



Validation/Qualification – Design
Review & DQ
A Scalable Process

Agenda

- Definitions
- Concept of scalable qualification
- Suggestions
- Examples

DQ from Annex 15

- "The documented verification that the proposed design of the facilities, systems and equipment is suitable for the intended purpose."

(EU-GMP/PIC-S Guideline, Annex 15)

A very broad remit – GMP, Process Critical not mentioned. (of course Annex 15 is a GMP related document)

Design Review from GAMP 5

- Design Reviews evaluate deliverables against standards and requirements, identify issues, and propose required corrective actions.
- They are planned and systematic reviews of specifications, design, and development performed at appropriate points throughout the life cycle of the system.
- They are an important part of the verification process.
- Design Review should be performed by appropriate Subject Matter Experts (SMEs). The individuals performing the review should be identified.
- The rigor of the design review process and the extent of documentation should be based on risk, complexity, and novelty.

Scalability from GAMP 5

- GAMP 5 is not prescriptive. All lifecycle activities and associated documentation are to be scaled according to risk, complexity, novelty. (Some examples):

Scalability from GAMP 5

- **PRODUCT RISK:**
 - manufacturing process control = high risk,
 - database containing training records = low risk.
- **Complexity:**
 - SAP = high complexity,
 - Excel spreadsheet calculating lab results = low complexity.
- **Novelty:**
 - Excel = used by millions worldwide, lab instrument, PC software = well established = low risk
 - In-house developed application - used only by the company that developed it = high risk

Scalability from GAMP 5

- GAMP 5 - all about risk.
- Increasing Product Criticality, complexity and/or novelty = higher risk = more effort and deliverables.

Scalability for Systems and Equipment – Scales Example

- Weigh scales
 - Balance on bench
 - = simple, standard, recognised vendor.
 - Automated dispensing weighing system; scales built in, connected to dispensing computerised system
 - = complex, unique, novel.

Scalability for Systems and Equipment

– Water System Example

- Purified water system
 - Complex
 - Unique – designs are different
 - Many different technical solutions possible

Scalability for Systems and Equipment – Sunscreen Example

- Sunscreen formulation system - Traditional Batch process
 - Relatively standard practice. Not novel.
 - Simple
- Sunscreen formulation system – Continuous process
 - Novel
 - Complex
 - Sophisticated process control and automation – mass flow metering, in-line mixing, on-line QC.

Scalability for Systems and Equipment - principle

- Potential for scalability principle:
 - 1. Product Quality Risk
N/S Sunscreen → Parenteral Cytotoxic.
 - 2. System Complexity
 - 3. System Novelty
 - 4. Vendor Confidence (only determined how much work to pass down, not what is done).

Impact of scale on Design Review

- The simple weigh scale
 - Low product quality risk.
 - Simple.
 - Standard kit.
 - Recognised vendor.
- All we need to do is a simple documented **"Specification Verification"**.

Impact of scale on Design Review

- The Pharma Purified Water System
 - High product quality risk.
 - Complex.
 - Unique system.
 - Recognised vendor.
- Need a rigorous process SME lead.
 - URS compliance check.
 - Walk-through analysis of functionality, suitability, and performance intentions. [Good example is microbiological control measures].

