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#sharing challenges
and solutions in practice

Integrated Commissioning and Qualification

with automated risk analyses in REXS

Part of PharmaCongress – Düsseldorf/Neuss, 31 May–1 June 2022

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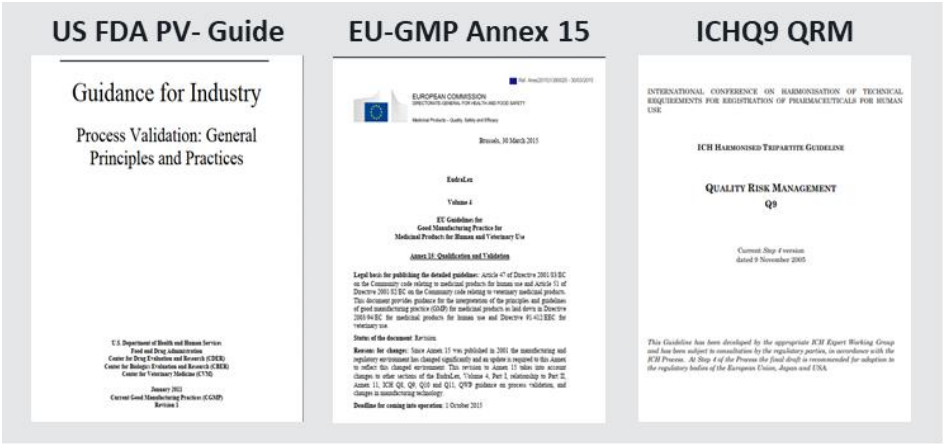
AGENDA

- MSD Animal Health in Krems - Video
- Integrated Commissioning & Qualification
  - Regulatory background
  - What is risk based iC&Q
- Traceability-matrix as basis for an agile iC&Q strategy
  - How to set up a risk-based life cycle traceability-matrix - right from the beginning
  - Paperless iC&Q - automated creation of (electronical) C&Q Documents

Legal basis and guidelines

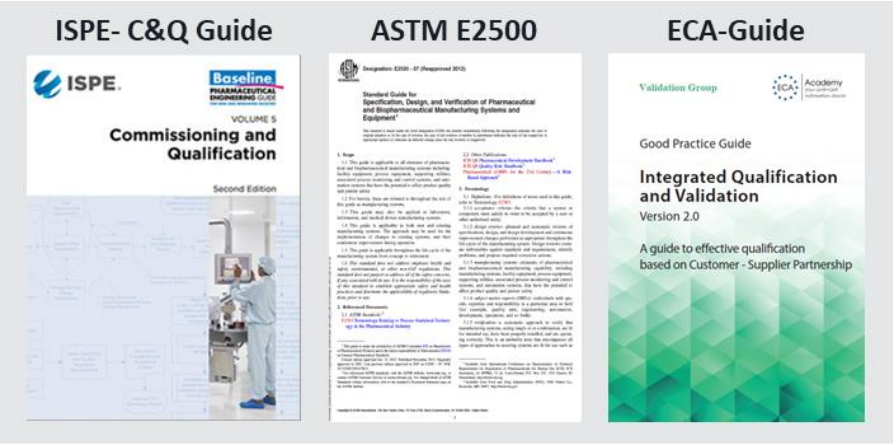
- Commissioning & Qualification
  - US FDA Guidance for Industry – Process Validation: General Principles and practices
  - EU- GMP-Guidelines - Annex 15
  - ICH Q9 Quality Risk Management



Risk based C&Q …

Legal basis and guidelines

- Integrated Commissioning & Qualification
  - ISPE Commissioning & Qualification Guide
  - ASTM E2500
  - ECA Good Practice Guide – Integrated Qualification and Validation

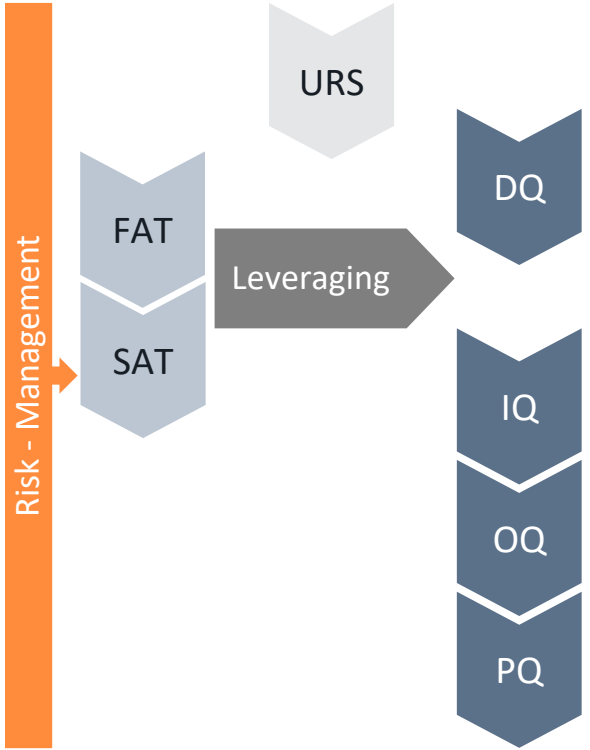


…and integrated C&Q

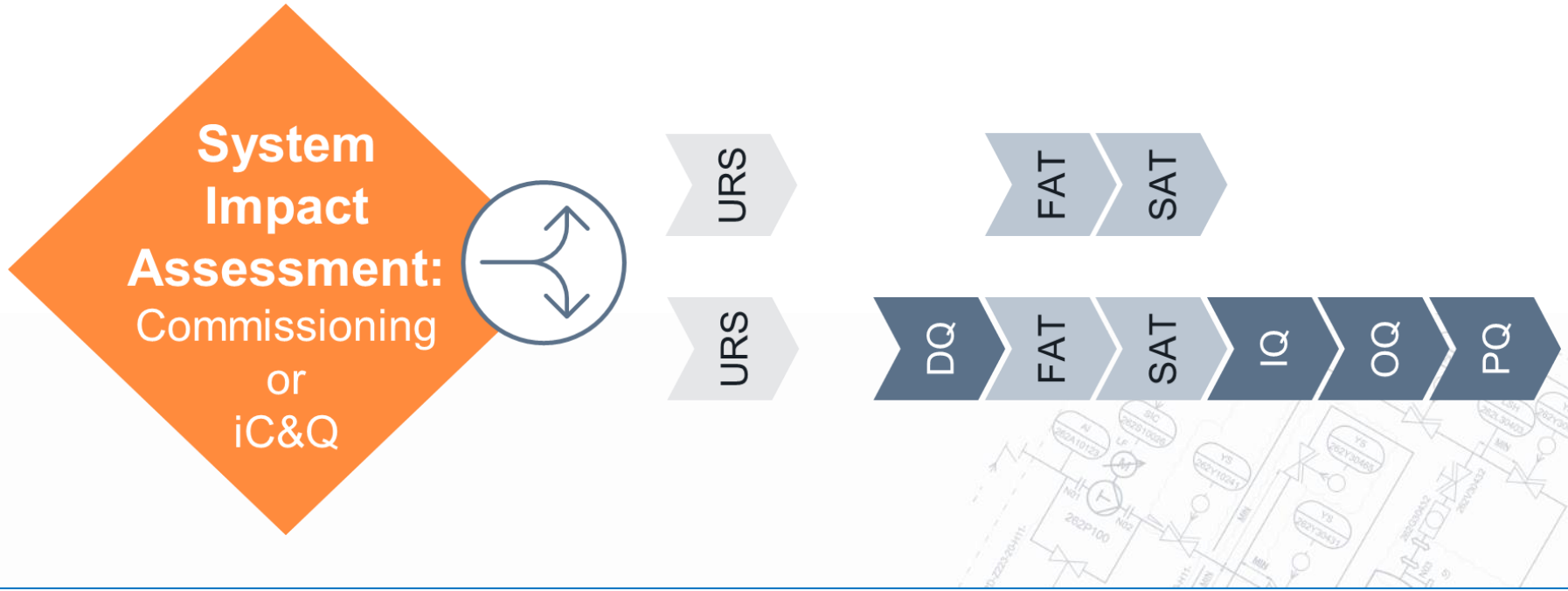
What is iC&Q?

