Key Considerations for SaaS eQMS Validation

TRAINING

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- 40+ years of experience in the Life Sciences including Pharma, Biotech, Medical Devices and Cell & Gene Therapy with expertise in in GLP, GCP, GMP and 21 CFR 11 / Data Integrity @ Director, VP, C-Level & Board Level
- Past positions include IT Director, QA Director and Chief Compliance Officer
- Co-authored & prototyped 21 CFR 11 guidance with FDA and work with FDA on Data Integrity Regulations.
- Co-authored Computerized Systems in Clinical Research w/ FDA& DIA
- Co-authored Data Integrity book with SQA – due out in 4Q2024
- Patent on Virtual Validation of Software Systems
- Quoted in Wall Street Journal for using training to bring regulatory compliance to the Boardroom
- Published in European Biopharmaceutical Review: A Guiding Light in Jan2020:
- Published in Healthcare Packaging in March 2021:
- Member of “Think Tank” that helps FDA regulate new technologies, e.g., AI
- Creating templates for industry & FDA Computer Systems Validation Credentialing
- Adjunct Professor at UC Berkeley for Regulatory Affairs.
- Former President and Vice President of Pacific Regional Chapter of Society of Quality Assurance (PRCSQA).
- Stanford’s Who’s Who for LifeSciences.

CONTENTS

Introduction

01

Introduction

- An essential part of all LifeSciences companies is to **ensure patient safety and product quality**.
- Each company is required to have a **Quality Plan**, to ensure that the processes required for quality are clearly outlined.
- A Quality Plan is implemented with a **Quality Management System (QMS)** that documents all policies, protocols, and controls that are essential for the creation and delivery of high-quality products and services to customers.

Some Simple Concepts

What is a Quality Plan?

- The Prescription of how your company will achieve patient safety and product quality

What is a Quality Management System (QMS)?

- The system used for the implementation of your Quality Plan

What is an eQMS?

- An electronic QMS (as opposed to paper)

What is a SaaS eQMS system?

- An eQMS installed in someone else's data center

Validation Principles to Comply with GaMP 5

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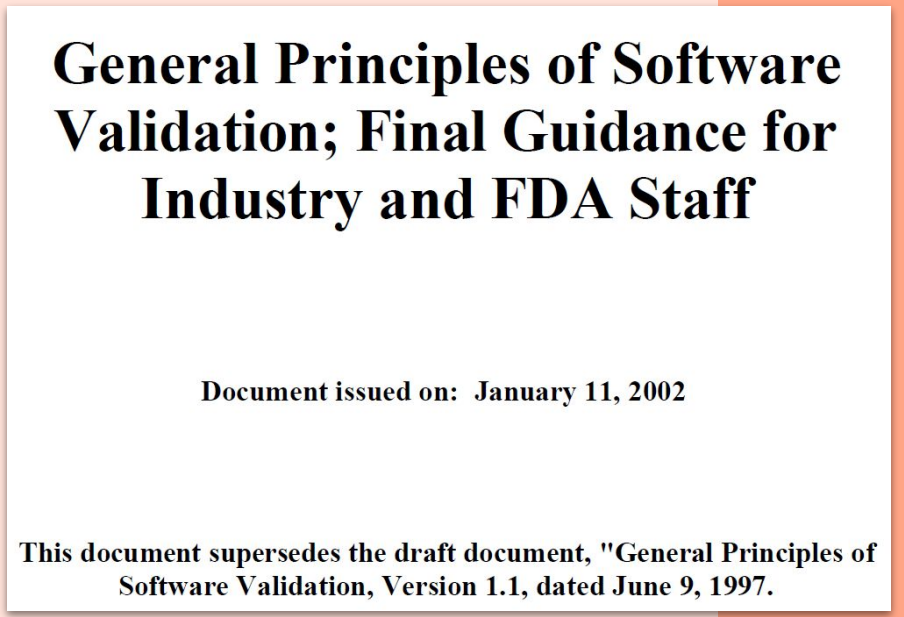
General Principles of Software Validation

- FDA general principle of software validation is the **confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through software can be consistently fulfilled**.

- This principle applies to the validation of <eQMS> software or the software used to design, develop, or manufacture <a product>. The validation process must be documented and meet the FDA's standards.

GaMP5

1. Regulation e.g., 21 CFR 11
2. Guidance Documents e.g.,
3. General Principles of Software Validation – 21 CFR 11.10(a)
4. GaMP5
5. Computer Systems Validation SOP (within your company)
6. Validation Plan ---other deliverables---
   Validation Report, etc.

