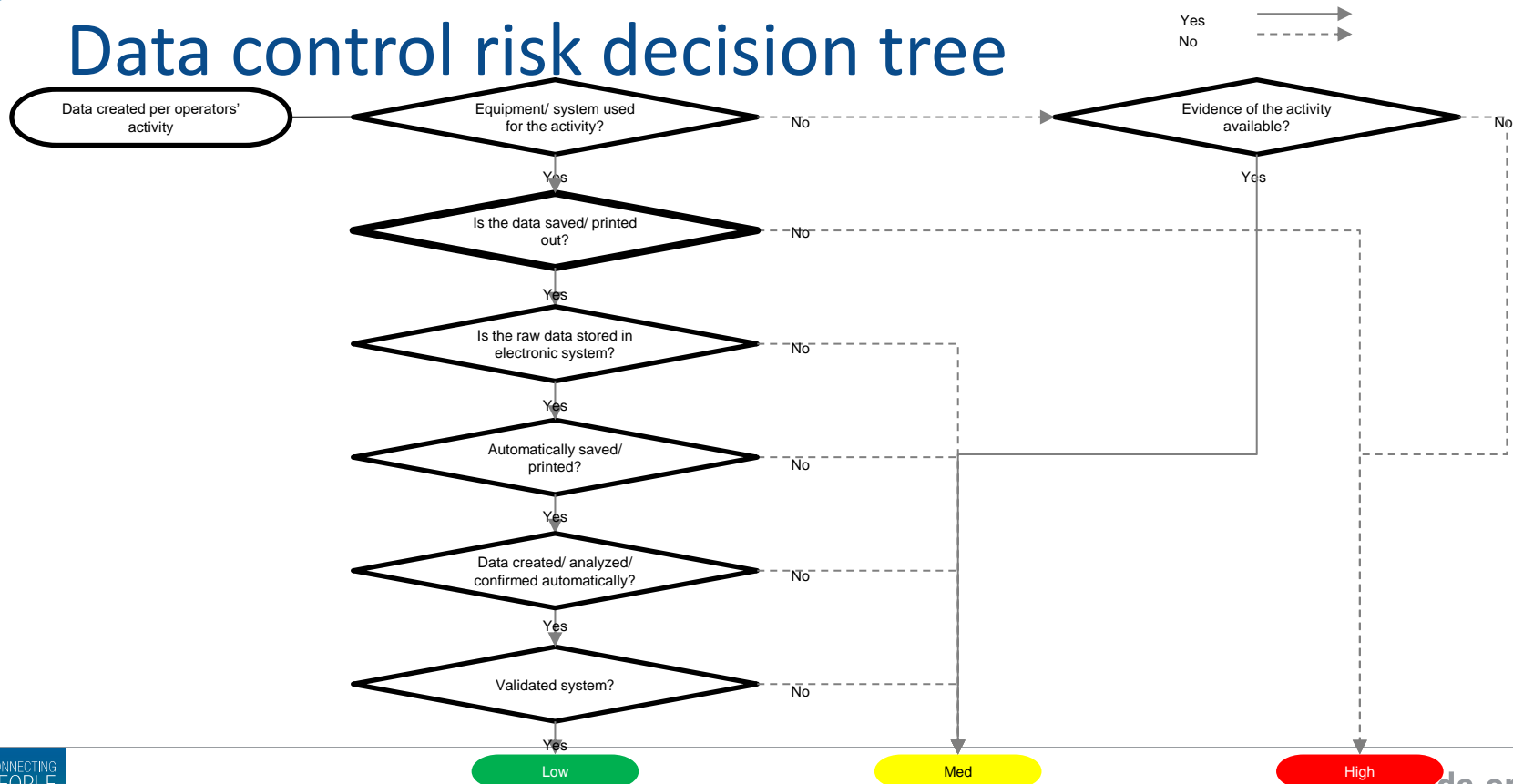
If
 C = High criticality
 AND
 A and B are not (n)CPP/CQA,
 THEN
A and B = High?



