MIDDLE EAST
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Computerized system validation (CSV) as a Requirement for Good Manufacturing Practices

Presented by
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Target Audience

- IT Personnel and Managers

- Quality Personnel and Managers

- Auditors and Audit Managers

Contents

Purpose of CS/ PLC validation

Why is validation needed?

Who cares about CSV?

List of Guidance Documents.

General Principles of Software Validation.

Introduction to Validation Master Plan

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Validation life cycle

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Introduction to CSA

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GMP definition

- ***WHO*** defines ***Good Manufacturing Practices (GMP)*** as ***"that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization."***

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Validation definition

- ***Validation (USFDA) is defined as the establishing of documented evidence which provides a high degree of assurance that a planned process will consistently perform according to the intended specified outcomes.***

Software Validation definition

- Software Validation is a process of evaluating software product, so as to ensure that the software meets the pre-defined and specified business requirements as well as the end users/customers' demands and expectations.

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Objectives

Computer System risk assessment

Risk based validation approaches.

Software and hardware Categories

Documentation Examples and discussions

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Purpose of CS/ PLC validation

- The purpose of the validation process is to provide a high degree of assurance that a specific process (or in this case computer system) will consistently produce a product (control information's or data which meets predetermined specifications and quality attributes.

WHY IS VALIDATION NEEDED?

- **To comply with the FDA regulations**

- **To avoid Failing an FDA audit which can result in FDA inspectional observations (“483s”) and warning letters.**

- **Failure to take corrective action in a timely manner can result in shutting down manufacturing facilities, and this will cause a financial penalties.**

Benefits of CSV conducting

- Cost of compliance is low comparing with the cost of non- compliance .
- Provides documentation required by FDA,EMEA, other regulatory agencies.
- Maximizes the value of the computer system and the employees that use it.
- Reduces labor costs by increasing employee's efficiency and effectiveness.
- Saves money by discovering defects early
- Reduces risk.
- Promotes continual process improvement.

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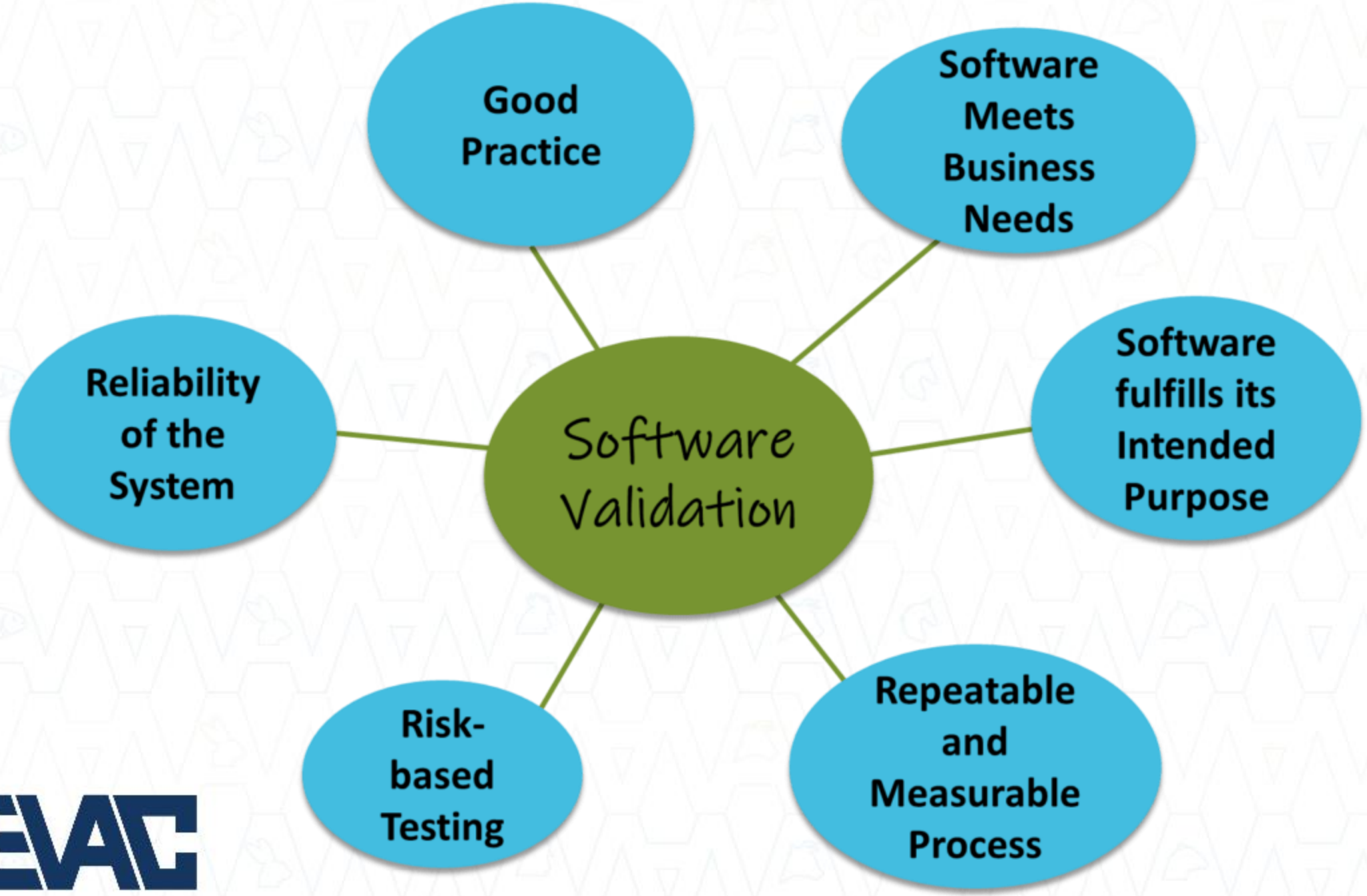
Key Objectives of CSV