DQ/Design Review Tools

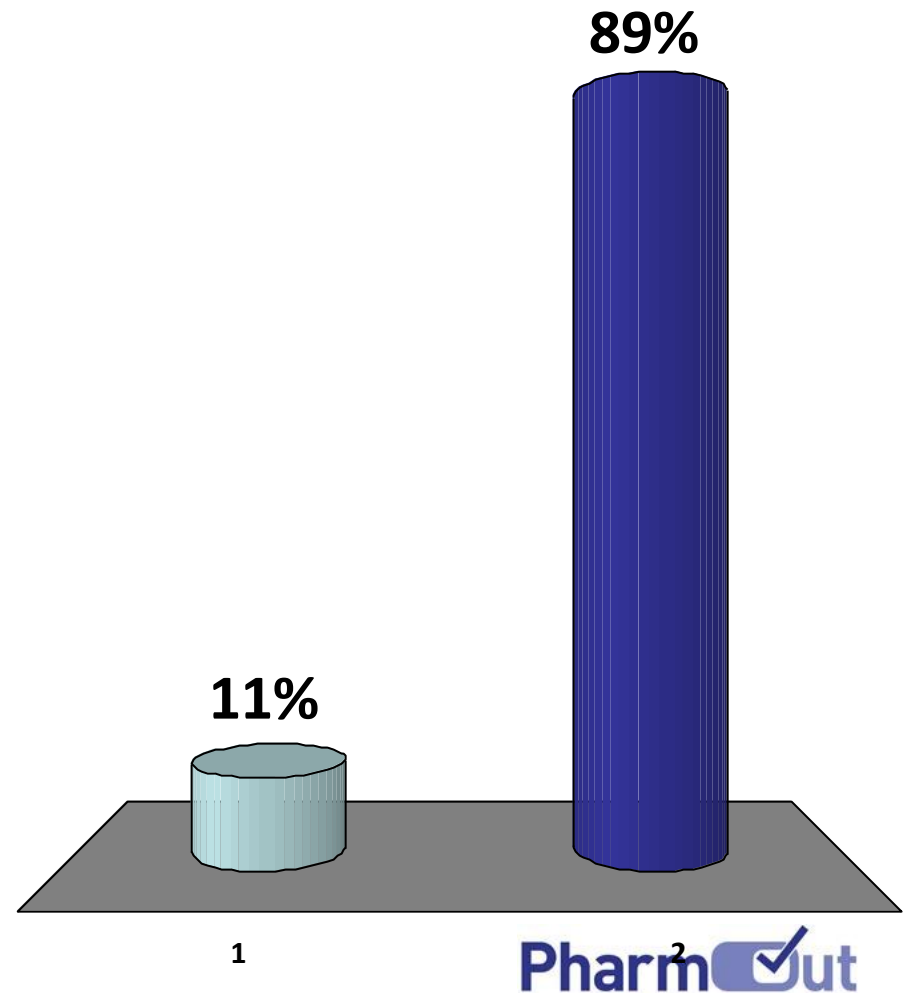
Confirming URS

Figure 2 : Example of a trace matrix [4]

UR no.	UR text	TR no.	TR text	Spec. no.	Specification	Test number	Comments
UR 1.1	Use of rust-free stainless steel	TA 1.1.1	1.4571 or higher is to be used.	SP 1.1	1.4435	IQ 1.1	Material is high quality and is therefore accepted.
		TA 1.1.2	The material must be verified.	SP 1.2	3.1B Attestation	IQ 1.1	-
				SP 1.3	Material confusion test	IQ 1.1	to be carried out with documentation
UR 1.2	Smooth surface	TA 1.2.1	Roughness depth \square Ra < 0.8 μ m	SP 1.4	Hand cut with grain 400	IQ 1.2	-
				SP 1.5	Surface roughness measurements with record	IQ 1.2	Record and number of test points is to be defined.

From what you have heard, and the workshops which feels best to you?

1. Scale validation effort based on Product Risk/Criticality
2. Scale validation effort by some measure of product Risk/Criticality + System Complexity + Novelty



Equipment vendors. Do you qualify them in some way?