Data flow examples



Data control risk decision tree

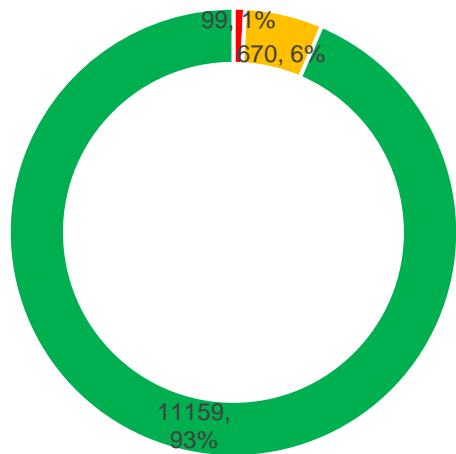


Data control risk examples

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						Data control risk	Vulnerability level
Sub-process	Step	Data Name	Data format	Data criticality	Hazardous situation	Current technical & procedural controls to minimize the hazard				
Vial washer and Depyrogenation Tunnel	Tunnel preparation	Heating Zone 2 temp. (°C)	Hybrid	High (Critical Material Attribute control)	Operator mis transcribe the data	<ol style="list-style-type: none"> The data is verified by second person in real time 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 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	<ol style="list-style-type: none"> The data is not saved to check the accuracy afterward. (Cleaning start date/time of filling equipment) Calculation formula is specified in BR 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	<ol style="list-style-type: none"> The data is not saved to check the accuracy afterward. 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	<ol style="list-style-type: none"> The data is verified by second person The alarm is triggered, and the machine is halted if fill volume criteria is exceeded. The data is automatically recorded in the batch report by the validated system Filling report is saved and printed and attached 		Medium	H/M (Orange)	

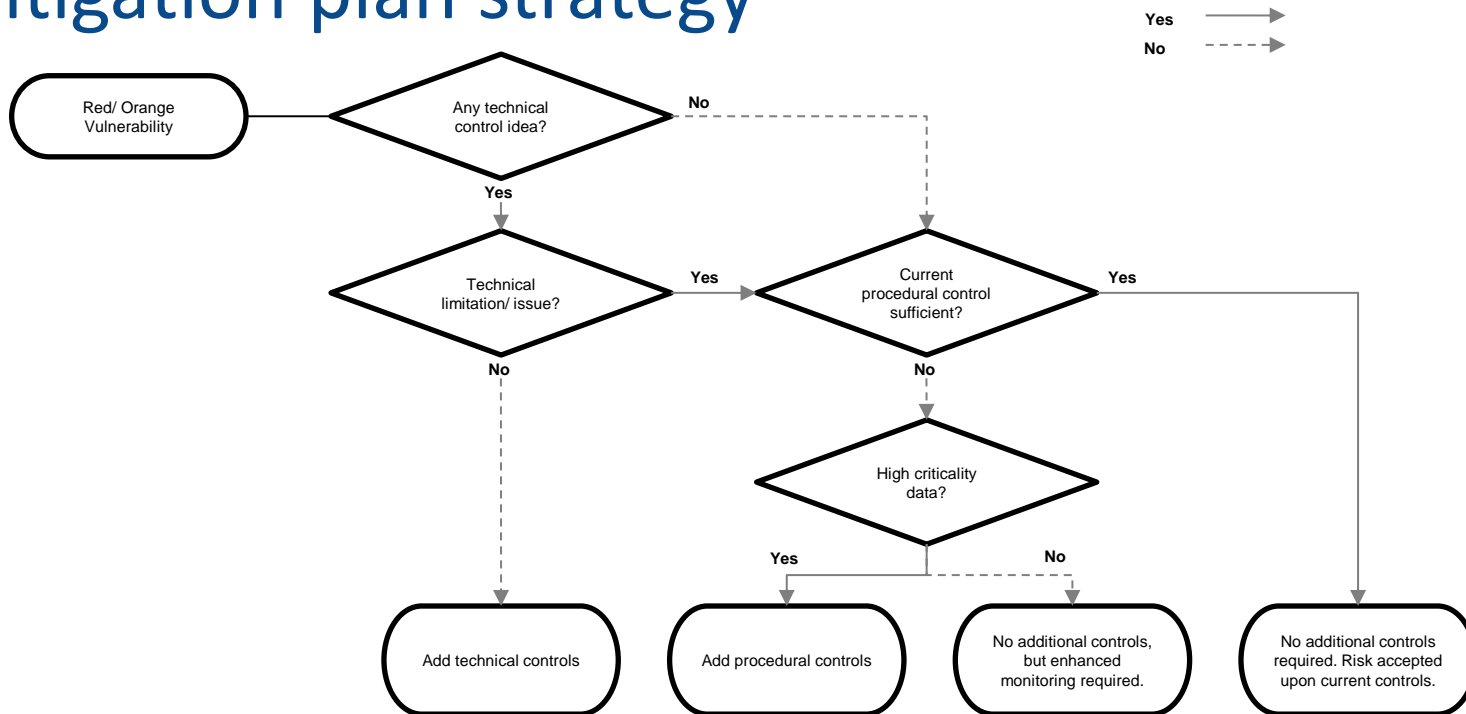
Result



Unit: # of data points

Control Risk \ Data Criticality	Control Risk			Total
	Low	Medium	High	
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>