- Patient safety
- Product quality
- Data integrity


Software Validation
Good Practice
Software Meets Business Needs
Reliability of the System
Software fulfills its Intended Purpose
Risk-based Testing
Repeatable and Measurable Process

Who cares about CSV?

Resources involved in any way with IT, computer or automated systems is affected:

- Developers
- Maintainers
- Users
- Regulatory Authorities
- QA

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The Regulatory Requirements can be grouped as below:

Quality System: related to the Quality System and to the associated documentation

Security: related to the general features of System Security and Security of Regulated Electronic Record managed by the system

Integrity: related to the Integrity of the Regulated Electronic Record managed by the system and associated Validation documentation

Traceability: related to the Traceability of the Regulated Electronic Record managed by the system

Accountability: related to the Regulated Electronic Signatures managed by the system

Regulatory Framework

- EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines. Volume 4 annex 11 computerized systems. https://ec.europa.eu
- Guidelines on validation – Appendix 5 . Validation of computerized systems (May 2018) https://www.who.int
- GAMP® 5: A Risk-Based Approach to Compliant GxP Computerized Systems https://ispe.org/publications/guidance-documents/gamp-5
- FDA 21 CFR 11
- FDA 21 CFR 820
- etc.

Examples from regulatory / guidelines requirement for CSV

Regulation or Guideline	Requirement
21 CFR 820.30 (g)	Design validation shall include software validation and risk analysis, where appropriate.
FDA 21 CFR 11.10	Controls for closed systems. Such procedures and controls **shall include** the following: (a) **Validation of systems** to ensure accuracy, reliability,…..
FDA 21 CFR 211.68(b)	Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy.
FDA 21 CFR 1271. 160(d)	You must validate the performance of computer software for the intended use, and the performance of any changes to that software for the intended use
EU- GMP – Annex 11	The application should be validated; IT infrastructure should be qualified
COUNCIL DIRECTIVE 93/42/EEC 12.(1a)	The software must be validated

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Examples from regulatory / guidelines requirement for CSV

Regulation	Requirement
WHO GMP for Pharmaceutical Products: Main Principles 4.11	Particular attention should be paid to the validation of analytical test methods, automated systems and cleaning procedures
WHO Specifications for Pharmaceutical Preparations 6.3	Critical computerized systems should be validated before use.
PIC/S PE 009-11 Guide to GMP for Medicinal Products 5.40	GMP related computerized systems should be validated. The depth and scope of validation depends on the diversity, complexity and criticality of the computerized application.
PIC/S PE 011-1 Guide to Good Distribution Practice for medicinal products	Before a computerized system is brought into use, it should be demonstrated, through appropriate validation or verification studies
ICH Q7A GMPs for Active Pharmaceutical Ingredients	GMP-related computerized systems should be validated
COUNCIL DIRECTIVE 93/42/EEC 12.(1a)	The software must be validated

