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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 micro-biological 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 there-fore 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 sur-face	TA 1.2.1	Roughness depth Ra < 0.8 µm	SP 1.4	Hand cut with grain 400	IQ 1.2	-
				SP 1.5	Surface rough-ness measure-ments with record	IQ 1.2	Record and number of test points is to be defined.

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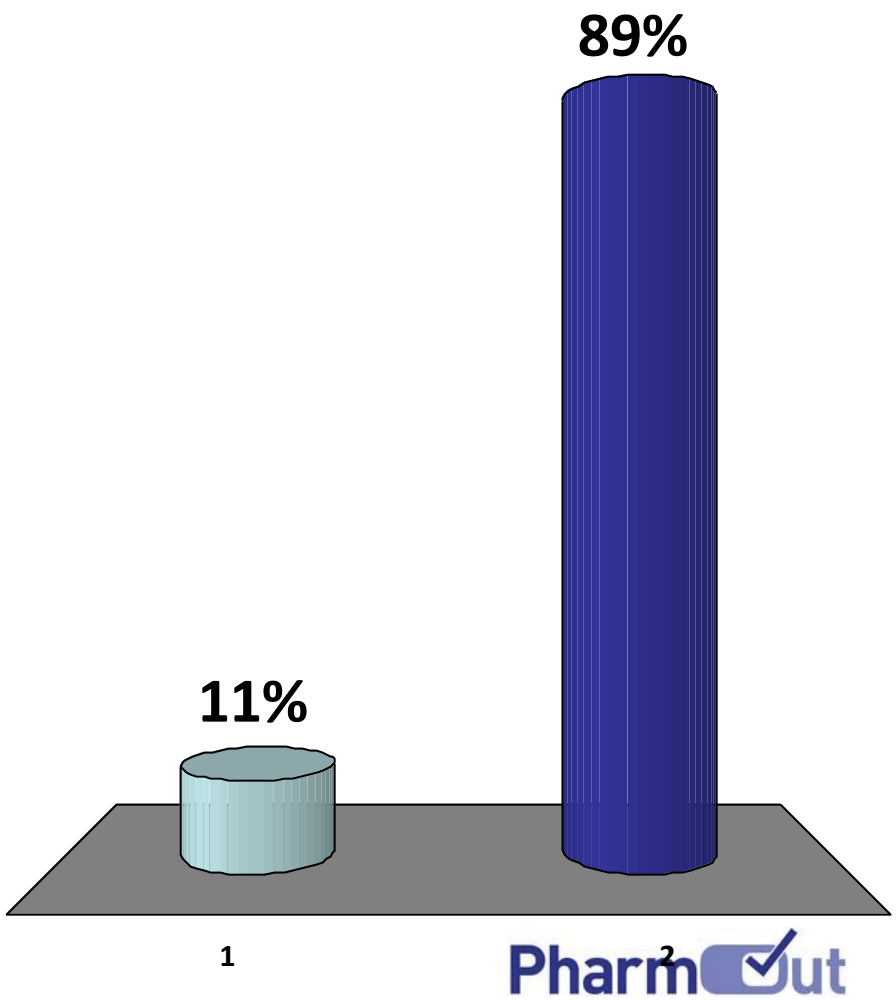
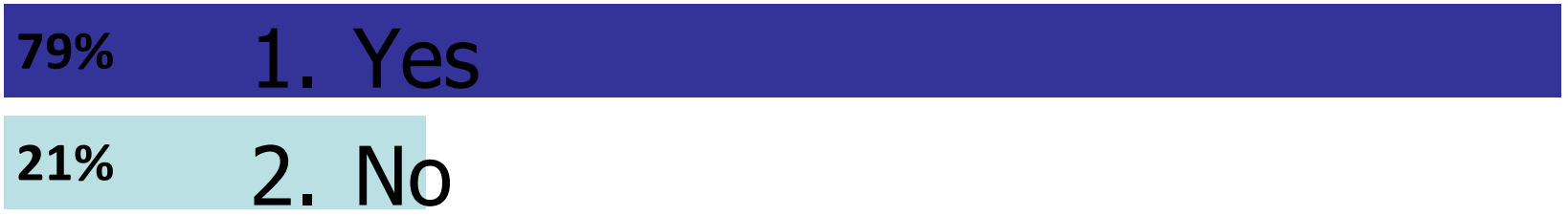
From what you have heard, and the workshops which feels best to you?