- Commissioning - **by supplier**
  - GEP/ GMP relevant manufacturing system [1)]
  - URS, FAT, SAT
- Qualification - **by drug manufacturer**
  - GMP relevant manufacturing system [1)]
  - URS, DQ, IQ, OQ, PQ
- Integrated C&Q:
  - fully integration of supplier tests / documentation
  - based on quality risk management and product- / process understanding

1) manufacturing system: equipment, facilities, utilities or systems



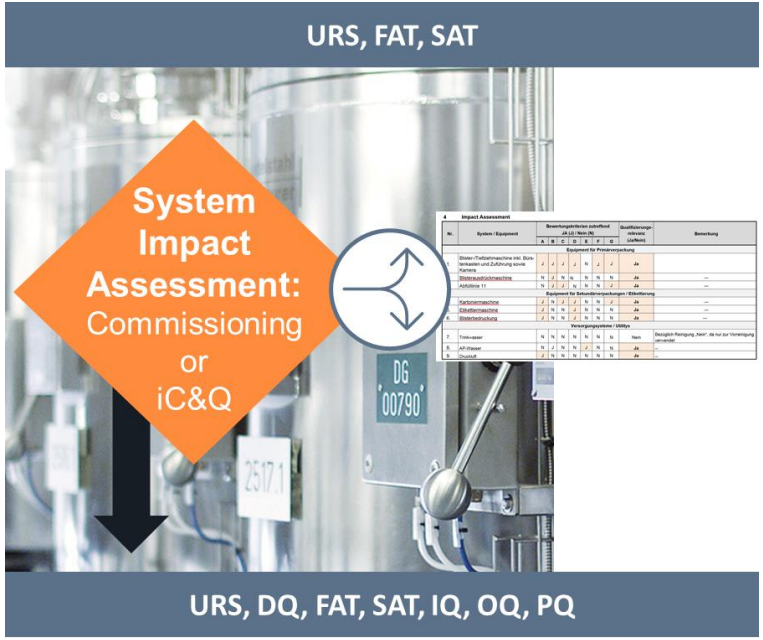
Scope of Commissioning / Commissioning & Qualification?



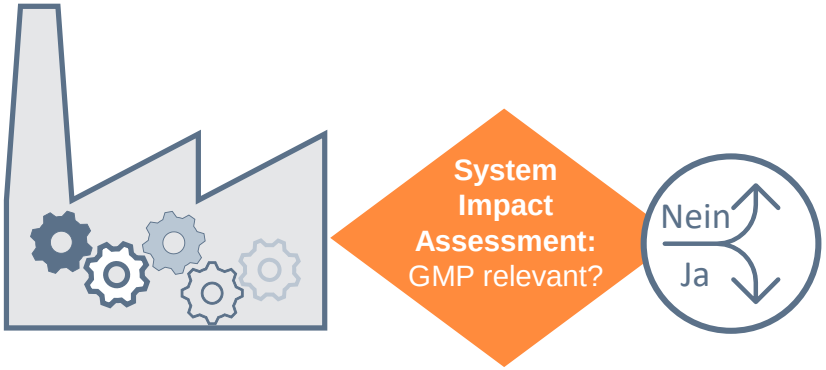
Impact Assessment

The following criteria are used by VTU

- The system can have direct contact with the product
- The system performs functions for critical process parameters
- The system produces/regenerates or contains product, product components, reagents or solvent
- The system influences the success of cleaning, sanitization or sterilization
- The system conserves product quality
- The system provides or saves relevant data for product evaluation
- The system includes or is a control system which influences product quality (without independent superior monitoring)
- The system provides or is used to verify information about product identification (e.g. batch number, ...) without independent verification