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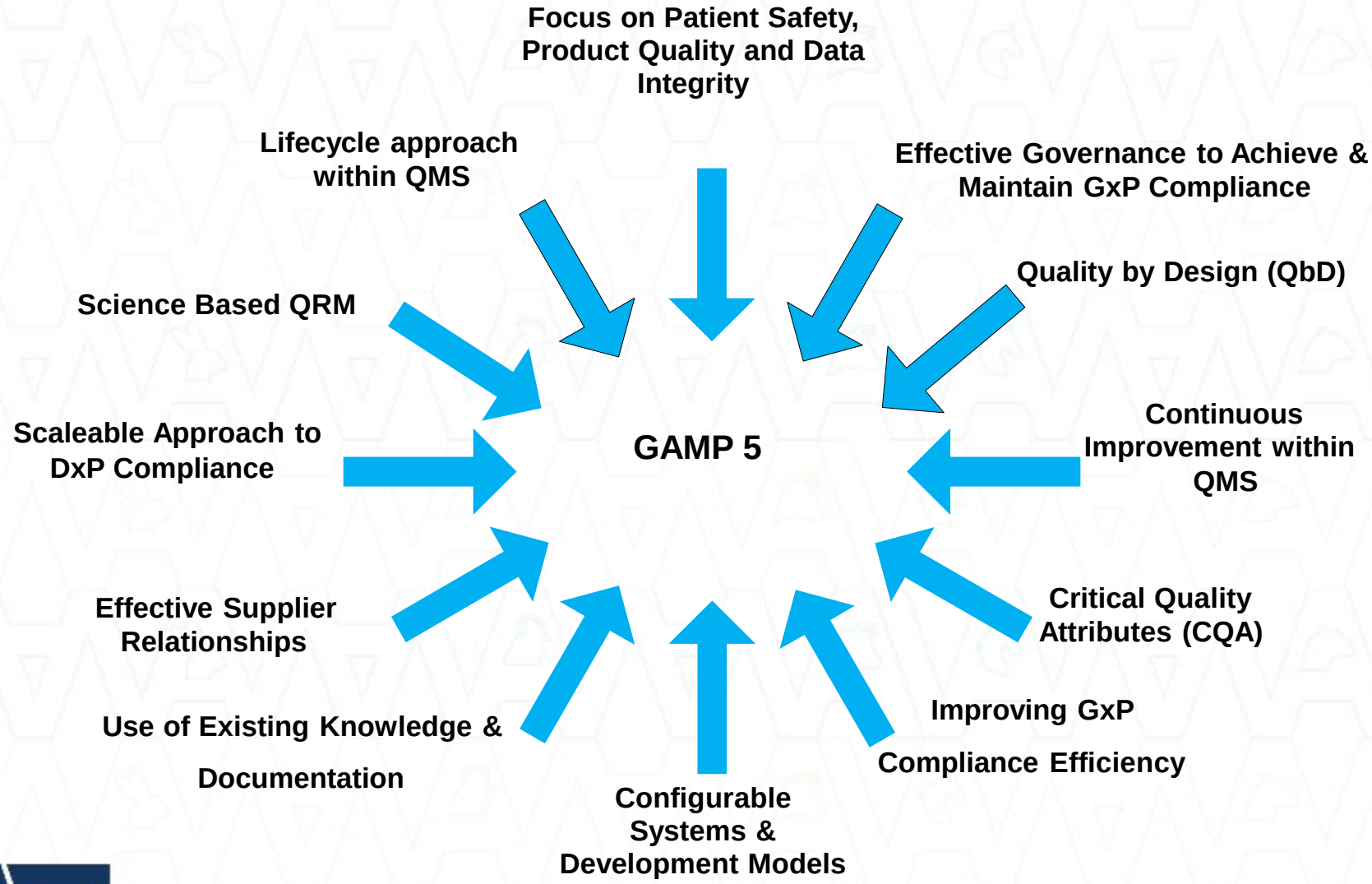
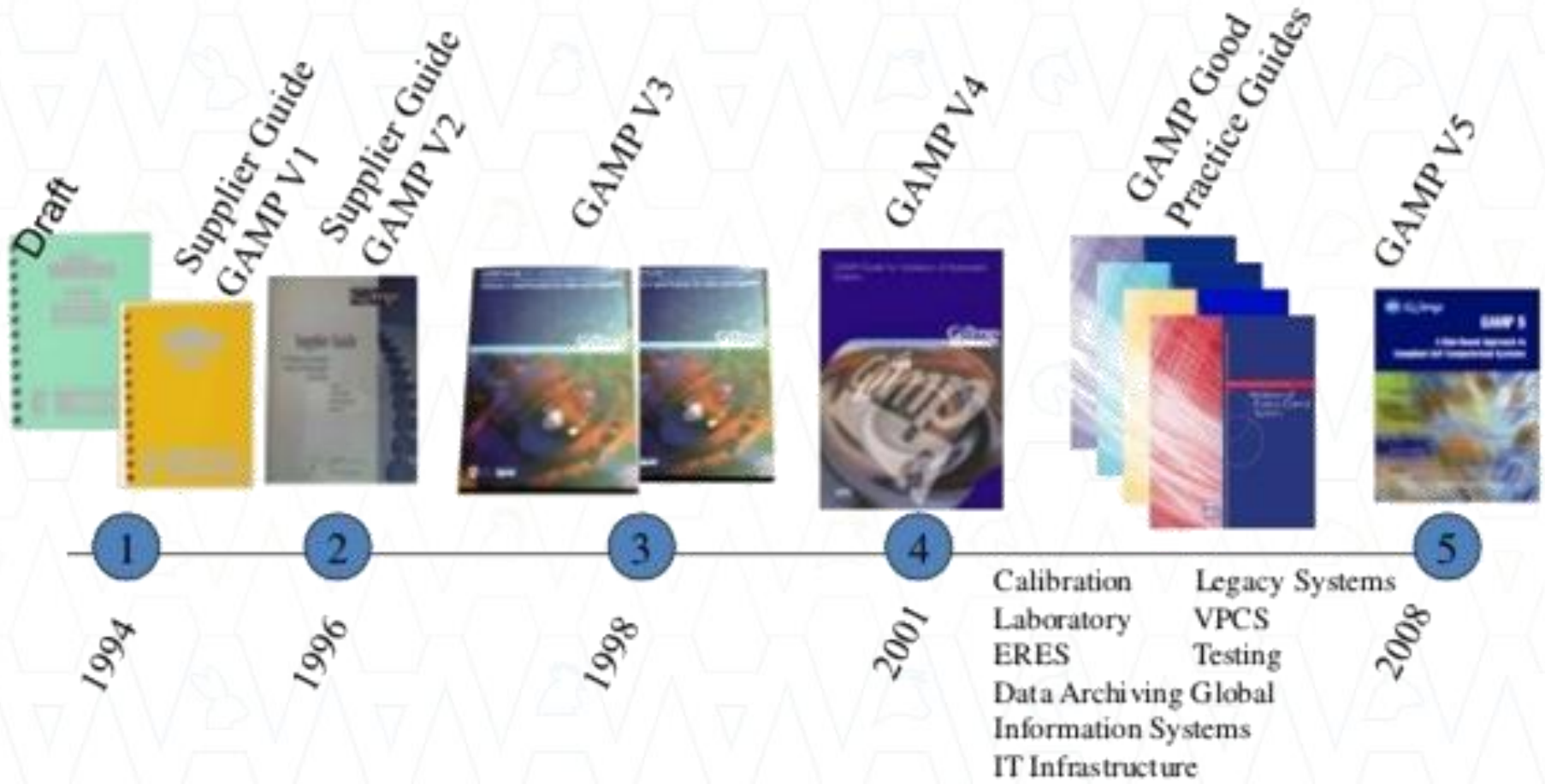
Compliance Strategy

