Computer System Validation in the Pharma Laboratory - 10 years of GAMP 5, Pitfalls and Best Practices

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Presentation Overview

Approach to CSV and common challenges with implementing GAMP 5

My Bio...

I am currently the Global SME for Computer System Validation and the Practice Manager for PerkinElmer's Compliance and Validation Services.

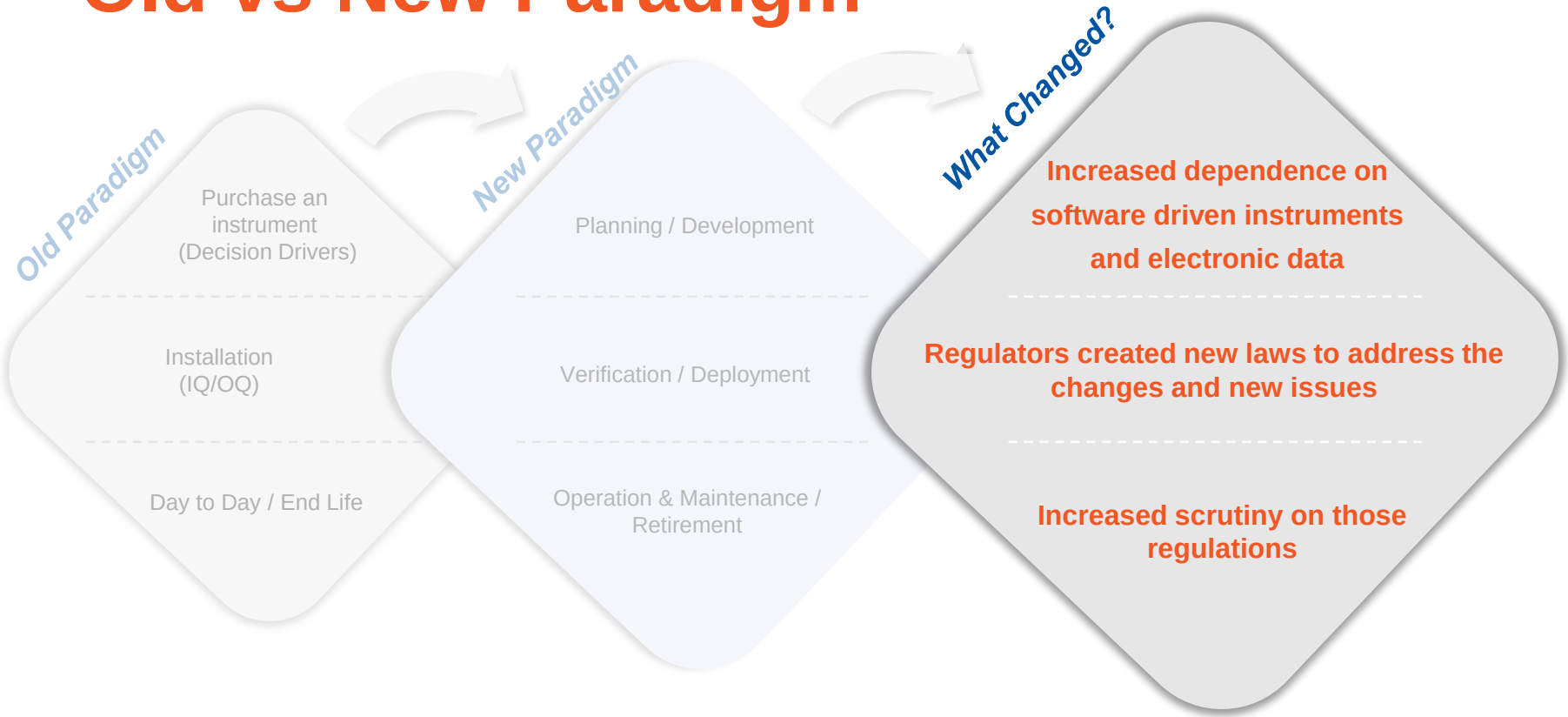
I have over 25 years of experience in a variety of FDA regulated environments focusing on CSV, Data Integrity, and 21CFR Part 11 - especially as pertaining to Laboratory Instruments, Systems, Software, and processes.