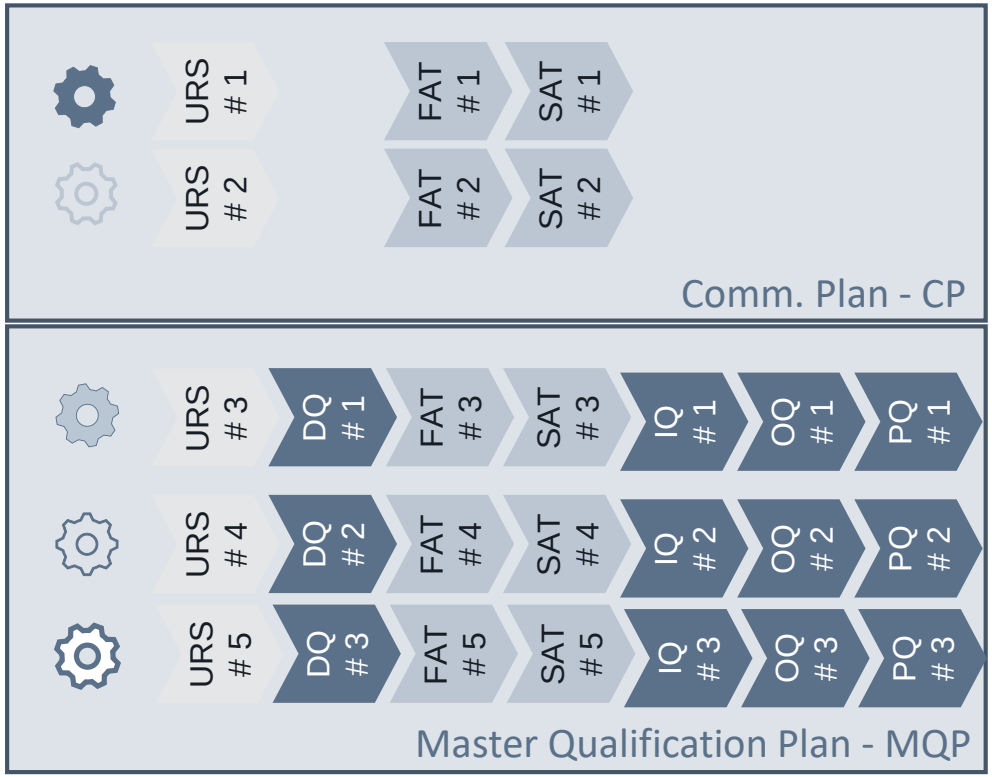


Commissioning & Qualification Planning

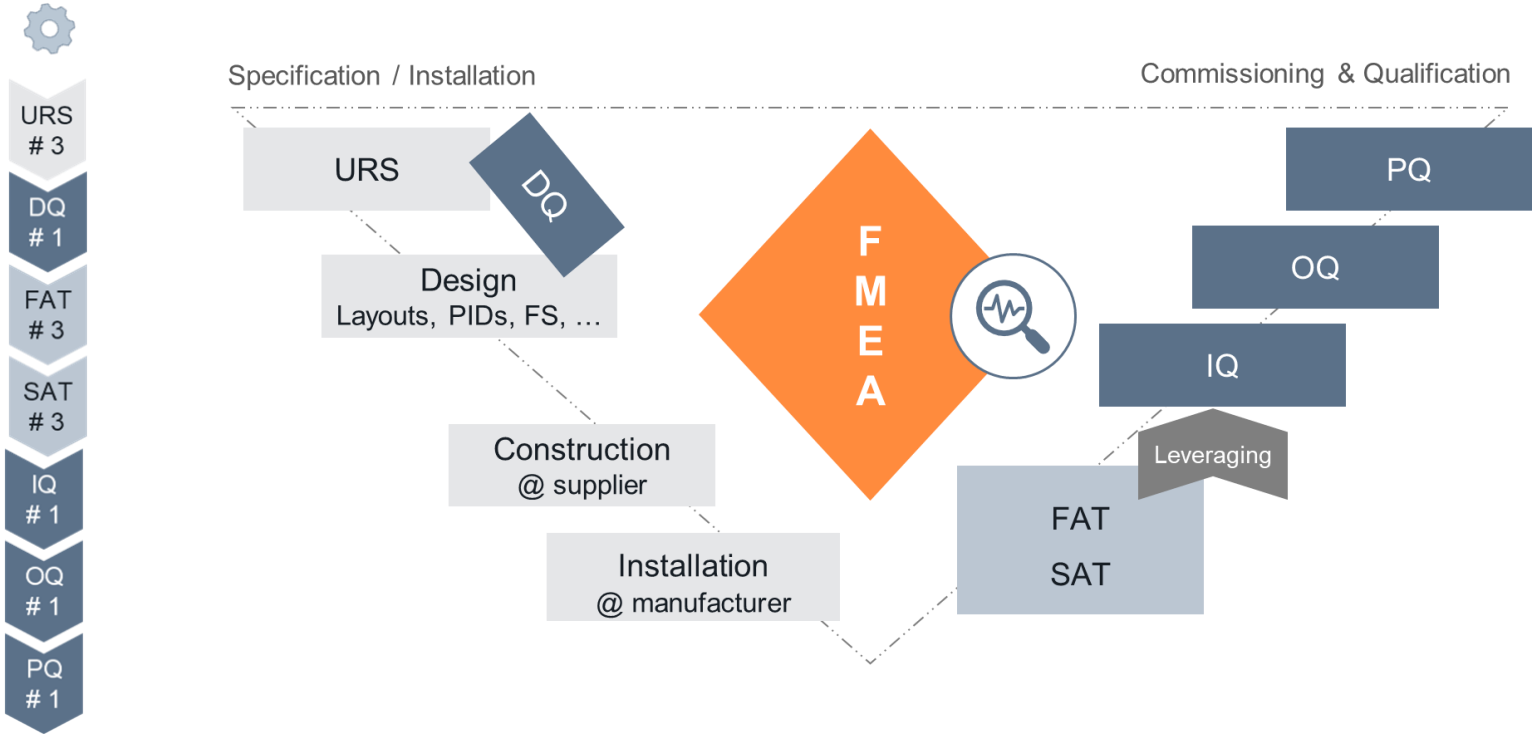


Manufacturing Plant:

- production equipment
- production / storage rooms
- media systems
- ...



FMEA - central planning tool for iC&Q extend

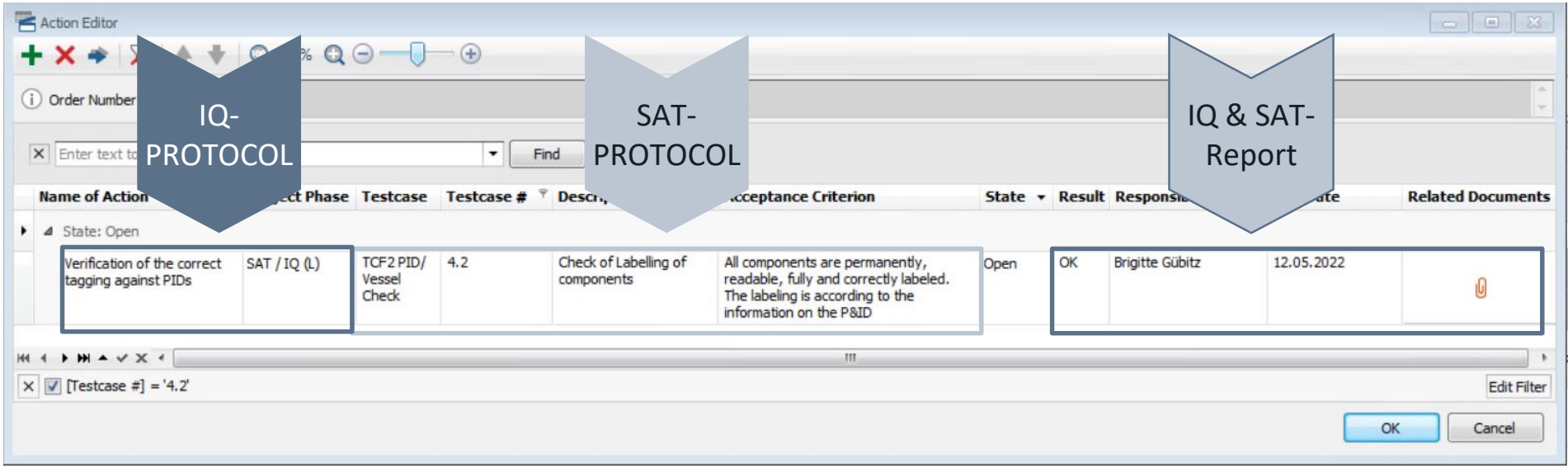


FMEA – incl. planning of “leveraging”

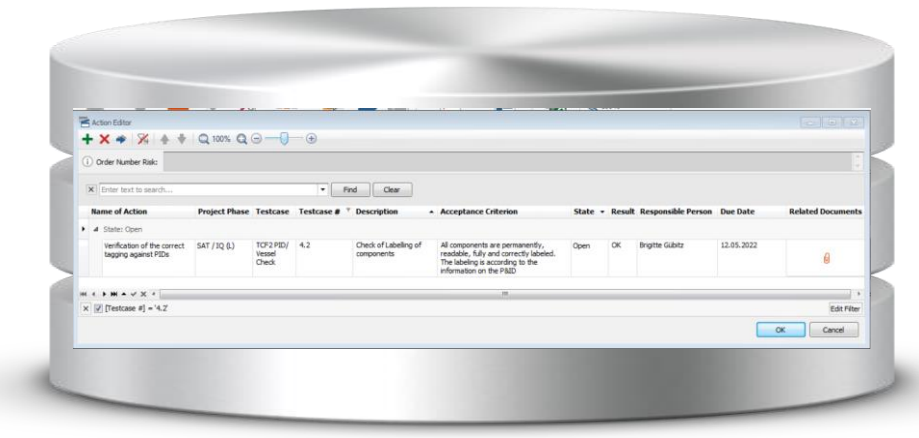
Number	UR.No.	UR Requirement	Effect	S1	FailureMode	Cause
URS: KRE-URS145-QA-102-Bacto_and_Central_Utility_Piping_DL_PL-01.00						
Installation of system						
7	UR-028 (QP)	The equipment requires a tagging number according to the MSD Krems tagging SOP KRE-SOP-xxxx	GMP conform maintenance is not possible	3	Installations are not tagged according to MSD SOP KRE-SOP-xxxx	Improper installation of tags

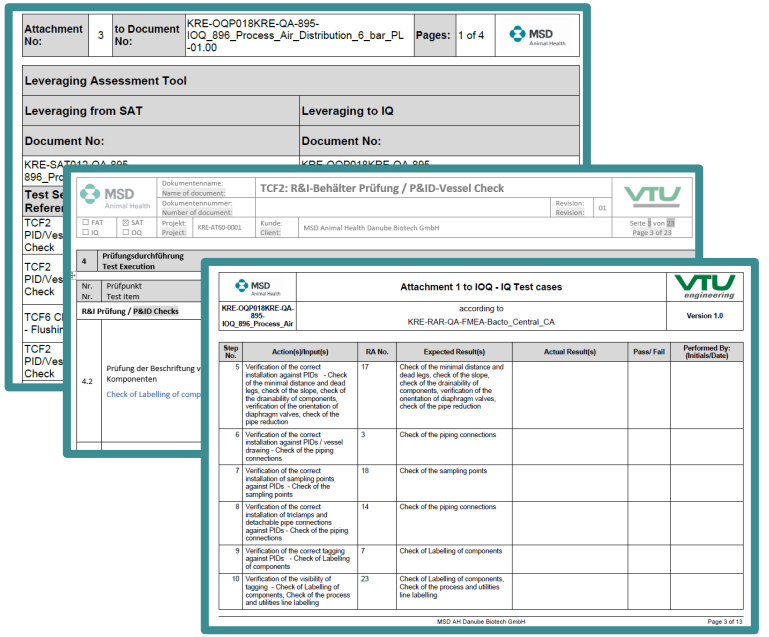
O1	D1	RPN1	Open Actions	O2	S2	D2	RPN2
4	4	48	▶ DQ: Verification of the correct tagging against PIDs ▶ SAT / IQ (L): Verification of the correct tagging against PIDs	1	3	1	3