The objective must be to achieve compliance as cost effectively as possible.


Focus on Patient Safety, Product Quality and Data Integrity
Lifecycle approach within QMS
Effective Governance to Achieve & Maintain GxP Compliance
Science Based QRM
Quality by Design (QbD)
Scaleable Approach to DxP Compliance
GAMP 5
Continuous Improvement within QMS
Effective Supplier Relationships
Critical Quality Attributes (CQA)
Use of Existing Knowledge & Documentation
Improving GxP Compliance Efficiency
Configurable Systems & Development Models


Draft
Supplier Guide GAMP V1
Supplier Guide GAMP V2
GAMP V3
GAMP V4
GAMP Good Practice Guides
GAMP V5
1
2
3
4
5
1994
1996
1998
2001
2008
Calibration
Laboratory
ERES
Data Archiving
Information Systems
IT Infrastructure
Legacy Systems
VPCS
Testing
Global

GAMP Aim

GAMP describes a set of principles and procedures that help ensure that pharmaceutical Software have required quality.

Computer system validation (CSV) following GAMP guidelines require users and suppliers to work together so that responsibilities regarding the validation process are understood.

What Software Requires CSV?

- Medical Device Software
- Production software
- Quality management software
- Software for FDA-Regulated Records

Examples for Quality Management Software

- Change control software
- Calibration Software
- Document management software
- Deviation tracking software
- CAPA tracking software

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Software for FDA-Regulated Records

- Electronic Submission Software
- Warehouse Management Software
- Validation Records software
- Supplier approval software
- Clinical Trails Records software