With PerkinElmer I have developed a validation team of over 50 people across the globe, which have supported the validation and compliance efforts of many dozens of pharmaceutical companies.

Presentation Content

1) SDLC (System Development Lifecycle) Paradigm: Old and New
2) Changes and Influencing factors
3) GAMP (Good Automated Manufacturing Process) History and Basics
4) Most Common GAMP 5 Implementation Pitfalls and Corresponding Best Practices
5) Path Forward
6) Conclusion
7) Questions

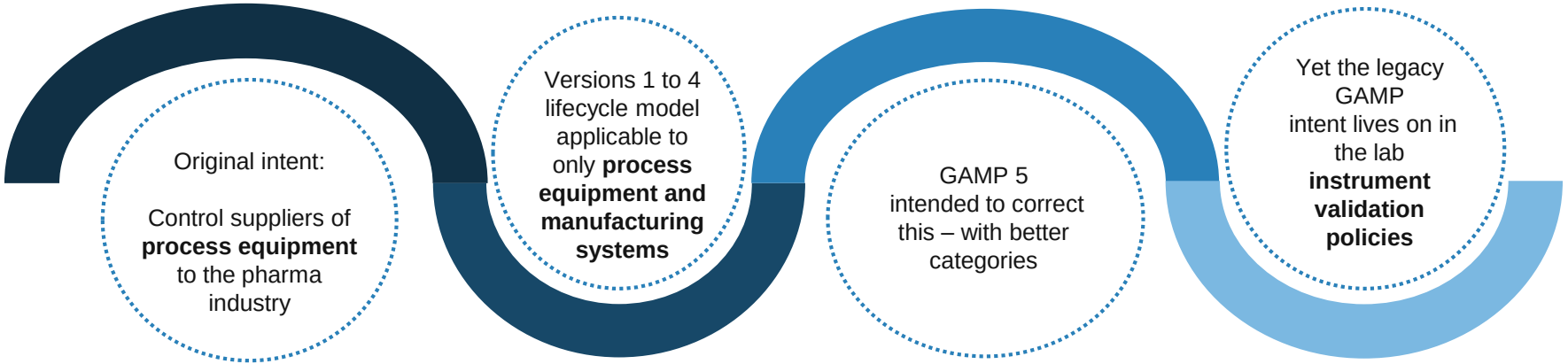
Old vs New Paradigm



Industry Response

- ❑ USP 1058 was considered insufficient guidance for computerized lab systems
- ❑ GAMP model (ISPE) embraced as best approach to encompass expanding validation needs
- ❑ GAMP 4 published in 2001
  - Solved some problems but caused others
- ❑ GAMP 5 published in 2008
  - With increased focus on risk-based approach and validation streamlining