Leveraging in FMEA – detail action list



FMEA – detail action list





One Data Source for

- all Comm. & Qualification protocols & reports
- results of C&Q execution

Example - SAT Protocol

MSD Animal Health	Dokumentenname: Name of document:	TCF2: R&I-Behälter Prüfung / P&ID-Vessel Check			VTU
	Dokumentennummer: Number of document:		Revision: Revision:	01	
☐ FAT ☐ IQ ☒ SAT ☐ OQ	Projekt: Project: KRE-AT60-0001	Kunde: Client: MSD Animal Health Danube Biotech GmbH			Seite 3 von 23 Page 3 of 23

4	**Prüfungsdurchführung** **Test Execution**

Nr. Nr.	Prüfpunkt Test item	Akzeptanzkriterium Acceptance criterion	Ergebnis Result	Kommentar Comment	Datum, Kürzel Date, Sign
R&I Prüfung / P&ID Checks					
4.2	Prüfung der Beschriftung von Komponenten Check of Labelling of components	Alle Komponenten sind dauerhaft und lesbar beschriftet. Die Beschriftung stimmt mit den Angaben des R&I-Schemas überein All components are permanently, readable, fully and correctly labeled. The labeling is according to the information on the P&ID	☐ OK ☐ NOK ☐ N/A		

Example – IQ - Protocol

MSD Animal Health	Attachment 1 to IOQ - IQ Test cases	VTU engineering
KRE-OQP018KRE-QA-895-IOQ_896_Process_Air	according to KRE-RAR-QA-FMEA-Bacto_Central_CA	Version 1.0

Step No.	Action(s)/Input(s)	RA No.	Expected Result(s)	Actual Result(s)	Pass/ Fail	Performed By: (Initials/Date)
5	Verification of the correct installation against PIDs - Check of the minimal distance and dead legs, check of the slope, check of the drainability of components, verification of the orientation of diaphragm valves, check of the pipe reduction	17	Check of the minimal distance and dead legs, check of the slope, check of the drainability of components, verification of the orientation of diaphragm valves, check of the pipe reduction			
6	Verification of the correct installation against PIDs / vessel drawing - Check of the piping connections	3	Check of the piping connections			
7	Verification of the correct installation of sampling points against PIDs - Check of the sampling points	18	Check of the sampling points			
8	Verification of the correct installation of triclamps and detachable pipe connections against PIDs - Check of the piping connections	14	Check of the piping connections			
9	Verification of the correct tagging against PIDs - Check of Labelling of components	7	Check of Labelling of components			
10	Verification of the visibility of tagging - Check of Labelling of components, Check of the process and utilities line labelling	23	Check of Labelling of components, Check of the process and utilities line labelling			

MSD AH Danube Biotech GmbH

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Example Leveraging Assessment - SAT/ IQ

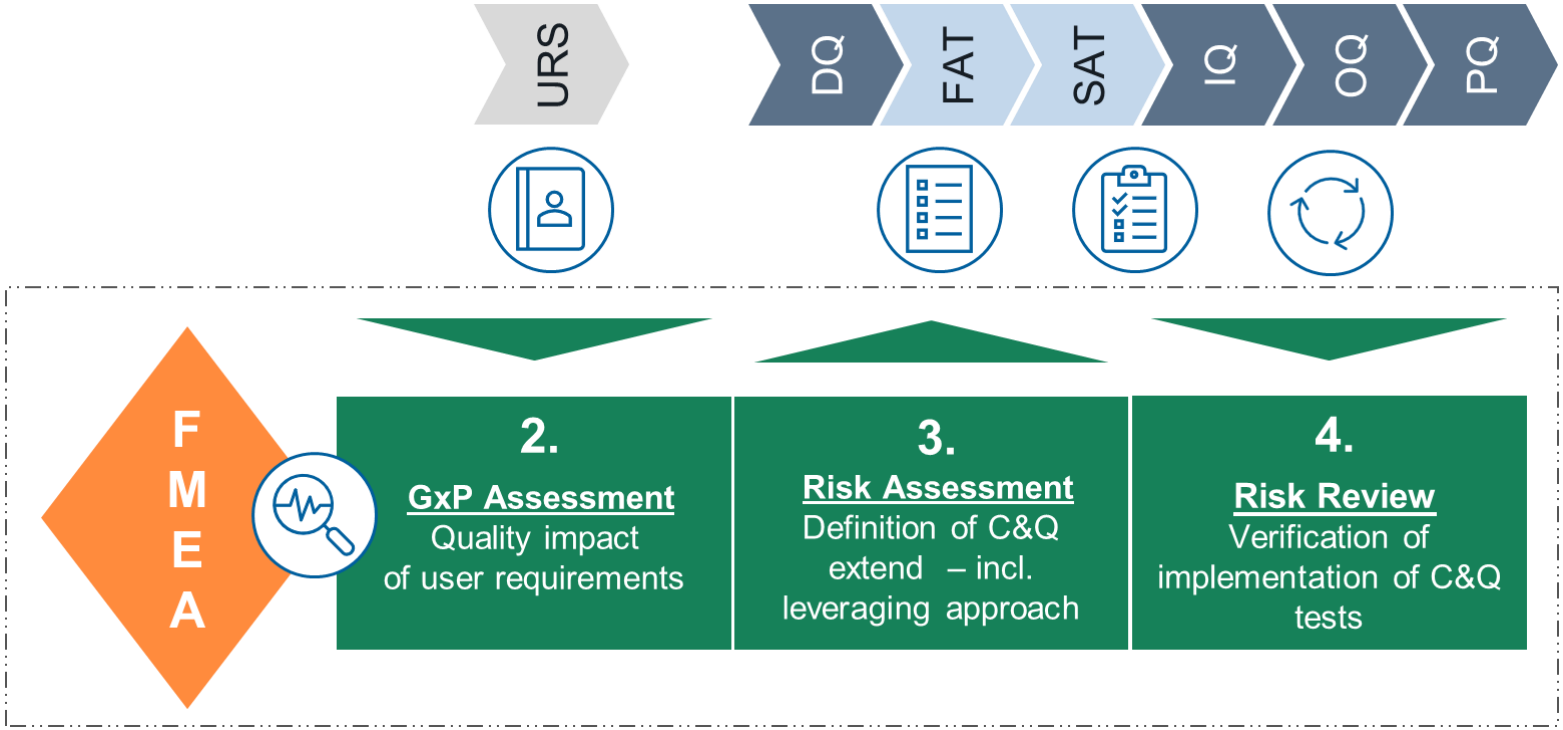
Attachment No:	3	to Document No:	IOQ_896_Process_Air_Distribution_6_bar_PL-01.00	Pages:	1 of 4	MSD Animal Health