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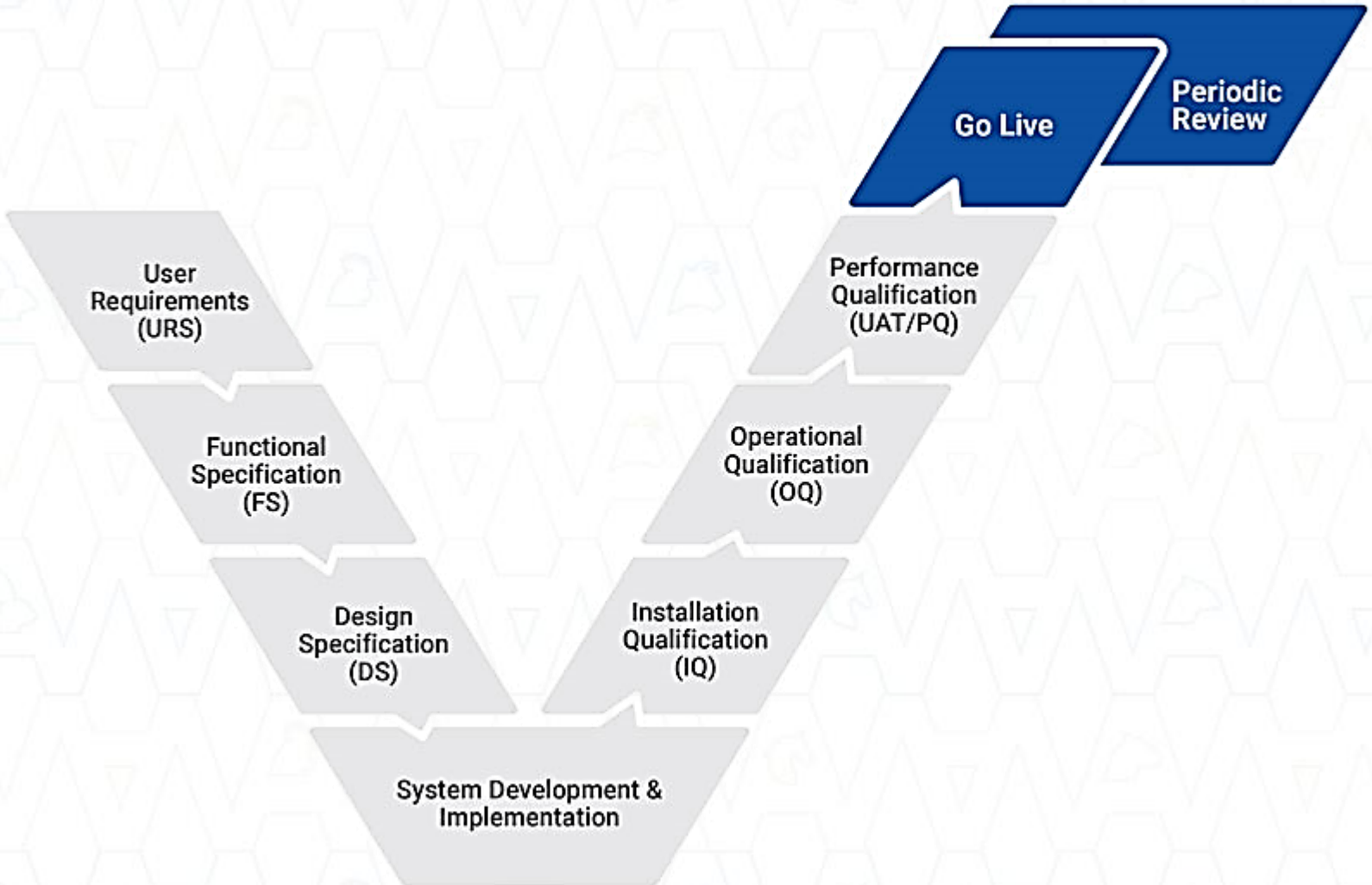
Validation life cycle



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User Requirement Specifications (URS)

Describes what the system should do. The user requirements contain scientific, business, legal, regulatory, safety, performance and quality aspects of the future system. The user requirements serve as the basis for the Performance Qualification (PQ).

DQ (Design Qualification):
Documented verification that the proposed design of facilities, systems, and equipment is suitable for the intended purpose

IQ (Installation qualification):
Documented verification that a system is installed according to written and pre-approved specifications

OQ (Operational qualification):
Documented verification that a system operates according to written and pre-approved specifications throughout specified operating ranges at the customer.

PQ (Performance qualification) or User Acceptance Testing (UAT):
Documented verification that a system is capable of performing the activities of the processes it is required to perform, according to written and pre-approved specifications, within the scope of the business process and operating environment

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Required documents for CSV

- Validation Plans and Protocols
- Documented Risk Assessment
- Documented Requirements, Specifications and Designs
- Verification activities such as Testing or Qualification according to approved plans or protocols (e.g.; IQ, OQ, PQ)
- Control mechanisms to ensure integrity and completeness during the validation or qualification process
- Procedures and/or other mechanisms to maintain the system in a controlled state after initial implementation
- Reports that provide summaries and conclusions of validation/qualification.

Category	GAMP 4	GAMP 5
1	Operating system	**Infrastructure software** (OS, middleware, DB managers, etc.)
2	Firmware	No longer used – Firmware is no longer functionally distinguishable
3	Standard software	**Non-configured software** – Includes default configurable SW
4	Configurable software packages	**Configured software** – configured to satisfy business process
5	Custom software	Custom Software