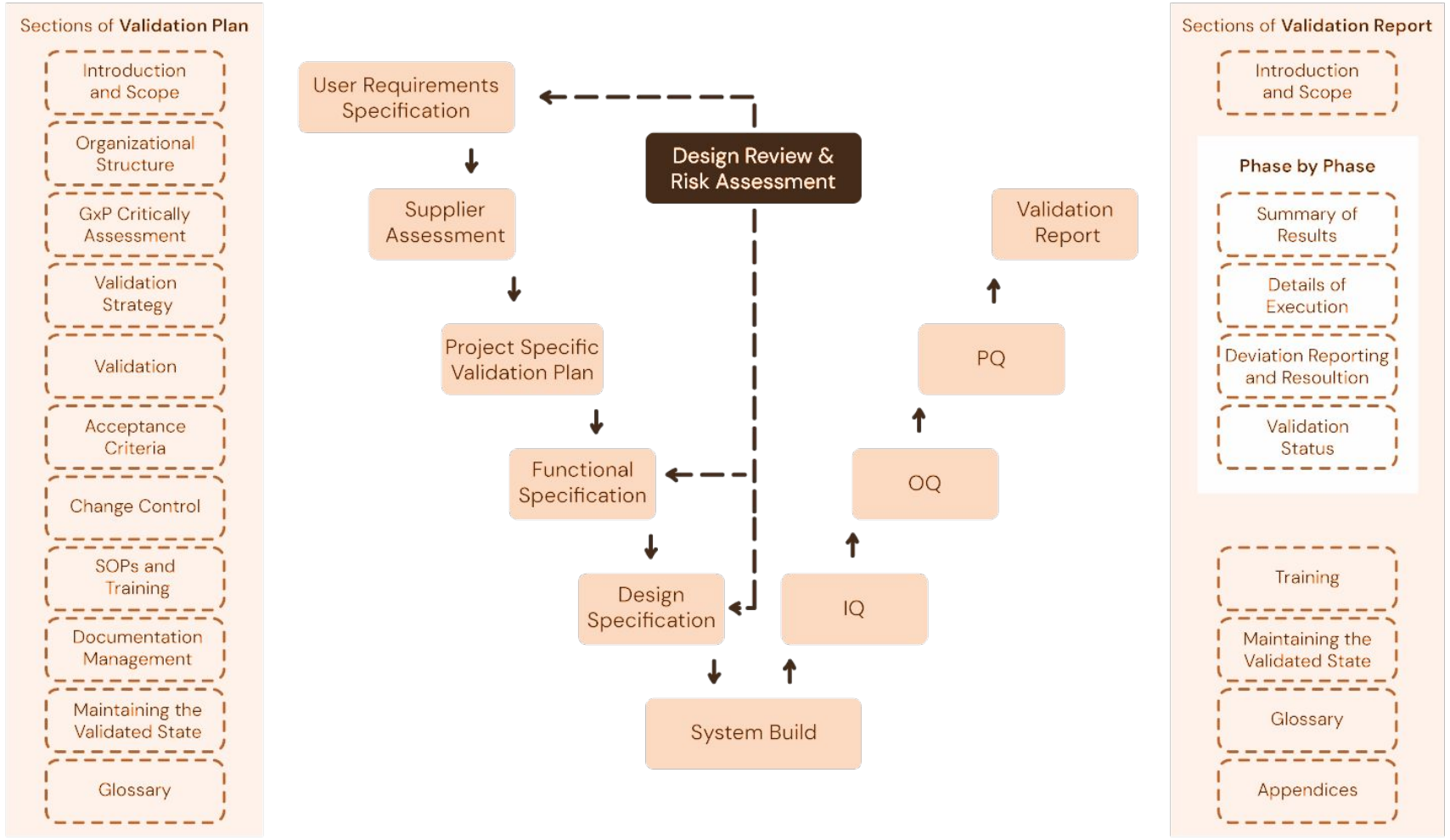


General Principles of Software Validation; Final Guidance for Industry and FDA Staff

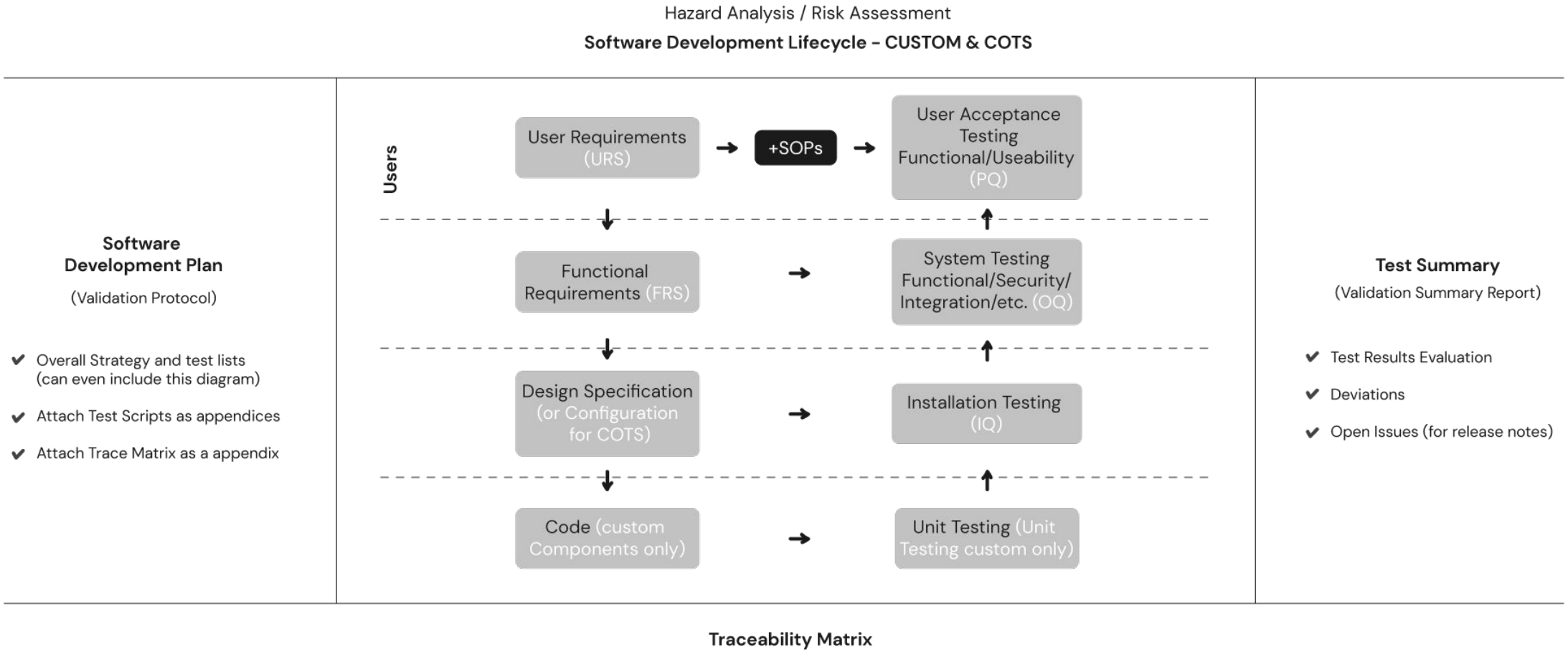
Document issued on: January 11, 2002

This document supersedes the draft document, "General Principles of Software Validation, Version 1.1, dated June 9, 1997.