Leveraging Assessment Tool			
Leveraging from SAT		**Leveraging to IQ**	
Document No:		**Document No:**	
KRE-SAT012-QA-895-896_Process_Air_Distribution_6_bar_PL-01.00		KRE-OQP018KRE-QA-895-IOQ_896_Process_Air_Distribution_6_bar_PL-01.00	
Test Sections Reference	**Test Reference / Title**	**Test Sections Reference**	**Test Reference / Title**
TCF2 PID/Vessel Check	RA - No.: 1 Verification of the correct installation against PIDs - AC: according to 4.1	PID/Vessel Check	RA - No.: 1 Verification of the correct installation against PIDs
TCF2 PID/Vessel Check	RA - No.: 3 Verification of the correct installation against PIDs / vessel drawing - AC: according to 4.8	PID/Vessel Check	RA - No.: 3 Verification of the correct installation against PIDs / vessel drawing
TCF6 Cleaning - Flushing	RA - No.: 6 Verification of cleaning / flushing protocol - AC: according to 4.1 - 4.4	Cleaning - Flushing	RA - No.: 6 Verification of cleaning / flushing protocol
TCF2 PID/Vessel Check	RA - No.: 7 Verification of the correct tagging against PIDs - AC: according to 4.2	PID/Vessel Check	RA - No.: 7 Verification of the correct tagging against PIDs

AGENDA

- MSD Animal Health in Krems - Video
- Integrated Commissioning & Qualification
  - Regulatory background
  - What is science & risk based iC&Q
- **Traceability-matrix as basis for an agile iC&Q strategy**
  - How to set up a risk-based life cycle traceability-matrix - right from the beginning
  - Paperless iC&Q - automated creation of (electronical) C&Q Documents

Risk based Commissioning & Qualification



2. GxP Assessment

- Evaluation of quality impact of each single user requirement
  - to identify they „critical aspects & design elements“
- User requirement are linked with the effects of the risk assessment
  - relation to product quality, critical process parameters, GMP requirements
  - quality influence is defined by the rating of the severity “S"

2. GxP Assessment

User requirement	Effect in FMEA	Severity
The quality of AP must meet the requirements for Purified Water ▪ Heavy metals: ≤ 0.1 ppm ▪ Nitrate: ≤ 0.2 ppm ▪ Conductivity: ≤ 4.3 µS/cm (20°C) ▪ Bioburden: ≤ 100 CFU/ml ▪ TOC: ≤ 500 ppb	Quality of media (AP) is not within specification	**5:** There may be adverse effects on product quality with damaging effects on health; recall of products

2. GxP Assessment - as part of FMEA

- Integration of URS / GxP Assessment into the FMEA

2-step Risk Analysis

REXS Risk Expert System

RPN2 :

Number	UR.No.	UR Requirement	Effect	S1	GxP relevance	FailureMode
3_Materials						
5	UR-008	The piping, equipment and valves should meet the requirements of the pipe classes and valve specs	Contamination of medium is possible/ insufficient cleaning	4	GMP critical	The equipment and piping does not comply with the process parameters specified in the pipe classes
4_Process relevant points						
6	UR-009	The quality of the medium produced (AP) must meet the requirements for purified water: - heavy metals: ≤ 0.1 ppm - nitrate: ≤ 0.2 ppm - conductivity: 4.3 µS/cm (20°C) - bioburden: ≤ 100 CFU/ml - TOC: ≤ 500 ppb	Quality of media is not within specification	5	GMP critical	Specification-compliant medium cannot be distributed (composition/ concentration/ purity)

3. Risk Assessment - as part of FMEA

- Risk Assessment defines
  - extend of commissioning & qualification testing
  - where & when C&Q tests are performed – incl. “leveraging approach”

2-step Risk Analysis

RPN2 :

REXS Risk Expert System

Number	UR.No.	UR Requirement	Effect	S1	GxP relevance	FailureMode	Cause	O1	D1	RPN1	Open Actions				
3_Materials															
5	UR-008	The piping, equipment and valves should meet the requirements of the pipe classes and valve specs	Contamination of medium is possible/ insufficient cleaning	4	GMP critical	The equipment and piping does not comply with the process parameters specified in the pipe classes	Wrong specification / implementation of materials	3	3	36	▸ DQ: Verification of specification (pipe class, valve specs) ▸ SAT / IQ (L): Verification material certificates (3.1) for stainless steel surfaces with product contact ▸ SAT / IQ (L): Verification material certificates for elastomers with product contact (USP Class VI)	1	4	1	4
4_Process relevant points															
6	UR-009	The quality of the medium produced (AP) must meet the requirements for purified water: - heavy metals: ≤ 0.1 ppm - nitrate: ≤ 0.2 ppm - conductivity: 4.3 µS/cm (20°C) - bioburden: ≤ 100 CFU/ml - TOC: ≤ 500 ppb	Quality of media is not within specification	5	GMP critical	Specification-compliant medium cannot be distributed (composition/ concentration/ purity)	Wrong specification / implementation of hygienic design / sterile process equipment	4	4	80	▸ SAT / IQ (L): Cleaning before commissioning ▸ SAT / OQ (L): Test run incl. AP-sampling / testing ▸ SAT / OQ (L): Verification of system sanitisation ▸ OQ: Verification of SOP sanitisation ▸ OQ: Verification of SOP sampling ▸ PQ: Performance Qualification of AP-system	1	5	1	5

3. Standardization in the FMEA

- Standardization supports
  - identical assessment of severity for same effect
  - Define consistent actions for risk mitigation

2-step Risk Analysis

GxP relevance :

Number	UR.No.	UR Requirement	Effect	S1	GxP relevance	FailureMode	Cause	O1	D1	RPN1	Open Actions	S2	O2	D2	RPN2
92	UR-032	Stainless steel used for product contact parts has a minimal quality of 1.4435 (ASTM 316L).	Contamination of medium is possible	4	GMP critical	Use of unsuitable metallic materials (with GW contact); use of reactive and shedding materials	Wrong specification / implementation of materials	4	4	64	► DQ: Verification of design/specification of metallic materials (with medium contact) ► SAT / IQ (L): Verification material certificates / surface finishing for stainless steel surfaces with product contact ► SAT / IQ (L): Verification of the correct installation against material and component list	4	1	1	4
93	UR-038	For all elastomers in direct contact with GW, material certificates according to USP class VI must be delivered.	Contamination of medium is possible	4	GMP critical	Use of non-compliant sealing materials / plastics (with product contact)	Wrong specification / implementation of materials	4	4	64	► DQ: Verification of design/specification of elastomers ► SAT / IQ (L): Verification material certificates of the supplier for elastomers with product contact (USP Class VI) ► SAT / IQ (L): Verification of the correct installation against material list	4	1	1	4
94	UR-019	A Control System to reduce the maximum withdrawal of PW needs to be installed to ensure a save supply to all users	Contamination of medium is possible	4	GMP critical	Turbulent flow in return line cannot be maintained	Wrong specification of withdrawal management	3	4	48	► DQ: Verification of design/specification ► SAT: Functional test of withdrawal management (setpoints, alarm, warnings, sequence of operations)	4	1	1	4
95	UR-119	For PW storage and distribution an ozon-strategy must be implemeted	Contamination of medium is possible	4	GMP critical	Ozon-strategy is not implemented for GW Central storage and distribution	Wrong specification / implementation of system	4	4	64	► SAT / OQ (L): Functional test of ozone measurement (setpoint, alarm, warnings, sequence of operations) ► SAT / OQ (L): Phase testing - sequence of operation: "permanent ozonisation without loop" ► SAT / OQ (L): Verification of software validation report ► SAT / OQ (L): Phase testing - sequence of operation: " periodic ozonisation of loop" ► PQ: Verification of ozonisation concept	4	1	1	4

3. Leveraging-Approach“ of FMEA

- No double testing:
  Commissioning tests (FAT/ SAT) are referenced in Qualification (IQ, OQ, PQ)
  - GEP relevant requirements → verification only during Commissioning
  - GMP relevant requirements → verification during Comm. & Qualification

The quality of AP must meet the requirements for Purified Water Heavymetalls: <0.1 ppm Nitrate: <0.2 ppm Conductivity: 4.3 µS/cm (20°C) Bioburden: 100 CFU/ml Endo Toxin: <0.25 EU/ml TOC: 500 ppb	5 QP	80	▶ SAT / IQ (L): Cleaning before commissioning ▶ SAT / OQ (L): Test run incl. AP-sampling / testing ▶ SAT / OQ (L): Verification of system sanitisation ▶ OQ: Verification of SOP sanitisation ▶ OQ: Verification of SOP sampling ▶ PQ: Performance Qualification of GW system