History of GAMP



Intent of GAMP 5

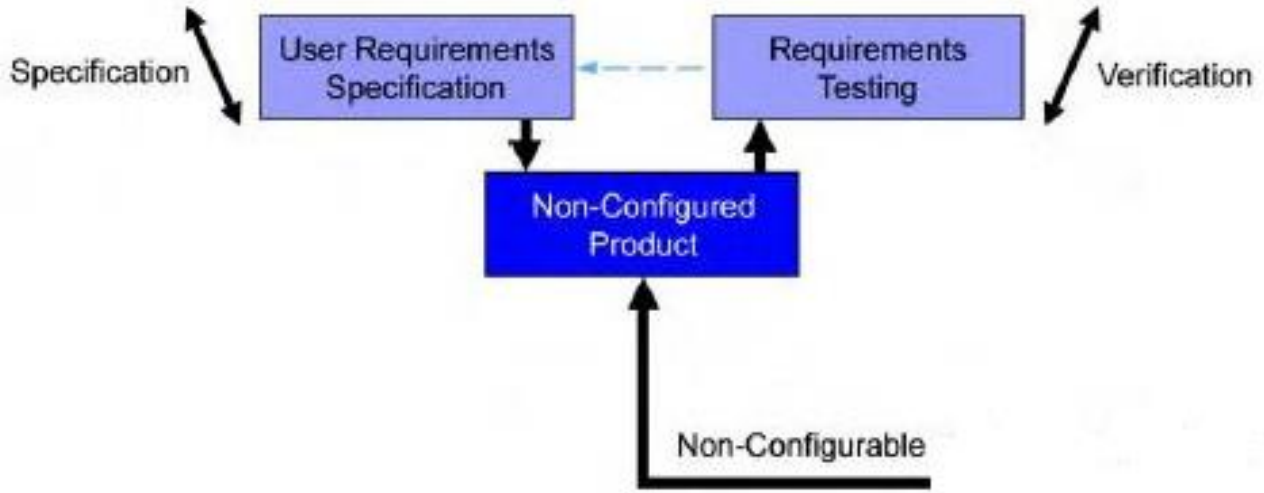
- Particular emphasis is given in GAMP 5 on providing a cost effective approach to compliance and demonstrating fitness for intended use.

- The GAMP Guide has been significantly updated to align with the concepts and terminology of recent regulatory and industry developments.

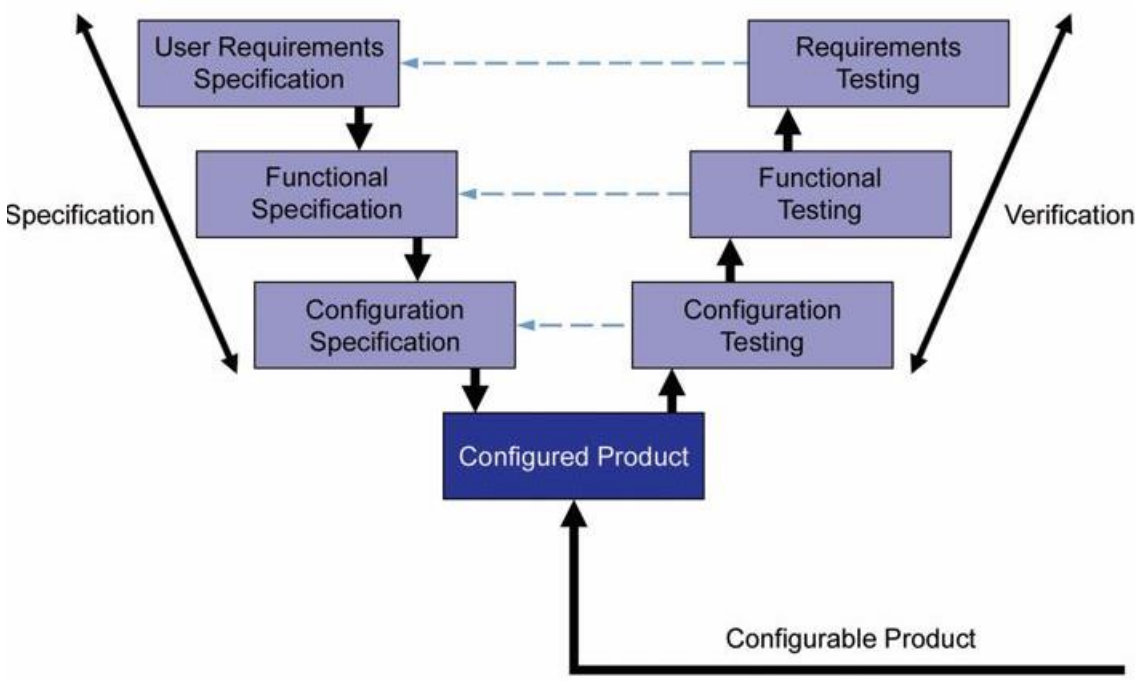
- These regulatory and industry developments focus attention on patient safety, product quality, and data integrity. This is a key driver for GAMP 5.