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)



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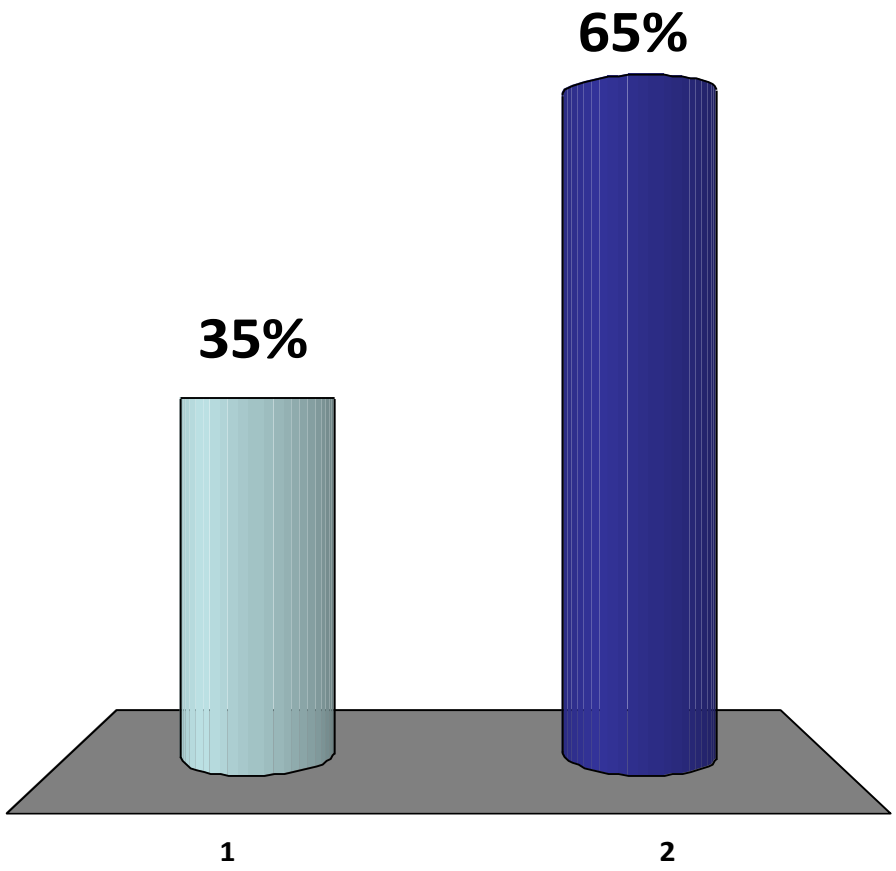
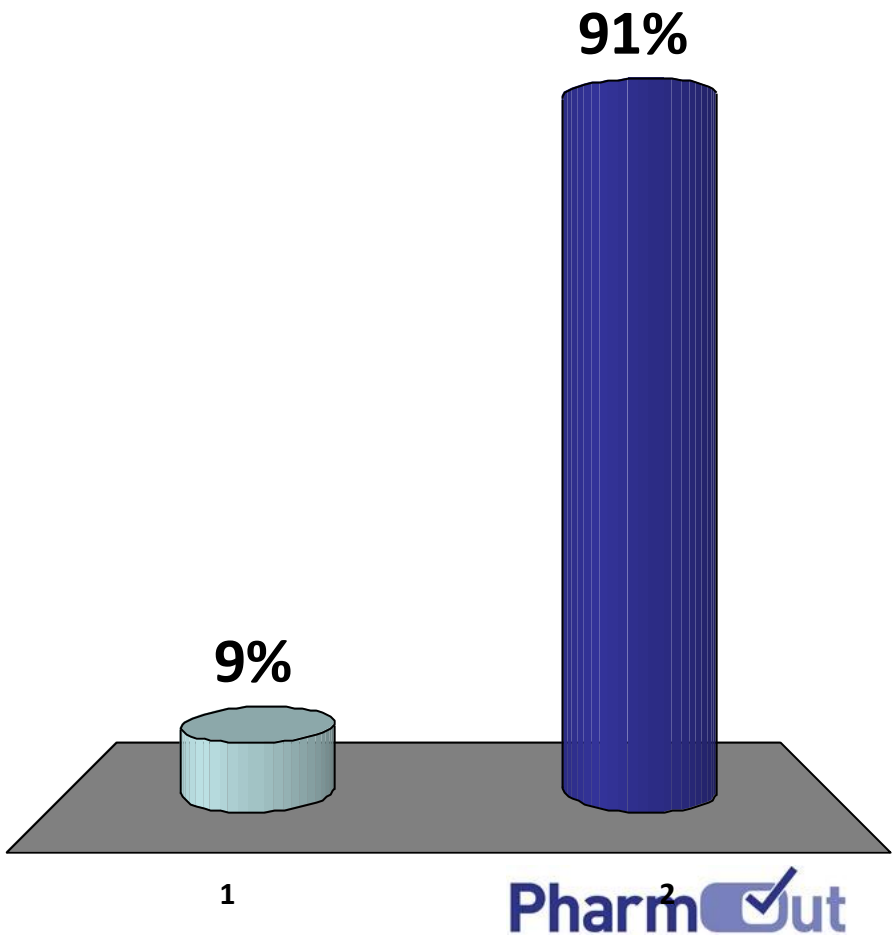
Product contact materials certificate evidence:

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

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Are you aware of this WHO Guidance

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

69% 1. Not aware

25% 2. Heard about it before today

5% 3. Use it for non-sterile OSD

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Thanks for your attention

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