3. Points to consider

- Include leveraging already in C&Q strategy
- Close alignment with supplier in case of vendor commissioning
  - Prepare and align vendor commissioning/documents with FMEA actions and qualification requirements
- Quality oversight already during commissioning
- Tracking of non-critical deficiencies from commissioning to qualification

3. Lessons learned from the Project

- Cluster identical tests to reduce number of open actions
- Be one step ahead the project schedule with C&Q activities

2-step Risk Analysis

Implemented Actions :

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Number	UR.No.	UR Requirement	Effect	S1	GxP relevance	FailureMode	Cause	O1	D1	RPN1	Open Actions	S2	O2	D2	RPN2
111	UR-010 (QP)	In the GW return line a temperature measurement needs to installed to control the GW-Loop Temperature	Preparation and distribution of a specification conform media is not possible	4	GMP critical	Temperature in the system (return line) can not be measured / controlled correctly	Wrong specification / implementation regarding measuring sensor, defect of measuring sensor; malfunction of automated process; incorrect calibration	4	4	64	► DQ: Verification of design/specification in PIDs ► SAT / IQ (L): Verification of the correct installation against PIDs ► SAT / IQ (L): Verification of calibration certificates of vendor ► SAT / IQ (L): Definition of re-calibration intervals (by vendor) ► SAT / OQ (L): Functional test of temperature measurement (setpoint, alarm, warnings, sequence of operations) ► OQ: Verification of SOP calibration incl. Recalibration	4	1	1	4
112	UR-011 (BEA)	After the Loop pump in the supply line a pressure measurement needs to be installed	EHS risk - no GMP risk	1	not critical	Pressure in the system (return line) can not be measured / controlled correctly	Wrong specification / implementation regarding measuring sensor, defect of measuring sensor; malfunction of automated process; incorrect calibration	4	4	16	► DQ: Verification of design/specification in PIDs ► SAT: Verification of the correct installation against PIDs ► SAT: Verification of calibration certificates of vendor ► SAT: Functional test of pressure measurement (setpoint, alarm, warnings, sequence of operations) ► SAT: Definition of re-calibration intervals (by vendor) ► OQ: Verification of SOP calibration incl. Recalibration	1	1	1	1
113	UR-013 (QP)	A conductivity measurement in the loop return line needs to be installed.	Preparation and distribution of a specification conform media is not possible	4	GMP critical	Conductivity in the system (return line) can not be measured / controlled correctly	Wrong specification / implementation regarding measuring sensor, defect of measuring sensor; malfunction of automated process; incorrect calibration	4	4	64	► DQ: Verification of design/specification in PIDs ► SAT / IQ (L): Verification of the correct installation against PIDs ► SAT / IQ (L): Verification of calibration certificates of vendor ► SAT / IQ (L): Definition of re-calibration intervals (by vendor) ► SAT / OQ (L): Functional test of conductivity measurement (setpoint, alarm, warnings, sequence of operations) ► OQ: Verification of SOP calibration incl. Recalibration	4	1	1	4

4. Risk Review

- Verification of correct implementation of measures during C&Q phases
  - update of test status in traceability matrix (open → implemented)
  - actual project status is available during project life cycle at any time

REXS Risk Expert System

Location	Project Phase	Name of Action	Description	Acceptance Criterion	Responsible Person
IR 5	DQ	Verification of specification (pipe class, valve specs)	Verification that requirements specified in vessel datasheet comply to vessel	Requirements specified in vessel datasheet comply to vessel drawing	Brigitte Gübitz
IR 5	SAT / IQ (L)	Verification of material certificates (3.1) for stainless steel surfaces with product contact	Verification of material certificates (3.1) / surface finishing testing for all metallic surfaces with direct product contact	All re surfa mate class	
IR 5	SAT / IQ (L)	Verification of material certificates for elastomers with product contact (USP Class VI)	Verification of certificate for all seals, O-rings, membranes - FDA, USP Class VI, <87> or <88> certificates	All re elast avail	

State	Due Date	Reference
Implemented	04.04.2022	DQ Report 12345 - # 27
Open		
Open		

From FMEA to Trace matrix

URS
- Integrated & evaluated in FMEA

FMEA
- Planning of C&Q tests

Output of FMEA
- C&Q documents

Execution of C&Q
- Documentation in FMEA

Risk Review
- Documentation of execution and changes in FMEA
- Review of finalization of C&Q measures

FMEA → Tracematrix

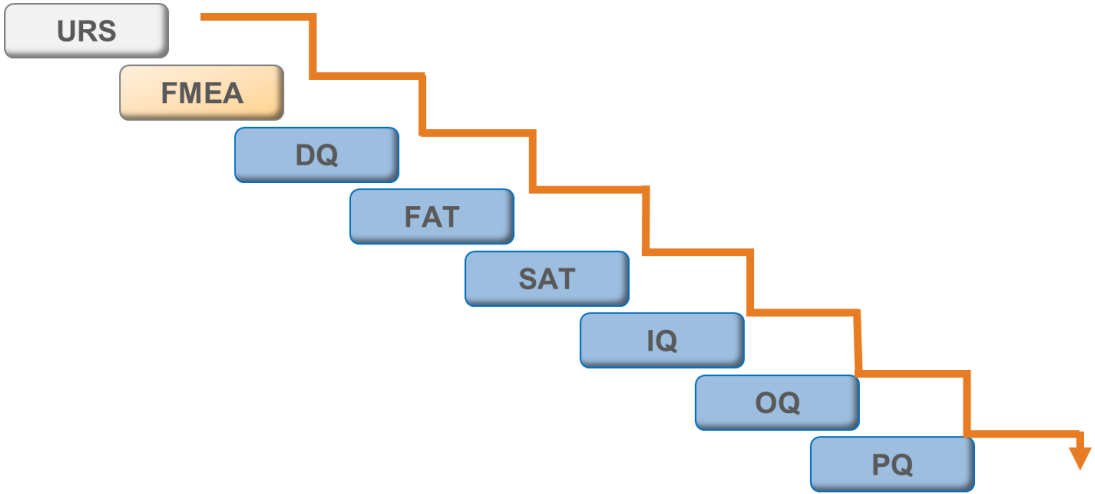
No.	Equipment/ Process	URS Requirement	Analysis: Failuremode	Analysis: Cause	Analysis: Effect	Implemented Actions	Rating: O	Rating: S	Rating: D	Rating: RPN	Open Actions	Final Rating: O	Final Rating: S	Final Rating: D	Final Rating: RPN
Configuration system															
1	- AP utility piping	DEMO_URS_567_AP_Utility_Piping-01.00 - UR-001 (QP) The following items must be available for the AP System: 1. Connection from the AP distribution System to AP tank 2. One pump and loop system suppling the AP Users 3. Gas inlet/exhaust with two redundant filters and CO2 traps 4. Ozone Generator 5. UV-Lamp 6. Heat exchanger for cooling 7. Connection to CS system to sanitize tank an pumps 8. Rupture disc and safety valve at vessel 9. Automated Sampling points at strategic locations in the API Loop return	Configuration / Installation does not comply with approved planning documents	Improper installation	Preparation and distribution of a specification conform media is not possible		3	4	4	48	► DQ: Verification of design/specification in PIDs ► SAT / IQ (L): Verification of the correct installation against PIDs or vessel drawing	1	4	1	4
2	- AP tank	DEMO_URS_123_AP_tank-01.00 - UR-009 (BEA) The following top items must be available on the vessel: 1. Transfer line for receiving of AP from existing loop 2. Gas inlet/exhaust. 3. Rupture disc with safety valve 4. Pressure gauge 5. Pressure switch 6. Sight glass and light 7. Two Additional spare ports for Validation purposes 8. Level gauge 9. Level switch for overfill protection 10. Manhole	Configuration / Installation does not comply with approved planning documents	Improper installation	Preparation and distribution of a specification conform media is not possible		3	4	2	24	► DQ: Verification of design/specification in PIDs or vessel drawing ► SAT: Verification of the correct installation against PIDs or vessel drawing	1	4	1	4
3	- AP utility piping	DEMO_URS_567_AP_Utility_Piping-01.00 - URS: RA-004 (QP) System has to be connected to following systems: - Clean steam - Prozess drain - compressed air / process air - chilled water supply/return - HVAC cooling water	Configuration / Installation of media connections does not comply with approved planning documents	Improper installation	Preparation of a specification conform media is not possible		3	4	3	36	► SAT / IQ (L): Verification of the correct installation against PIDs	1	4	1	4
4	- AP tank	DEMO_URS_123_AP_tank-01.00 - UR-010 (BEA) The following items must be available for the lower part of the vessel 1.A route from the bottom for transfer of vessel contents 2.Temperature probe should be located in a way to monitor the temperature at the minimum working volume	Configuration / Installation does not comply with approved planning documents	Improper installation	Preparation and distribution of a specification conform media is not possible		3	4	2	24	► DQ: Verification of design/specification in PIDs or vessel drawing ► SAT: Verification of the correct installation against PIDs or vessel drawing	1	4	1	4
5	- AP tank	DEMO_URS_123_AP_tank-01.00 - UR-014 (BEA) The vessel must be equipped with a sight glass with clear visibility of the contents and a light switch in close proximity.	Content of tank is not visible from outside	Wrong specification/ implementation regarding system	Business risk, no GMP risk		3	1	2	6	► DQ: Verification of design/specification in PIDs or vessel drawing ► SAT: Verification of the correct installation against PIDs or vessel drawing	1	1	1	1