Ambitiously Broad

GAMP 5 Category 3 Recommendations



GAMP Category 4 Recommendations



GAMP 5 Categories

Category	Description	Typical Examples
1. Infrastructure Software	Layered Software upone which applications are built. Software to manage the operating environment	Operating Systems
3. Non-Configured	"Run-time" parameters may be entered and stored but the software not "configurable"	Firmware Based Applications, COTS Systems, Instruments
4. Configured	Software often very complex, that can be configured by the user to meet the specific needs of the user's business process. Software code is not altered	LIMS, ERP systems
5. Custom	Software custom designed and coded to suit the business process	Internally or externally developed IT ot proccess applications

Five GAMP 5 Problems

1	2	3	4	5
Wrong GAMP 5 Category	Improper Use of Risk Assessment (not used to streamline)	Inefficient Process Sequence of Events	Lack of Validation Governance	Emphasis on Total Automation

Problem 1: Wrong GAMP 5 Category

- The vast majority of Laboratory Instrumentation is Commercial off the Shelf (COTS)
- GAMP is very clear – this is category 3! Reduced Deliverables
- Yet – the approach of most of the industry resembles GAMP category 4

WHY?

WHY the complexity?

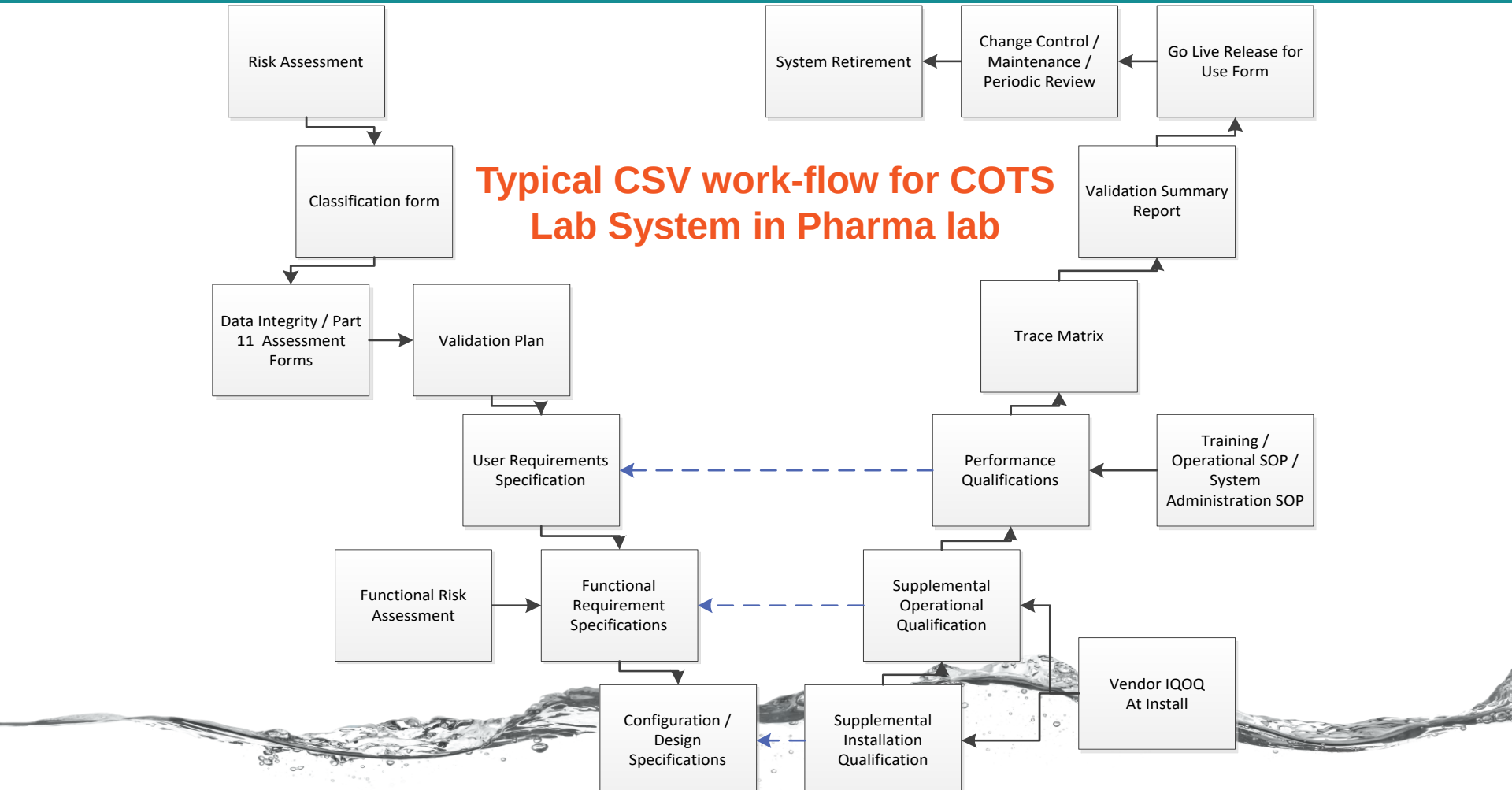
- Origin and Legacy of GAMP
- COTS systems “present” as being configurable, though not by GAMP definitions – this can be confusing
- Quality and Validation Policy can be are hard to change – often only gets added to