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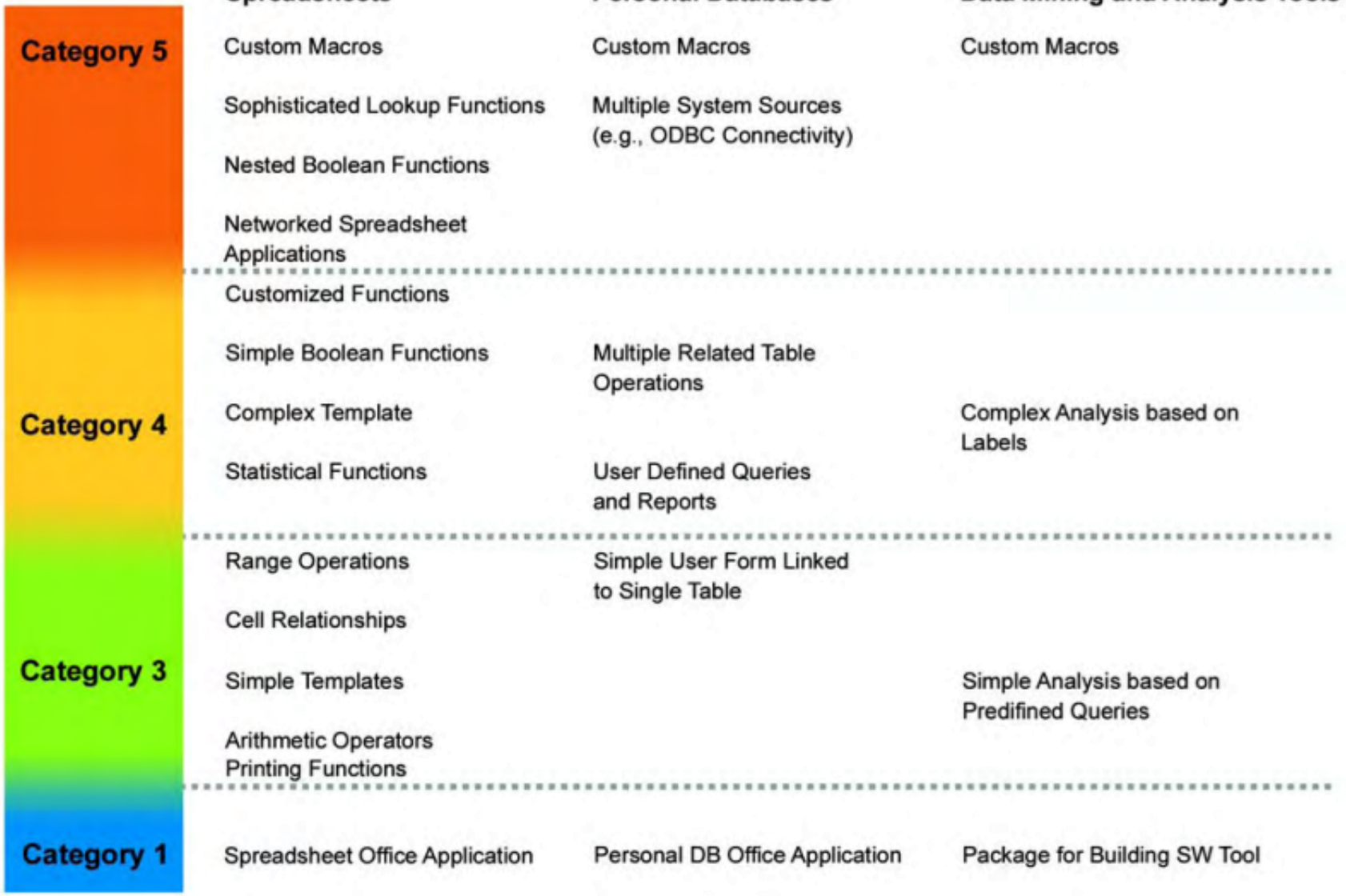
GAMP 5 – software categories

Continuum of Categories for End User Applications



Category	Hardware type	Validation Approach	Example
Category-1	Standard hardware components	Standard hardware components should be documented including make or supplier details and version number.	PLC, Controller, Scanner.
		Hardware details can be taken from the hardware data sheet or specification material.	
Category-2	Custom built hardware components	Hardware should have design specification and be subjected to acceptance testing.	PCB etc.
		Any hardware configuration should be defined in the design documentation and verify in the IQ.	

GAMP 5 – Hardware categories

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Regulatory Guidance on Software Validation

Computerized System validation plan

01

Shall be an approved document, which describes the validation activities and responsibilities.