What is a Traceability Matrix?

- Should demonstrate the relationship between
  - the user requirements
  - the risk assessment
  - the commissioning and qualification test and their results
- Used to
  - Track requirements & prove that requirements have been fulfilled

What is a Traceability Matrix?

- In C&Q projects the TM is normally created to trace forward
  - from requirements → to risk analyses → to the test cases



Example of a Trace Matrix

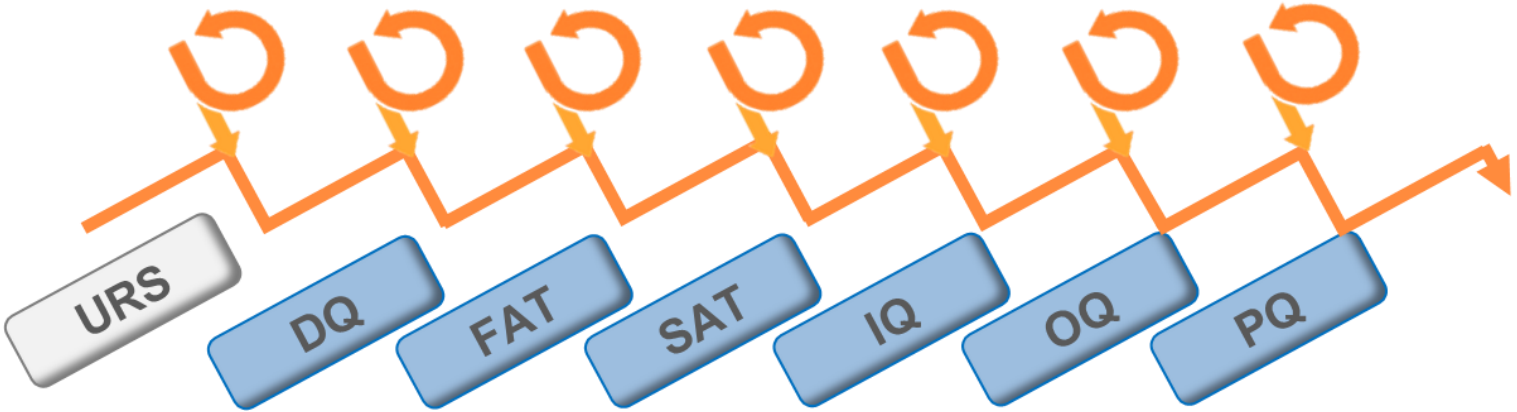
LOGO	Traceability Matrix according to FMEA 001 for Aqua purificata [example]	REXS Risk Expert System	VTU engineering
Created with: REXS	CQTM_01.00		Version 1.0

1. Traceability Matrix

URS Requirement	RA No.	Equipment / Failure Mode / Effect	Open Actions
URS001_AP_Storage_Tank-01			
UR-001 (QP) The following top items must be available on the vessel: 1. Gas inlet/exhaust. 2. Rupture disc with safety valve 3. Pressure gauge 4. Pressure switch 5. Sight glass and light 6. Additional spare ports 7. Level gauge 8. Level switch for overfill protection	2	T001 - AP Storage Tank Failure Mode: Configuration / Installation does not comply with approved planning documents Effect: Preparation and distribution of a specification conform media is not possible	**DQ:** Verification of design/specification in PIDs or vessel drawing; Status DQ: Released [Document: DQ–Report 001, Verification of components for the top part of vessel -Test #: 4; verified by: B. Gübitz, 13.01.21)] **SAT / IQ (L):** Verification of the correct installation against PIDs or vessel drawing Commissioning Status: Verified [Document: SAT-Report 3412, Testcaseform 1: PID/Vessel Check - Test #: 2; verified by: M. Muster, 14.05.21)] Qualification Status: Released [Document: IQ-Report 001 – Chapter 2: PID/Vessel Check Test # 3: Verification of installation of top components of vessel; verified by: B. Gübitz, 13.08.21)]
UR-002 (BEA) The following items must be available for the lower part of the vessel 1.A route from the bottom for transfer of vessel contents 2.Temperature probe 3. Additional spare ports	3	T001 - AP Storage Tank Failure Mode: Configuration / Installation does not comply with approved planning documents Effect: Preparation and distribution of a specification conform media is not possible	**DQ:** Verification of design/specification in PIDs or vessel drawing; Status DQ: Released [Document: DQ–Report 001, Verification of components for the lower part of vessel -Test #: 5; verified by: B. Gübitz, 13.01.21) **SAT / IQ (L):** Verification of the correct installation against PIDs or vessel drawing Commissioning Status Verified [Document: SAT-Report 3412, Testcaseform 1: PID/Vessel Check - Test #: 2; verified by: M. Muster, 14.05.21)] Qualification Status: Released [Document: IQ-Report 001 – Chapter 2: PID/Vessel Check Test # 4: Verification of installation of top components of vessel; verified by: B. Gübitz, 13.08.21)]
UR-003(QP) The vessel and the associated pipework should be completely drainable without local puddles of liquid.	8	T001 - AP Storage Tank Failure Mode: Piping, valves and equipment are not completely drainable Effect: Contamination of medium is possible/ insufficient cleaning	**SAT / IQ (L):** Verification of self-drainability of system Commissioning Status Verified [Document: SAT-Report 3412, Testcaseform 3: Verification of drainability of system - Test #: 1; verified by: T. Test, 21.05.21)] Qualification Status: Released [Document: IQ-Report 001 – Chapter 4: Installation Tests # 5: Verification of self-drainability of Storage tank; verified by: B. Gübitz, 19.08.21)]
UR-004 (QP) A logbook and SOPs must be created during the qualification of the unit	11	T001 - AP Storage Tank Failure Mode: Maintenance cannot be documented in a logbook Effect: GMP conform maintenance is not possible	**OQ:** Verification of existence of electronical logbook for GW system Qualification Status: Open

Trace Matrix as project management tool

- FMEA- Tracematrix bidirectional
  - Revision of FMEA at performance of each C&Q step
  - Documentation of results and changes