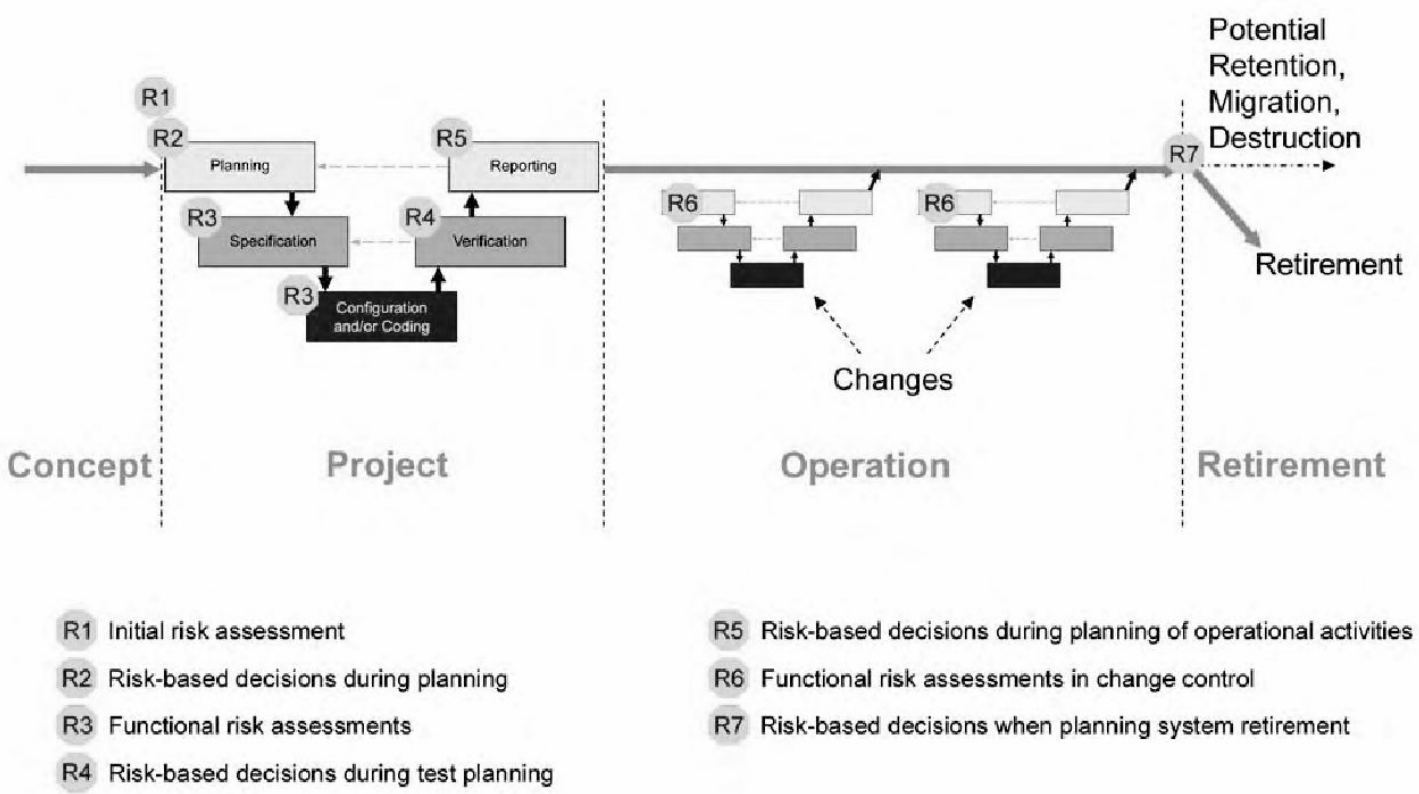
GaMP5 Deliverables



GaMP5 Deliverables

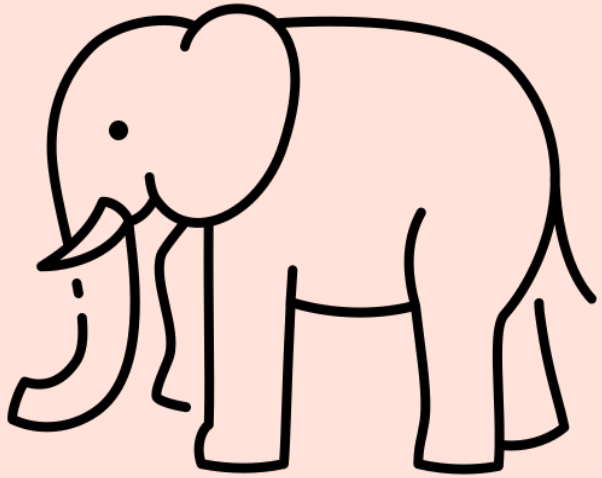


GaMP5 – Don’t Forget Risk



Elephants in the Room

- Requirements
- “Prevalidation”



Requirements:

But…. The Vendor Gives Us Requirements….!

Imagine going to a restaurant, whose system is that your waiter orders the food for you, and then tells you that you liked it.

Is this valid (a validated system)?

The answer is "No" because …

- "Validation is objective evidence that a system works per intended use"!
- No-one can determine your intended use other than yourself.

Requirements:

But… We Don’t Have Any Requirements

How do you find a needle in a haystack?

First you burn the haystack.