02

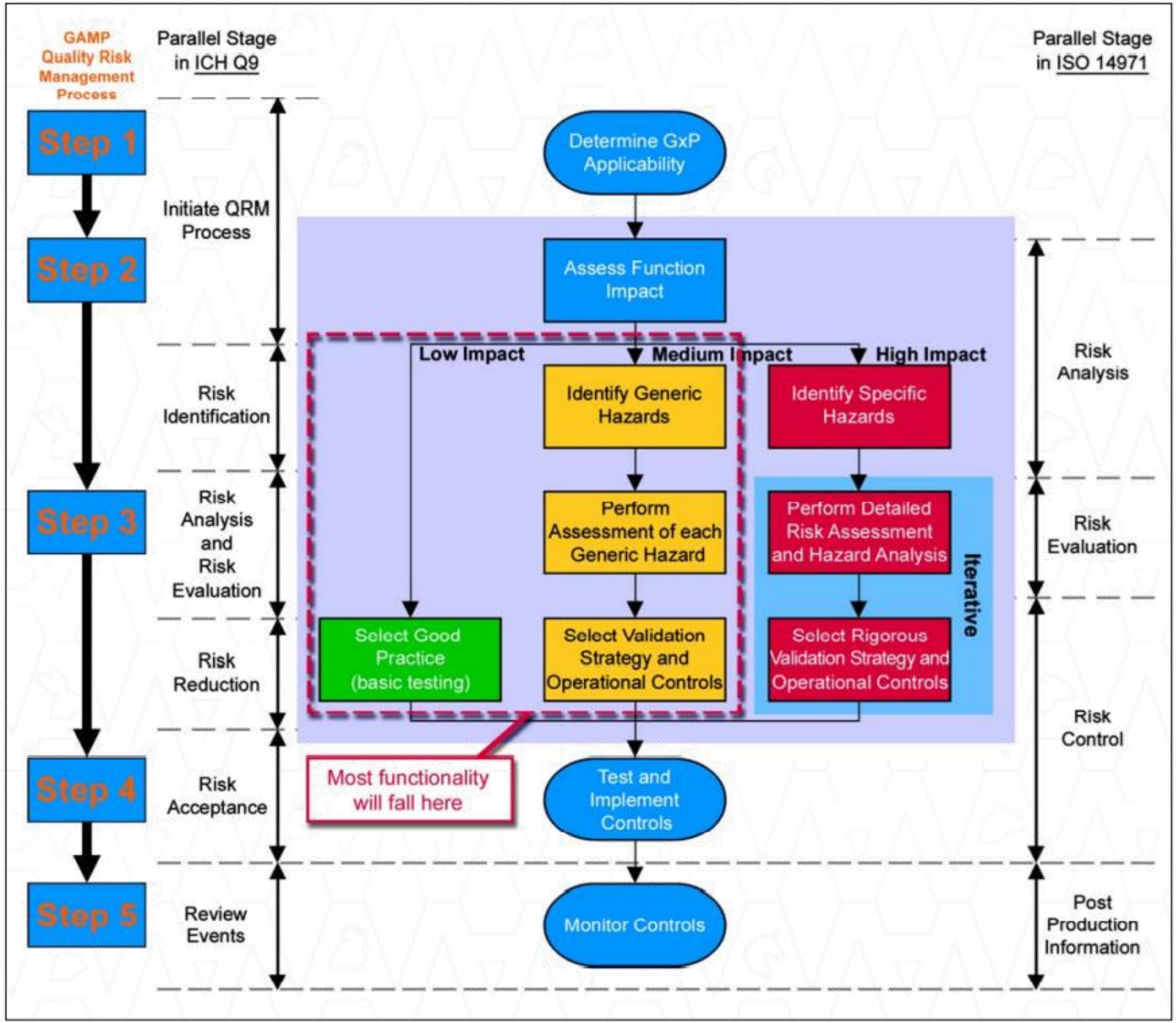
Specifies the Computerized System subjected to validation and compiles the validation activities to be performed and the validation targets/criteria to be fulfilled.

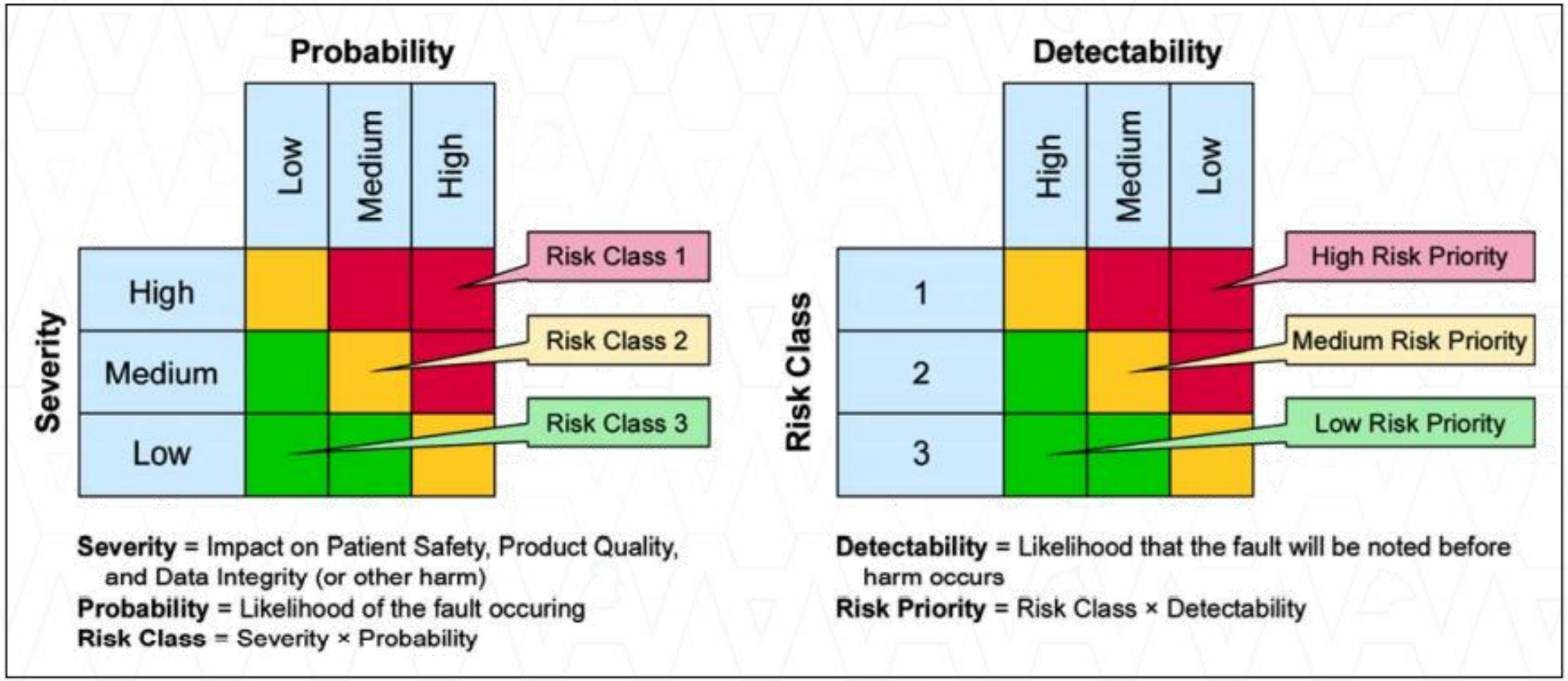
03

Shall be prepared and approved prior to conducting the test.