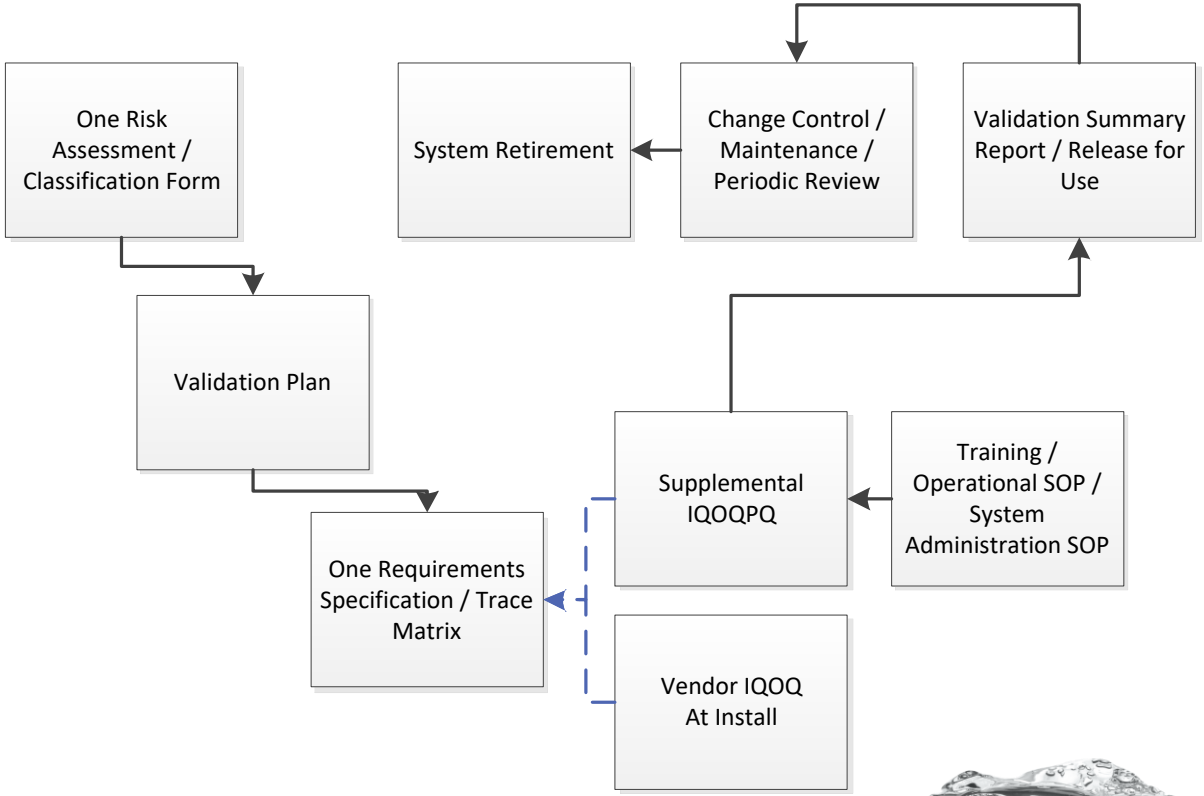
The industry is adverse to risk

Best Practice Solution

- Update company policies to reflect proper instrument categorization
- Streamline the process and the deliverables as necessary, especially for COTS systems
- Capture any “run-time” parameters or “configuration settings” in your requirements doc – but do not categorize as 4
    - May include combining documents and forms
    - Less documents = less review and approval time as well
- The recent revision if USP 1058 offers impetus to re-visit and update overly complex validation policies

Typical CSV work-flow for COTS Lab System in Pharma lab




One Risk Assessment / Classification Form
System Retirement
Change Control / Maintenance / Periodic Review
Validation Summary Report / Release for Use
Validation Plan
Supplemental IQOQPQ
Training / Operational SOP / System Administration SOP
One Requirements Specification / Trace Matrix
Vendor IQOQ At Install

Problem 2: Improper Use of Risk Assessment – not used to streamline

Intent of the Risk Assessment is to streamline the process

- GAMP presents a broad all encompassing approach to evaluate risk
- GAMP approach from the ICH Q9: Evaluation of Harm, Hazard, Risk, Severity

This 5 step ICH Q9 process is totally over-engineered for COTS lab equipment

- Even GAMP implies this can be simplified for Category 3 equipment but does not really explain how

GAMP 5 Risk Workflow

For typical Category 3 product these steps are combined in one assessment

Best Practice Solution

One Simple Assessment

- ✓Form-based
- ✓Checklist
- ✓Classify equipment
- ✓Determine whether validation is required
- ✓Determine which corporate policies and requirements apply

Problem 3: Inefficient Process/Sequence of Events

URS as a gate to instrument purchase

- ❑ Too general – the testing approach is hard to align with a non-specific requirement
- ❑ Too detailed – the instrument may never be purchased as the process stalls out in vendor selection
- ❑ Catch-22 scenarios

Sequential construction of validation documents, especially Requirements, Testing Protocol, and Trace Matrix docs

- ❑ Not robust or efficient process. Changes to later stage documents can cause major re-writes of all documents
- ❑ Creating and approving validation documents sequentially can result in circular rewrites and an endless review cycle

Best Practice Solution

URS

- Do not use a finalized URS as a gate to vendor / instrument selection
- But do use a draft URS to help vet the best option, or
- A specialized vendor qualification form for instrument purchase, which should generally assess:
    - Installation requirements are suited to your environment
    - Operational specs are suited toward intended use
    - Software was designed for GxP use
        - Part 11 requirements
        - Audit Trail capabilities
        - Security – different user groups and permissions, etc

Best Practice Solution, continued…

Validation Document Sequence

- Combine documents (if your policy allows)
- Create, submit, and review the Requirements document, the Testing protocols, and the trace matrix – **TOGETHER**

These documents are inextricably linked and should not be reviewed individually

Problem 4: Lack of Validation Governance

The problem: Validation projects can be complex projects that involve many people and moving parts – both internal and external to the company. As such, many validation projects suffer from a high degree of stalls and delays.