- If you don’t have any requirements, ALL features of a QMS need to be turned off.
- The features that you want turned on are your requirements
- If a feature is not needed, you must turn it off to avoid using it accidentally: which will break the validation of the system.

Requirements:

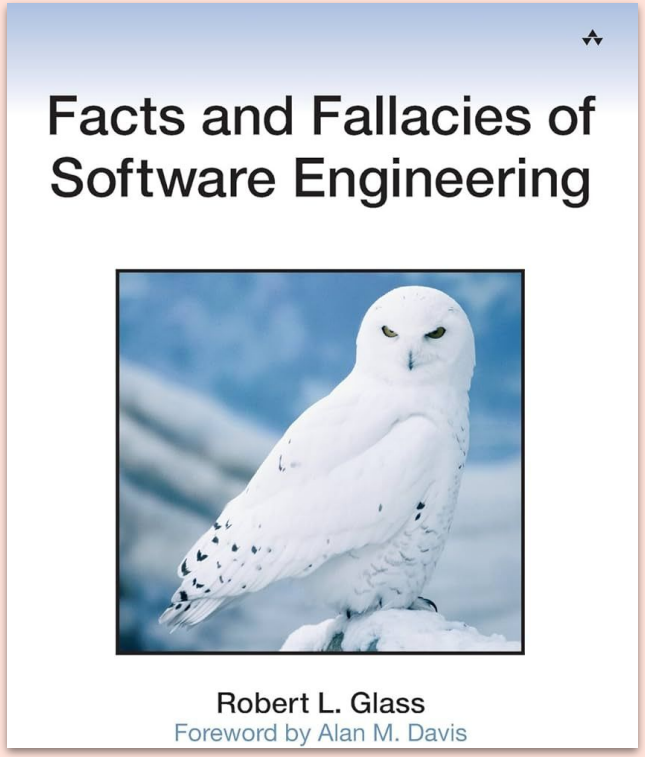
But...We Use Agile, etc. Methodology

The way that the requirements are captured is immaterial. The important thing is to have documented requirements.

Requirements:

But…It's a COTS / SaaS: We Do Not Need Requirements

- One of the two most common causes of runaway projects is **unstable requirements**
- The other one is **poor estimation**: poor estimation is a direct result of **estimating a project before you have requirements**
- Imagine going into a restaurant and the waiter orders food for you and then tells you that you liked it….



Requirements:

But…It's a COTS

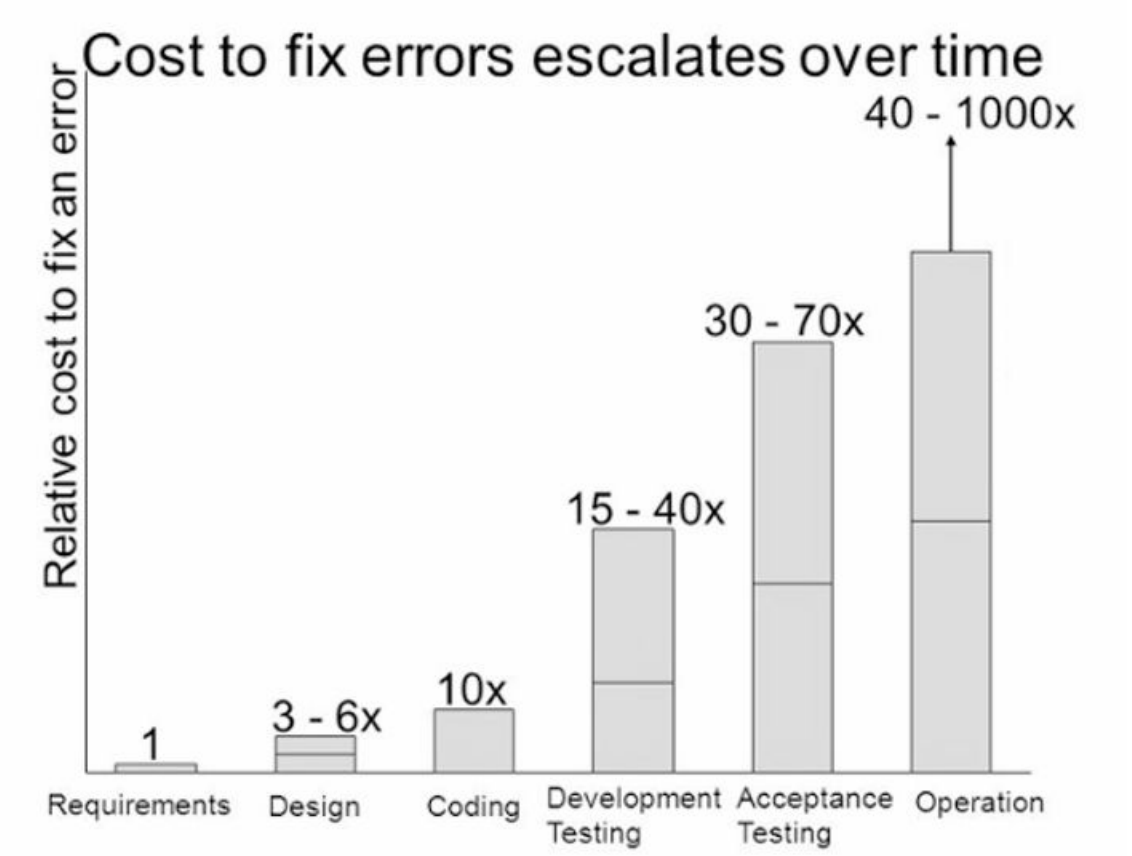
- Commercial-Off-The-Shelf (COTS) need requirements
- COTS vs Custom requirements are a matter of degree, not kind. E.g.,
- COTS requirement: Need an E-Signature Field
- Custom requirement: Need an E-Signature Field that is 90 characters wide and does not accept numbers or null values.