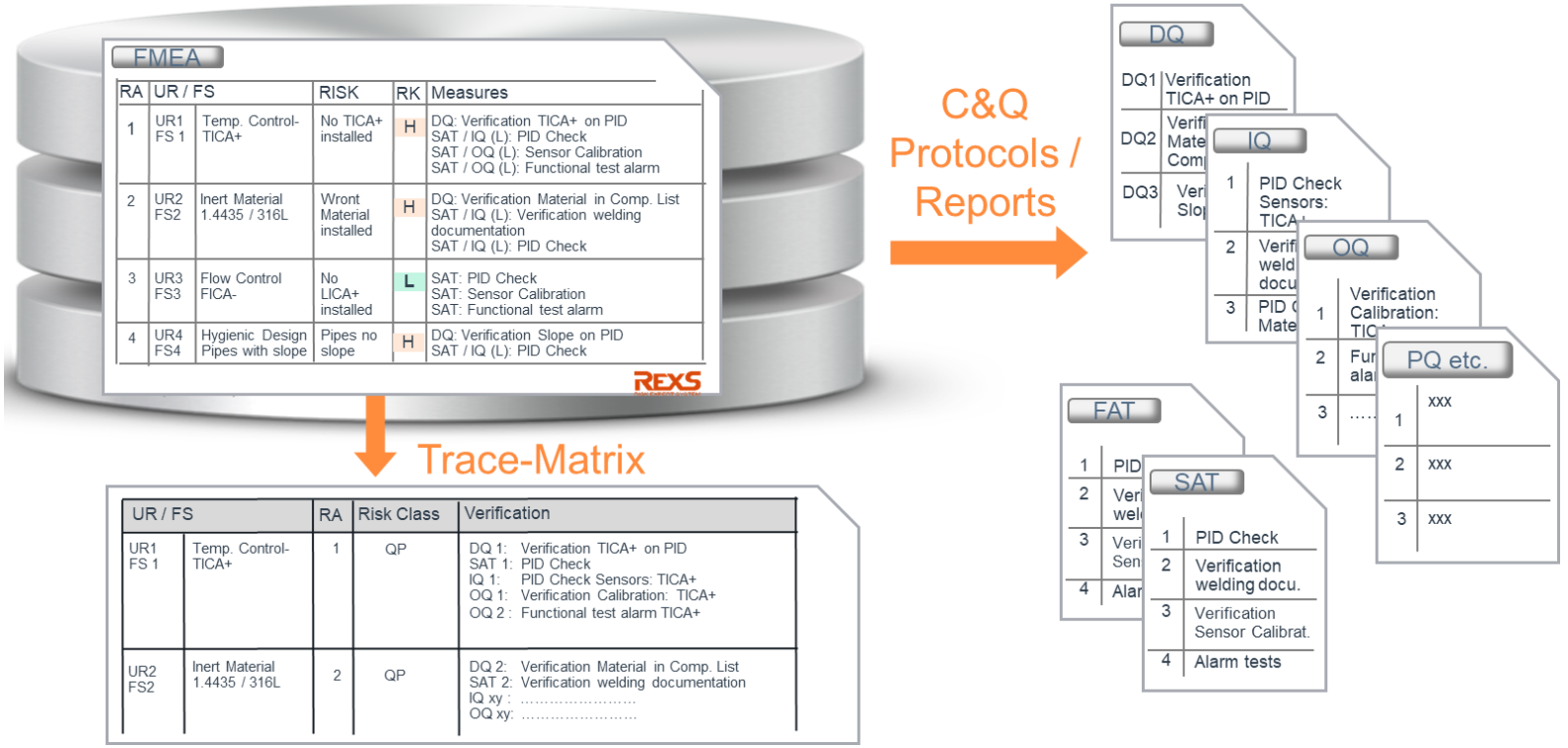


Risiko-Management 4.0 @ VTU

- Knowledge based creation of FMEAs / Tracematrix
  - by using the REXS knowledge database
- Automated creation of Comm. & Qualification documents
  - within a mouse- click from the FMEA

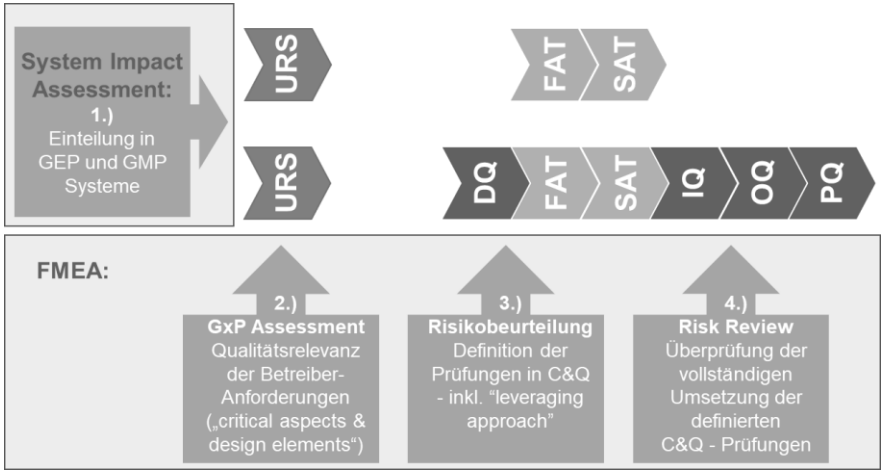
+ Higher quality, consistency and efficiency

Automated creation of documents @ VTU



Advantages risk based iC&Q

- Impact Assessment
  - Qualification only for GMP relevant systems / requirements
- FMEA defines C&Q extend
  - Commissioning (FAT/SAT) on the bases of product & process requirements
    → not only supplier „standard-tests“
  - Leveraging Approach: no “double – testing” by fully integration of suppliers FAT/SAT verifications into qualification

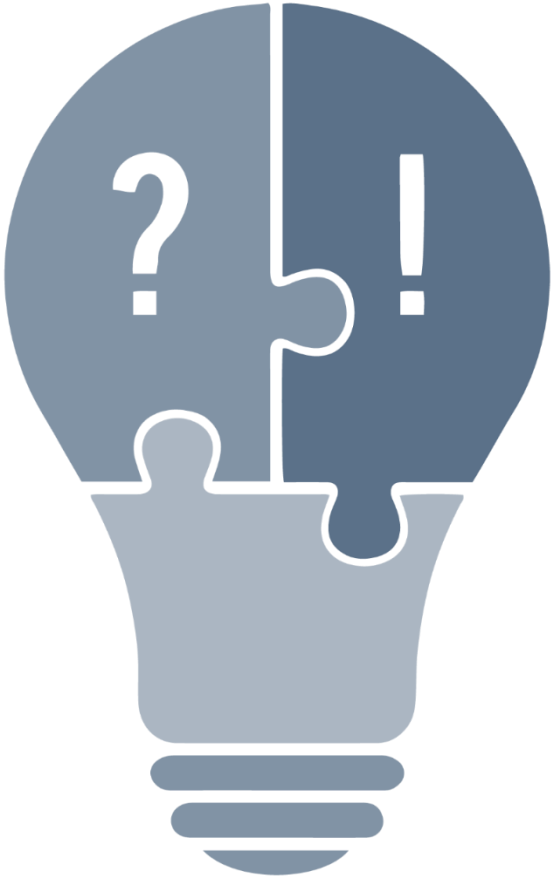


Advantages automated iC&Q

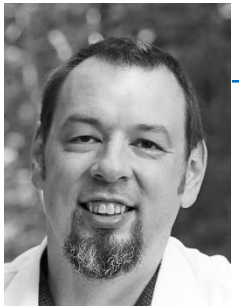
- Higher consistency, efficiency and easy change management
  - Automated creation of iC&Q documents → Time savings & no “copy” errors
  - Changes at a central point (FMEA) → automated update of all relevant documents
  - Traceability Matrix from the beginning → The implementation status of C&Q is visible at any time

Thank you for your attention

QUESTIONS ?



Thank you for your attention!



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