Common Stalls:

1) The system(s) to be validated are not ready
2) The validation team cannot agree on a path forward – Docs stalled or in circular review
3) Members of the validation team are totally un-engaged with the project
4) It's a new instrument and nobody knows how to use it or it's intended use
5) There is no clearly defined leader for the validation effort, no one to drive the project or move things forward

Problem 4: Lack of Validation Governance

From GAMP 5:

“SMEs should take the lead role in the verification of the computerized system. Responsibilities include planning and defining verification strategies, defining selection criteria, selection of appropriate test methods, execution of verification tests, and reviewing results”

Problem:

- GAMP guidance describes a technical lead, but not a project lead
- The SME’s for lab instruments are often scientists whom:
  - May not have the right background in validation or project management
  - May not view Validation as a priority or their “real” job

Best Practice Solution

Build governance and process into your validation policies – clearly define leadership and R&R

- Add the role of Project Manager to your validation team
- Use Project Management tools:
  - Kick-off meetings
  - R&R matrix
  - Communication and escalation plans
  - Readiness checklists
  - Set meeting cadence and required attendance
  - Hold a “project closure” or “lesson’s learned” meeting after challenging projects with a continuous improvement mind-set
- Limit the amount of time a document can be in review
- Limit the number of review cycles a document can be subjected to
- Use a “live-edit” meeting when a team cannot reach a consensus on validation documents

Problem 5: Emphasis on Total Automation

Inherent problem of GAMP

- ❑ Endless experimentation with the configuration of the instrument
- ❑ 3rd party softwares and other bandaids are explored – additional delay
- ❑ Project stalls because no consensus on optimum configuration
- ❑ Project stalls because the perception that the software is not compliant

Real world

There are no totally compliant softwares

Best Practice Solution: Define “ACLs”

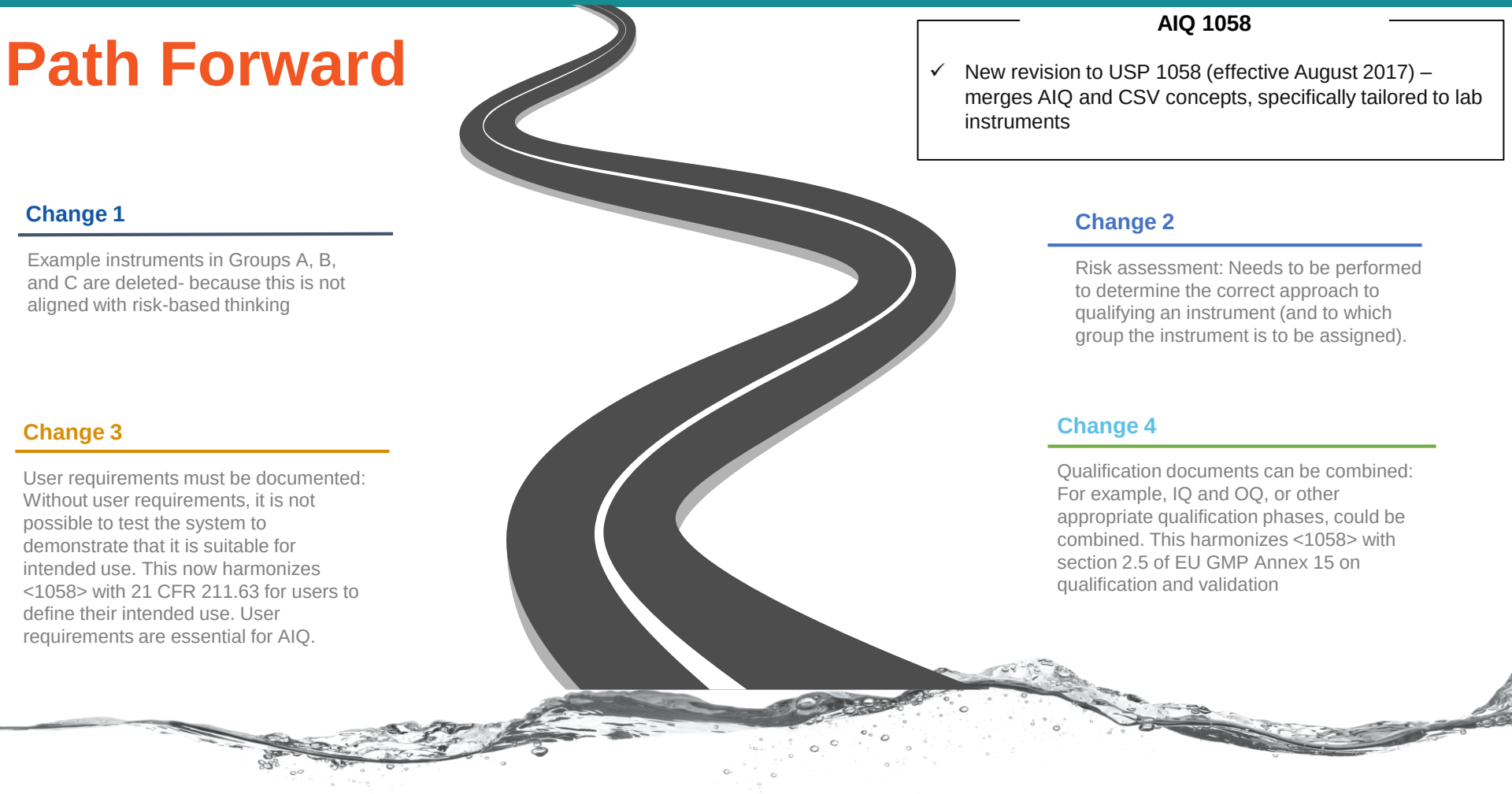
- Define “Acceptable Compliance Levels” for laboratory instrumentation
  - “ACLs” will help bring closure to an endless “sandbox” environment
- Embrace the concept of “proceduralization” when faced with an unexpected compliance gap
  - Ideally through training, SOPs, corporate policy, etc – many requirements are already met in non-automated fashion
  - To address specific compliance gaps in specific instrumentation, new training, SOPs, or policies may need to be created.