Requirements:

But…It's a COTS

- No COTS covers 100% of desired functionality.
- Often additional code / modules have to be added to cover automated functionality (SOPs are added for manual functionality)
- Requirements is WHAT the User WANTS. Design is WHAT the user GETS!
- COTS have configuration for the bulk of the design specification but can have additional design requirement for more detailed modules.

Requirements Are… Required

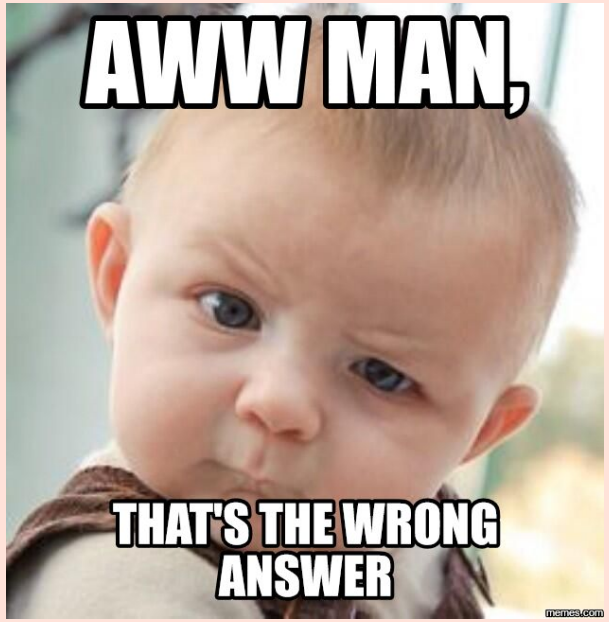


Prevalidation:

But…The SaaS System is Pre-Validated by the Vendor

Yeah….No! It is NOT!!!

- Vendors Test – Sponsors Validate (intended use)
- FDA has a rule against calling systems pre-validated
- Vendor can make system 21 CFR 11 Capable but the sponsor is responsible for everything (Ref: General Principles of Software Validation)



Deliverables Expected from SaaS Validation

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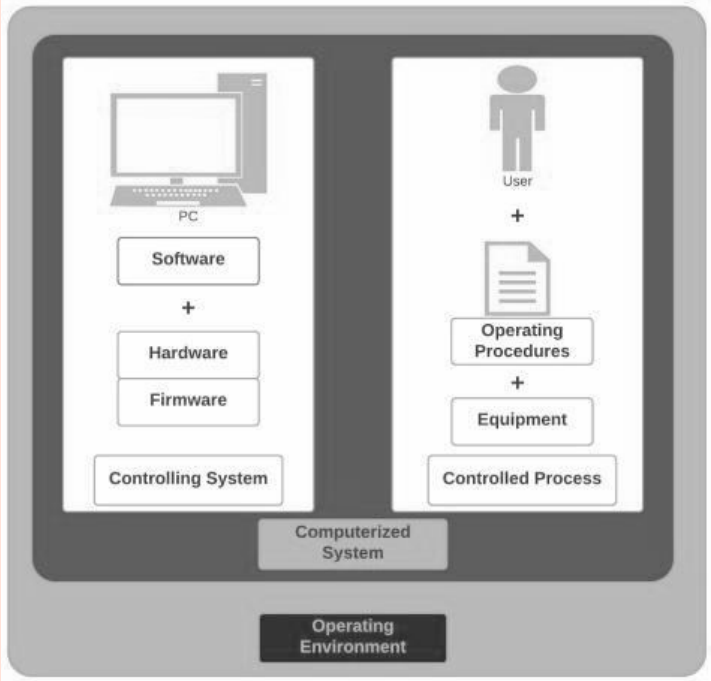
Definitions:

Computerized System

- Computerized System (System) consists of hardware, software, and network components and a controlled function or process that the computer system supports within a GxP operating environment.
- In other words, a computerized system is a **computer system and a controlled process or function**.
- The combination of the computer system and the controlled process is what produced the definition of a **GxP computerized system**.



SaaS System Deliverables:

Vendor Tests – Sponsor Validates

- To use an analogy, If a system were a bicycle, the actual system is, say, the gearbox, while the infrastructure, database, utilities, etc., would be the wheels, handlebars, saddle, and so on.
- The vendor then sells the gearbox to the sponsor, and the sponsor rebuilds the bicycle using the sponsor's technical environment.
- For example, the vendor may be testing the system on Oracle 12 and Windows 10, as the database and the O/S. However, the sponsor, may install the vendor software on Oracle 9 with Windows 8.
- Additionally, the system may have 1,000,000 functions, while the sponsor may only require 400.

SaaS System Deliverables:

Vendor Tests – Sponsor Validates

- Consequently, the vendor testing the system, does not necessarily reflect the intended use of the system, by the sponsor.
- To use another analogy, if the vendor is a restaurant, the sponsor orders from the menu, and then determines if the food meets the sponsor needs.
- You would not expect the restaurant waiter to order for you, or to decide whether you liked the food or not, based only on their requirements.
- Even if the vendor is doing the tasks for the validation, the sponsor is ultimately responsible in determining whether the deliverables meet the sponsor's intended use, and to ensure that the deliverables are created to a compliant standard, e.g., GaMP5