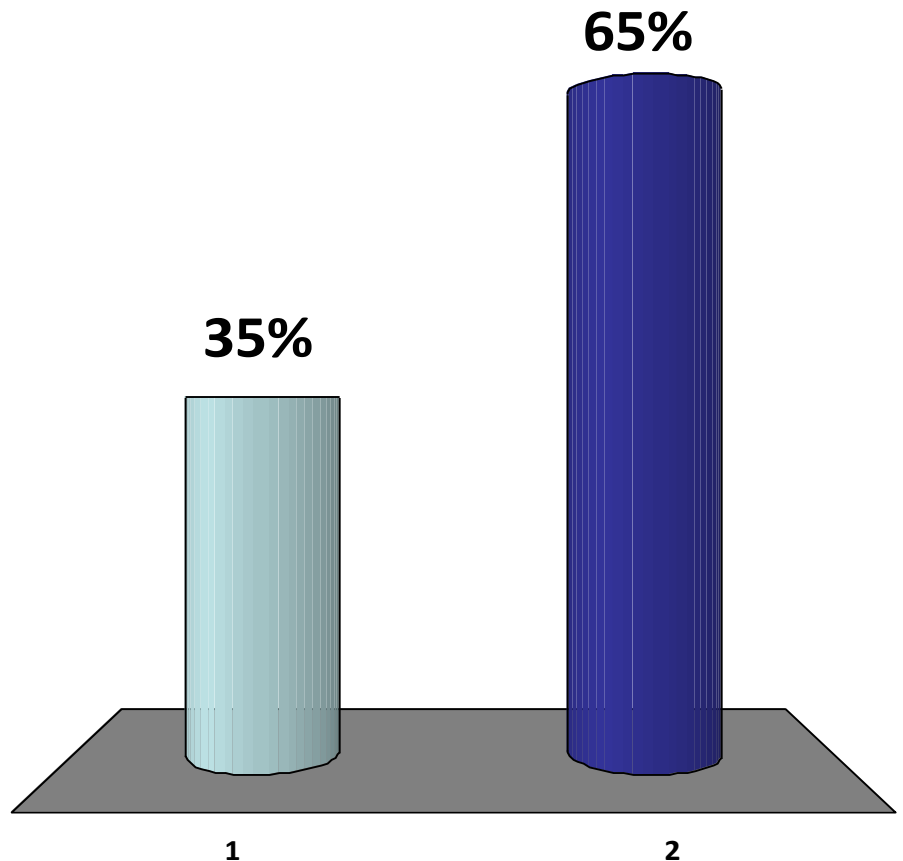
(could be previous experience → formal audit)

79% 1. Yes

21% 2. No

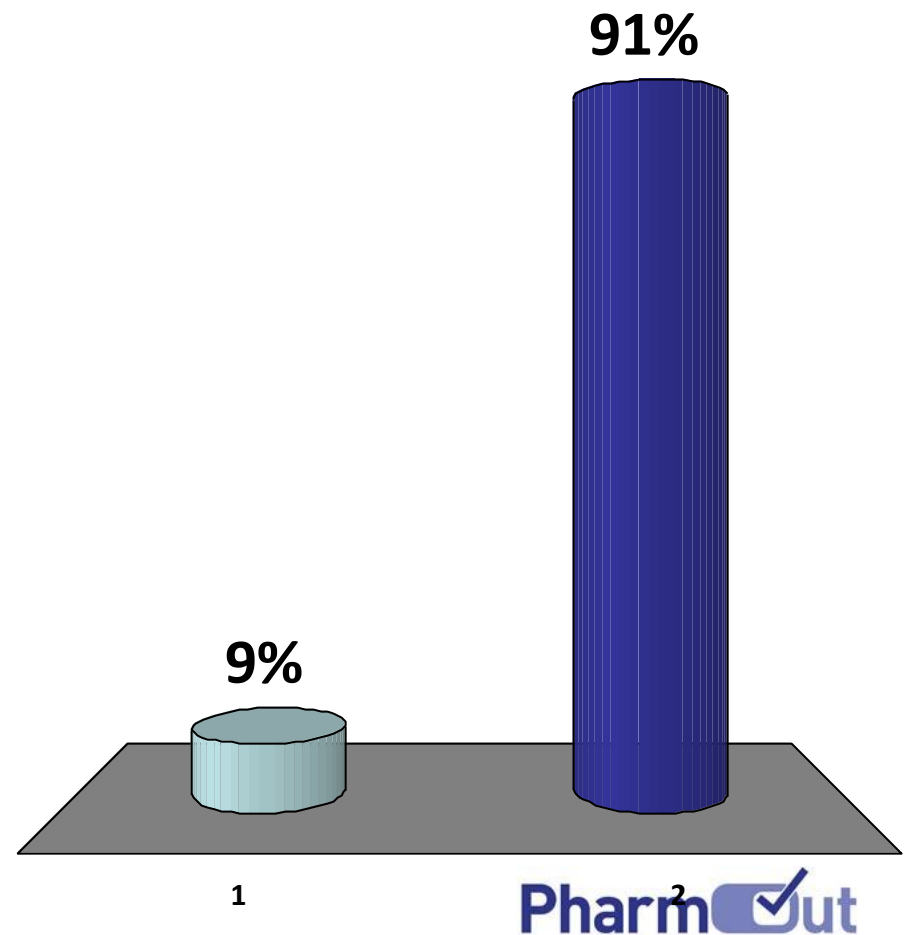
Product contact materials certificate evidence:

1. Required for all categories of product.
2. Different for different categories of products.



When considering a simple item of equipment (weigh scale), how would you qualify the vendor?

1. Visit the firm and review their quality system, manufacture/assembly operation, etc.
2. Arms length- Check track record and if necessary take up some references.



Conclusion

- Scalable approach
 - Fits Annex 15
 - Needs clear plan and rationale
 - Already accepted in GAMP 5
- Still need a VMP.
- Next step: Maybe should develop more examples of the scale and DR, Verification & Testing (IQ, OQ, PQ), scope for typical product types and equipment.
- What is the next step?

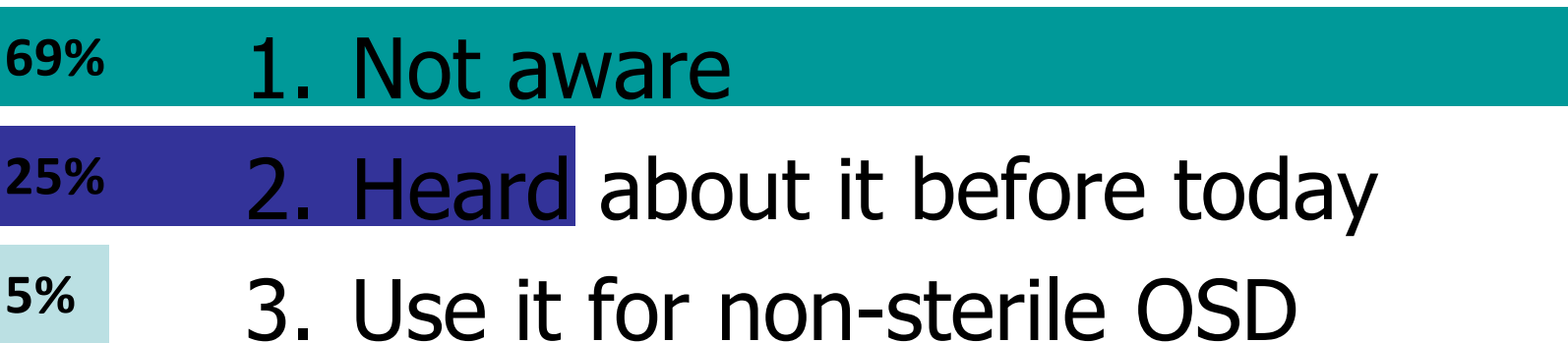
SOME OTHER QUESTIONS

Are you aware of this WHO Guidance

© World Health Organization
WHO Technical Report Series, No. 961, 2011

Annex 5

Supplementary guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms



Thanks for your attention