No software fully automates compliance – accept this!

Other helpful Best Practices for GAMP 5 implementation

- Have **strong corporate policies** on:
    - Data Integrity, Electronic Records and Signatures (Part 11)
    - System Security and Administration
    - Training
    - Instrument Administration
- Deploy a uniform operating system in your lab (**Win 10**)
- **Combine documentation** whenever possible
- Leverage existing validation work:
    - First and second in family approach to validating replicate equipment
    - Approved Software/Instrument combinations at Global Level

Path Forward



AIQ 1058

- ✓ New revision to USP 1058 (effective August 2017) – merges AIQ and CSV concepts, specifically tailored to lab instruments

Change 1

Example instruments in Groups A, B, and C are deleted- because this is not aligned with risk-based thinking

Change 2

Risk assessment: Needs to be performed to determine the correct approach to qualifying an instrument (and to which group the instrument is to be assigned).

Change 3

User requirements must be documented: Without user requirements, it is not possible to test the system to demonstrate that it is suitable for intended use. This now harmonizes <1058> with 21 CFR 211.63 for users to define their intended use. User requirements are essential for AIQ.

Change 4

Qualification documents can be combined: For example, IQ and OQ, or other appropriate qualification phases, could be combined. This harmonizes <1058> with section 2.5 of EU GMP Annex 15 on qualification and validation

In Conclusion:

- GAMP 5 is a broad guideline and before implementation needs to be tailored to the specific validation activity at hand in the specific environment
- Legacy GAMP versions and concepts live on in corporate policy.
- Mis-categorizing laboratory instrumentation dramatically complicates validation
- Ensure your validation workflow is well defined and logically ordered
- Combine validation documents, have strong policies, and add project management and governance to dramatically reduce validation project time and cost
- Accept that compliance is rarely 100% automated and establish corporate “ACLs” to assist with configuration decisions and verification approach – as well as proceduralizing any compliance gaps
- **The new version of AIQ 1058 offers impetus and an avenue to revisit corporate validation policies and process**

Questions?

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