Inherent DI Risks of Hybrid Documentation



Solution: Digital Validation System



21 CFR 11, Annex 11 Compliance



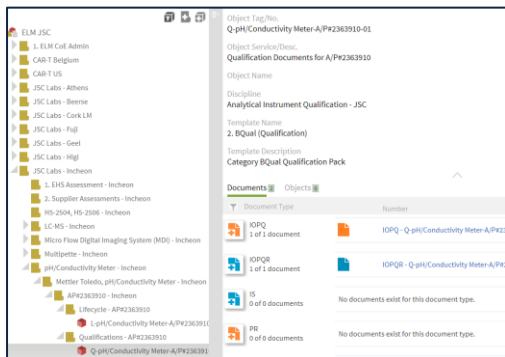
End-to-End Execution Online



Requirement Traceability Matrix (RTM)

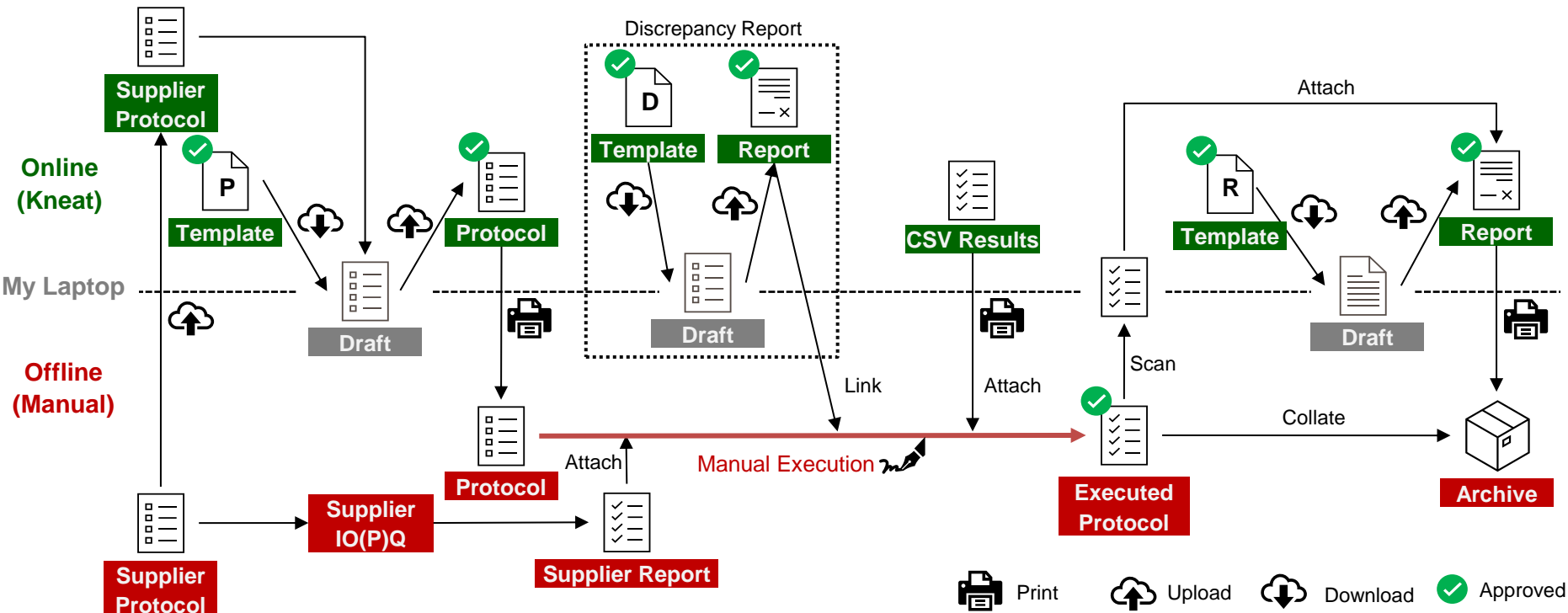


Efficient & Resource Saving

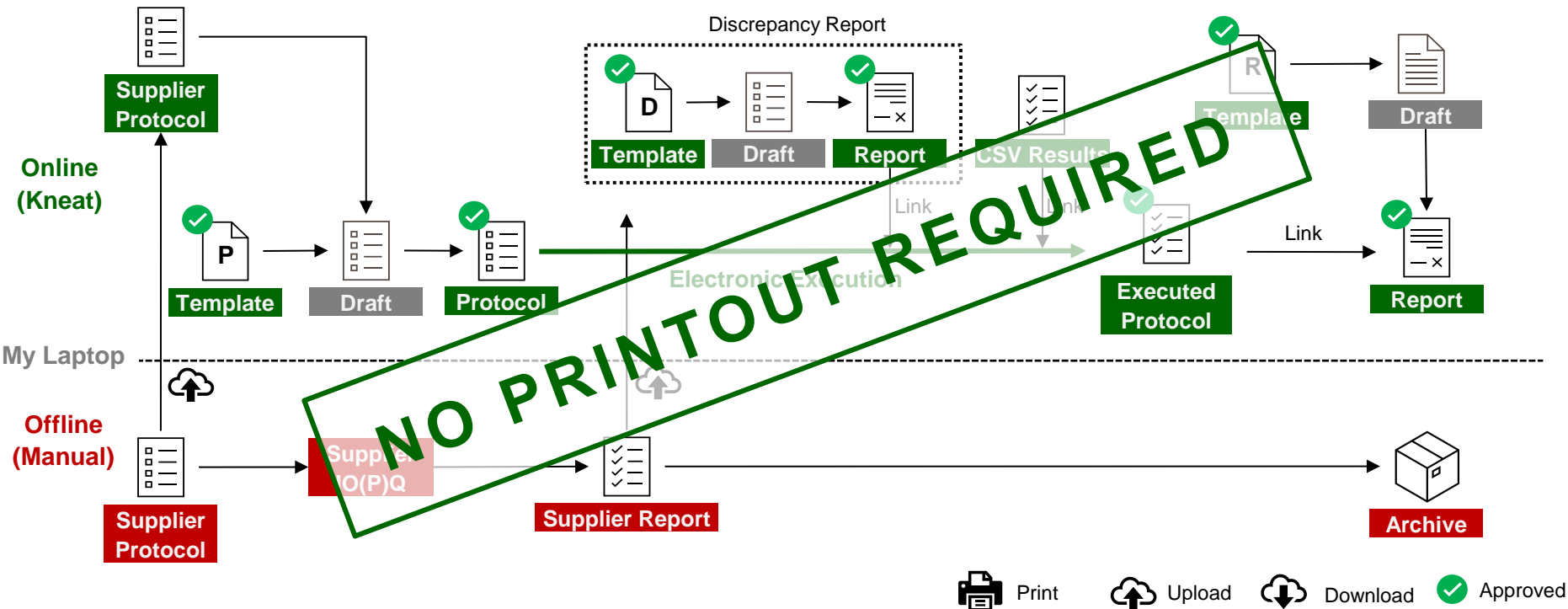


All qualification documents created during the lifecycle of an analytical instrument are accumulated under the same folder, allowing users to easily locate them and provide a clear view of lifecycle events that resulted in requalification activities.

Streamlined Process Flow with Kneat DVS



Streamlined Process Flow with Kneat DVS



Key Features

The screenshot displays a document review interface for a document titled "Installation, Operational and Performance Qualification for Q-Micro Flow Digital Imaging System (MDI)-A/P#2363908-01". The document is currently in "Review" mode. The interface includes a sidebar with a table of contents, a main document area, and a comments sidebar on the right.

Document Metadata Table:

Document Title:	Installation, Operational and Performance Qualification for Q-Micro Flow Digital Imaging System (MDI)-A/P#2363908-01
Document No.:	IQPC - Q-Micro Flow Digital Imaging System (MDI)-A/P#2363908-01
Document Version:	0.1

Section 7.1 System overview:

The MF1 5100 model is particle analysis instruments. They operate by capturing images of suspended particles in a flowing stream. During operation, images are displayed on the system monitor in real time. The images are analyzed to measure the suspended particles and to produce a particle database including count, size, intensity, and shape parameters. Pre-defined Methods and Reports ensure repeatability and consistency. Particle images are also stored for further investigation and analysis.