SaaS System Deliverables

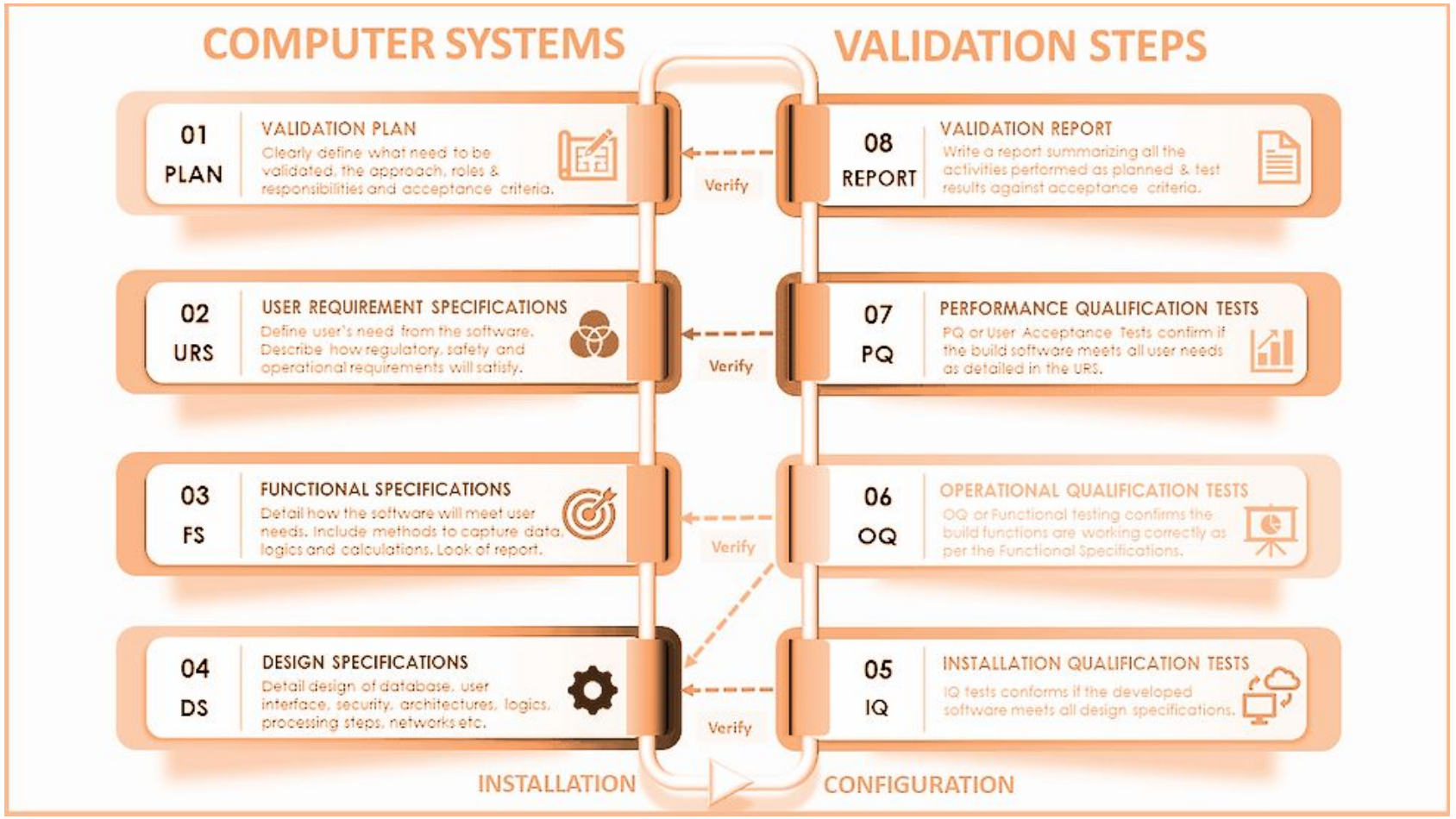
- SaaS systems are a combination of GaMP5: Category 4 (Configuration) and GaMP5 Category 5 (custom code).
- So the validation for the Category 4 parts would be lower risk than the validation for the Category 5 parts.
- The sponsor needs to ensure that the correct level of validation has been applied to each part of the system.
- There are 2 parts to the validation of SaaS eQMs Systems:
  - The part that meets 21 CFR 11 / Annex 11 deliverables.
  - The part that meets Quality Plan Deliverables.

Requirements:

21 CFR 11 / Annex 11

- System Agnostic
- Include User Processes
- Include Technical Requirements
- Include Regulatory Requirements
- Include anything else that is a requirement

GaMP5 Deliverables



Requirements Categories for SaaS QMS:

21 CFR 11 / Annex 11

1. **Configuration / System Parameters requirements** – these are the requirements that detail how the system is to be configured e.g., security.
2. **Data Design requirements** – these are requirements that prepare the tell the system what kind of data to expect e.g. number of patients, type of sample etc. These should include boundary conditions, e.g. number of files to be included etc. When possible an entity relationship diagram should be included.
3. **Data Collection Requirements** – these detail how the data will be collected and by whom. Will also detail where the data will be collected and, if the data is transmitted between locations or systems, how to assure that the transmitted data is identical to the originating data.
4. **Data Collection Tracking Requirements** – these detail how the tracking of the data that is being collected e.g. if there is an expectation of certain types of files to be collected these requirements detail what information needs to be captured ABOUT the data that is being collected.
5. **Data Cleanup Requirements** – these detail how data that does not meet the requirements for moving forward to processing will be handled and how the exceptions will be reported.

Requirements Categories for SaaS QMS:

21 CFR 11 / Annex 11

6. **Analysis Preparation Requirements** – these detail how the data will be prepared for analysis e.g. normalization.
7. **Analysis Requirements** – these include the algorithms that will be used to analyze the data as well as their input and output conditions.
8. **Results handling requirements –** these detail how the analysis results will be handled including the versioning of the results, where they would be saved etc.
9. **Results annotation requirements –** these detail how the results will annotated by the entity that is interpreting the data.
10. **Result Reporting requirements –** these detail the reports to be produced by the system and includes the report structure and boundary conditions, etc.