Comments:

- hjie** (1 day ago): does not meet
- mkim152** (18 hours ago): 수정하겠습니다.
- hjie** (1 day ago): 이 문구가 필요한지 확인 부탁드립니다.
- mkim152** (18 hours ago): 불필요하므로 삭제하겠습니다.
- hjie** (1 day ago): The images are used to analyze the suspended particles, producing a database that consists of count, size, intensity, and shape of the particles.
- mkim152** (18 hours ago): 재안 주신 문구로 수정하겠습니다.

Reviewer can leave comments and the Author can reply.

Key Features

URS - L - Material Verifier - G2-2769-01 (1.0)

Sections Approval

Export Compare

URS - L - Material Verifier - G2-2769-01 (1.0)

2.1 System Description

Review Closed (0.2)

For Approval (1.0) -48 removals +31 additions

Document Title: User Requirements Specifications for L - Material Verifier - G2-2769-01

Document No.: URS - L - Material Verifier - G2-2769-01

Document Version: 01

2.1 System Description

Enter equipment / system description.

This system description section must include:

- Instrument description
- Intended use of the system
- Connection to other applications/ software (example Empower, Citrix, Tiamo)
- Connection to other hardware (example: DAC /LACE box)
- Describe the process flow of data generated
- Diagram - picture of the system

Example of an Empower System

Document Title: User Requirements Specifications for L - Material Verifier - G2-2769-01

Document No.: URS - L - Material Verifier - G2-2769-01

Document Version: 1.02

2.1 System Description

Enter the equipment/MFI 5100 system model descriptions particle analysis instruments:

This system operates description by section capturing must include:

- Instrument description
- Intended use/images of the suspended system
- Connection/curves for others applications/flowing software stream (example During Empower operation, Citrix/images Tiamo)
- Connections are to display when hardware (example: DAC/LACE box)
- Describe the process flow of data generated
- Diagram - picture of the system

Example: monitor data several Empower time. The images are analyzed to measure the suspended particles and to produce a particle database including count, size, intensity, and shape parameters. Pre-defined Methods and Reports ensure repeatability and consistency. Particle images are also stored for further investigation and analysis.

The MIDI System is equipped with:

- MFI 5100 instrument
- MILL PC workstation

[Compare] button allows easy tracking of changed elements.

Key Features

The screenshot displays the ELM JSC software interface. On the left, a document viewer shows the '4.5 General Hardware and Software System specification' document. On the right, a test protocol table is visible. The table has columns for Step #, URS Reference, Procedure, Expected, Actual, Pass / Fail, Attachments / Comments, Performed By, and Verified By. The first three rows of the table are highlighted in blue, indicating they are locked. The fourth row is highlighted in orange, indicating it is editable. A callout box points to the orange row with the text: 'Orange-shaded area is editable after the Protocol is issued for test.' Another callout box points to the blue rows with the text: 'Blue-shaded area is locked after Protocol is approved.' A dropdown menu is visible in the 'Pass / Fail' column of the orange row, showing options: 'Please select an option', 'Pass', and 'Fail'.

Step #	URS Reference	Procedure	Expected	Actual	Pass / Fail	Attachments / Comments	Performed By	Verified By
1	URS-006 (1.0 App) 4.5.HURS-006-U.HS.1	Verify if the MLL PC meets the vendor minimum hardware specifications.	The MLL PC meets the vendor minimum hardware specifications. Add instrument specific information: Examples: 1) CPU speed 1.4 Ghz 2) 4 GB RAM 3) 10 GB Hard Disk 4) 1 USB port	The MLL PC meets - does not meet- the vendor minimum hardware specifications				
2	URS-006 (1.0 App) 4.5.HURS-006-U.HS.2	Verify that the MLL PC meets the vendor minimum software specifications.	The MLL PC meets the vendor minimum software specifications.	The MLL PC meets - does not meet- the vendor minimum software specifications				
3	URS-006 (1.0 App) 4.5.HURS-006-U.HS.3	Document the firmware version installed on the instrument.	The instrument firmware version is identified and documented on page 1 of this document.	Firmware version installed - is - is not- identified and documented on cover page of this document.				

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

Key Features

Traceability Matrix Report

Owning Document Number:	URS - L-OSMOMETER-A/P#2305065-01 (1.0)	Report data last updated: 25-Sep-2024 9:05 pm
Document Version:	1.0	
Reference Folder:	No References Exist	
Risk Assessment Document Number:		

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

Table Legend	
	Approved Documents
	Non Approved Documents

Document Number	Identifier	Description	Design	Test
			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 <i>and the correct steps are performed in the correct sequence.</i>	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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