Requirements Categories for SaaS QMS:

21 CFR 11 / Annex 11

11. **Document Management Requirements** – these detail the management by any of the documents that are produced by the system including the management, versioning, storage, labeling, etc.
12. **Workflow Requirements** – these detail the sequence or sequence combinations in which the different components of the system can be executed.
13. **Security Requirements** – these detail the roles and responsibilities for the individuals that will be using the system and how the system will prevent unauthorized access.
14. **Audit Trail Requirements** – these detail how the system will show that the data has not been altered or corrupted while the data is being handled by the system.
15. **Interface Requirements** – these detail how the system components interface with each other or how the system interfaces with other software or systems in an automated fashion.

Requirements Categories for SaaS QMS:

21 CFR 11 / Annex 11

20. **Import / Export Requirements** – these detail any interfaces that require the passing of a file between the system and other systems.
21. **Performance Requirements** – these detail any speed, memory usage etc requirements that are necessary for the system.
22. **Reproducibility Requirements** – these detail the expectations for reproducibility of results given the use of the same process and input.
23. **Technical Requirements** – these detail the technologies (both hardware and software) that will be employed in the implementation of the system.
24. **Backup and Recovery Requirement** – these detail the backup requirements for the system and how the system can be recovered in the case of non-catastrophic failure.
25. **Archive and De-Archive** – these detail the long term archival of data or documents and when necessary, how to dearchive these. Archive and De-Archive may also be used as data migration techniques of archiving the data / documents out of the source system and dearchiving into the target system.

Requirements:

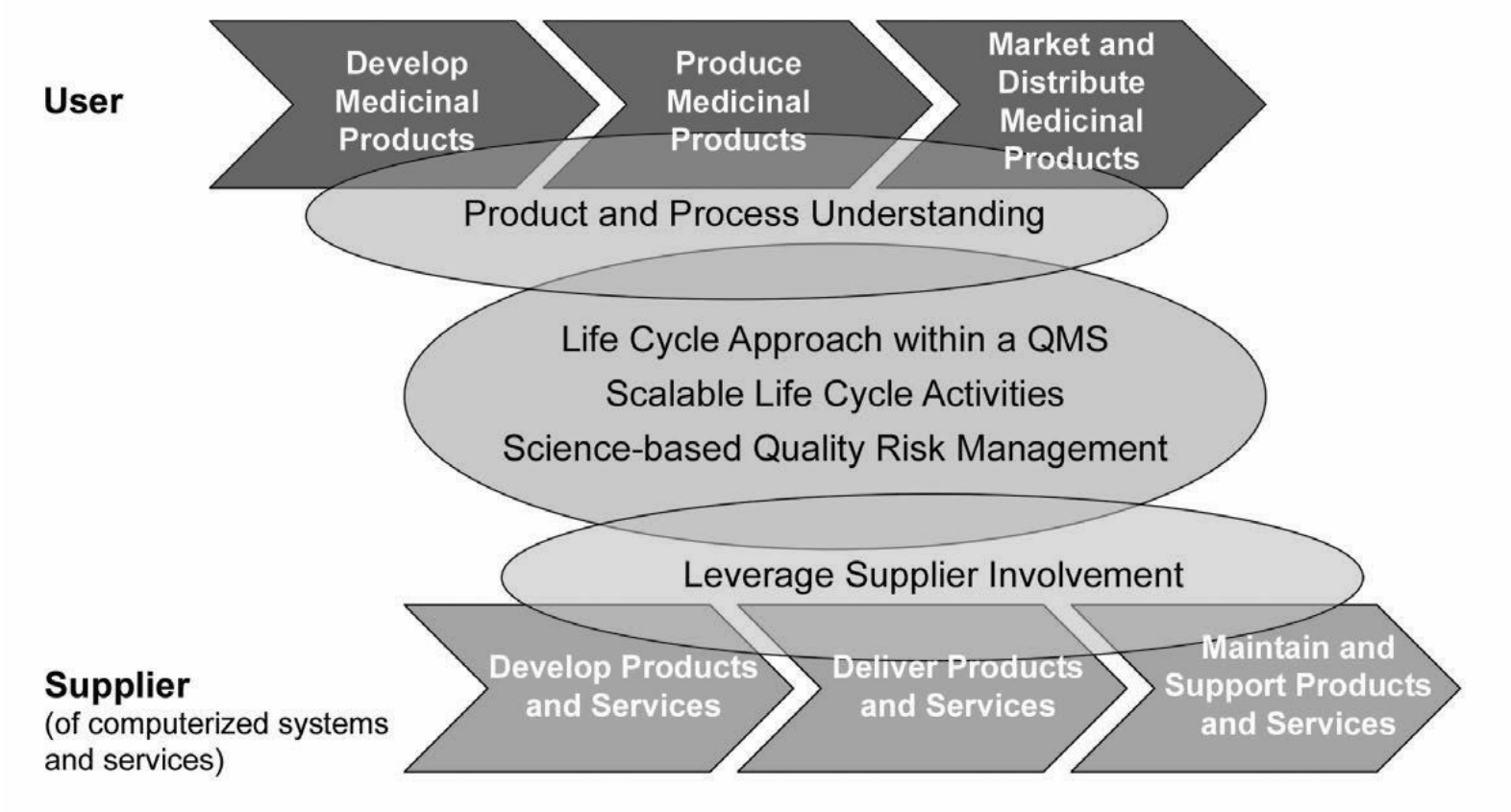
Quality Plan Processes

FEATURES	NOTES
CORE QMS MODULES	
Document Control	Mgmt. of Procedures (SOPs), Work Instructions, Supplier Reviews, Design Records, Complaints, CAPAs etc.
Training Management	Scheduling of training activities with automatic notifications and reminders. Overview of training complaince. Manage personal records and certificates within GDPR
CAPA Management	Identify, uncover, resolve, and report CAPAs and link to issues.. Assign tasks with instructions and follow-up on overdue CAPAs
Issue / PMS Management	Collect, document, route issues and escalate overdue activities. I.e. analyze complaints by product, component, process, customer, equipment, supplier etc
Audit Management	Create audit plans and manage internal and external audits. Submit findings into an automated flow, track and follow-up. Produce and share audit summaries
Equipment Management	Planning and scheduling of calibration and maintenance.
Supplier Management	Organise supplier documentation, schedule follow-ups, reviews, audits and manage finding. Automate selection, evaluation, qualification and monitor your suppliers
Product Management	Manage documentation and changes to products allowing full tracibility. Link complaints, production records, DMRs etc
Change Management	Manage changes with high flexibility and tracebility. Changes automatically trigger tasks and sends email notifications.
Design Control & Collection	Relate Design Control documents to multiple archives (i.e. DHF, DMR, TF, 510k, CE marking etc). Make "snapshots" for external submissions. Connect to other systems
Risk Management	Link risk mgmt. documentation with products, components, suppliers, customers etc. Access ISO 14971:2019 Risk Mgmt. procedures and forms such as Risk Management plan, Hazard Traceability Analysis, and Risk Report
Reporting	Use standard dashboards or create your own custom views. Follow-up on KPIs on training, issues, CAPAs etc

Who Is Responsible for What: Vendor vs Sponsor

04

GaMP5 Deliverables



Sponsor vs Vendor RACI

RACI Matrix for SaaS 21 CFR 11 Deliverables[1]: R=Responsible; A= Author; C=Consult; I=Inform			
Deliverable	**Sponsor**	**Vendor**	**Vendor's Cloud[2] Supplier[3]**
Vendor Audit of Vendor	RA		
Vendor Audit of Vendor's Cloud Supplier	RC	RA	
Qualification of Host Infrastructure	R	RC	RA
Validation Plan	RA		
User Requirements Specification	RA		
System Configuration	RC	RA	I
System Customization	RC	RA	I
Test Plan	RA		
Installation Qualification (IQ) of SaaS	RA		
Operational Qualification (OQ) of SaaS	RA[4]		
Performance Qualification (PQ) of SaaS	RA[5]		
Test Report	RA		
Traceability Matrix	RA		
Validation Summary Report	RA		
Validation Registry	RA		
System Release	RA		
SOPs – users	RA	C	
SOPs – admins	RA	RA	
Training - users	RA	C	
Training - admins	RA	RAC	
Operations & Maintenance	RC	RA	I

[1] Based on GaMP 5, Good Practice Guide: infrastructure Qualification and Control, GPG: Operations and Maintenance
[2] Or other infrastructure provider
[3] If different from vendor.
[4] Can use some of vendor's test cases
[5] Use Sponsor's SOPs

Leverage Vendor Deliverables

- Develop methodology for Computer Systems Validation (CSV).
- Develop templates for your company for each CSV Deliverable.
- Map eQMS components to QP deliverables by mapping existing SOPs to eQMS components.
- For each component, move functionality from Vendor Requirements to your requirements spec template. If templates do not match, update template ensuring a QA event is recorded in existing QMS, to document deviation from your templates.
- Map eQMS functions to other Requirements.

TURN OFF ANY eQMS FUNCTIONS THAT YOU ARE NOT USING!!!

Leverage Vendor Deliverables

- Select Vendor Deliverables to **meet QP and 21 CFR 11 Requirements.**
- Select Vendor tools to **meet requirements**.
- If you already have **test cases** to test parts of the system, use your test cases, else use vendor test cases.
- **Ok to use vendor proposed processes** (e.g., predefined processes) if improvement – update deliverables documentation as appropriate.
- **ALL DELIVERABLES NEED TO BE INCLUDED** - Validation is like being pregnant – you cannot be a 'little bit pregnant'

SaaS is Sharing of Validation But You Are Responsible !!!

- Use **FDA GMP quality agreement** between companies.
- Detailed **who is responsible for what.**
- Consider turning components on one or a couple at a time, so as not to get overwhelmed.

SaaS is Sharing of Validation But You Are Responsible !!!

- SaaS Vendor Management Best Practices
- Strong agreements for vendor services.
- **Regularly scheduled communication a must!**

Managing Vendor SubContractors

05

Vendor Subcontractors:

Who, What and Where

- SaaS Vendor hosts the eQMS on someone else Cloud.
- To host the eQMS on someone else's Cloud, the vendor typically hires one or more Cloud brokers who manage the data center providers.
- The data center providers or the data center brokers, hire other subcontractors to manage their backup and restore, disaster recovery, etc. functions.
- In your validation plan, ensure you have a WHO, WHAT & WHERE for each deliverable.
- Ensure to include operations and maintenance functions – e.g., if security is provided by third party – who, what & where.

Vendor Subcontractors:

Who, What and Where

- Where is your data?
- Is it supposed to be there? E.g., GDPR requirements
- Can you get ‘visit’ your data at the data center as you want to?
- Or is the data center burned down, the data center vendor has not notified you and the issue is found our by the MHRA inspector (True Story!!)
- Don’t forget training for dealing with all these moving parts.

You are responsible for all of these!!!

Special Considerations for SaaS eQMS vs Other eQMS

06

SaaS eQMS vs ‘Other’ SaaS Systems

- SaaS eQMS must be **industry specific to LifeSciences to ensure adherence to regulations** – generic QMS do not work
- Other SaaS systems are for a single function. SaaS eQMS needs to integrate with all those other systems
- SOPs for function AND governance to be considered.

Conclusion

07

Conclusion

- SaaS eQMS is an **efficient way to implement eQMS**.
- **Still needs full validation** per GaMP5.
- **Sponsor is responsible** for ALL vendor deliverables and actions.

Q&A session

08

Thanks!

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Scilife

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