Five steps risk management approach

GAMP 5 - A risk-based approach to compliant GxP computerized system



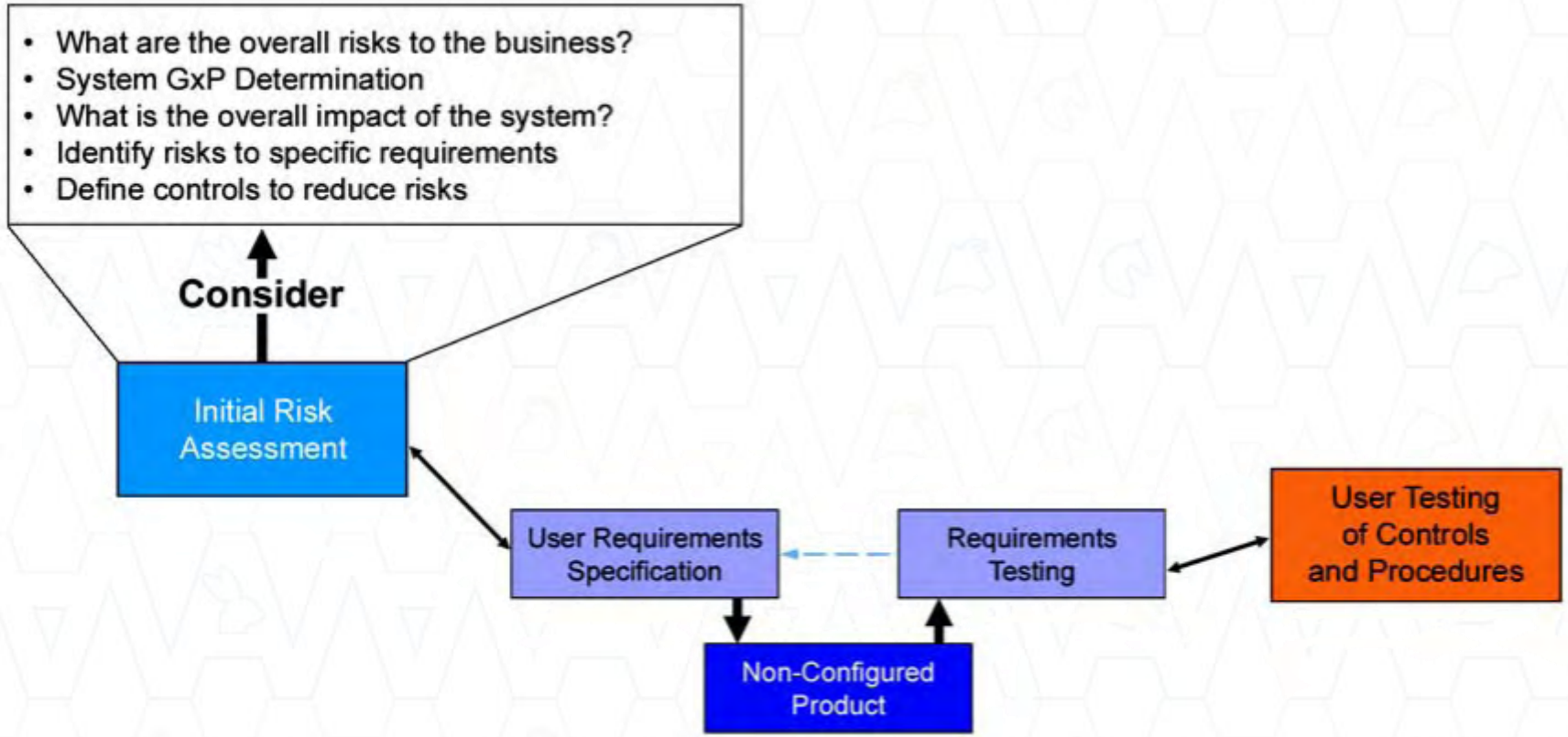

Probability
Low
Medium
High
Severity
High
Medium
Low
Risk Class 1
Risk Class 2
Risk Class 3
Detectability
High
Medium
Low
Risk Class
1
2
3
High Risk Priority
Medium Risk Priority
Low Risk Priority
Severity = Impact on Patient Safety, Product Quality, and Data Integrity (or other harm)
Probability = Likelihood of the fault occuring
Risk Class = Severity × Probability
Detectability = Likelihood that the fault will be noted before harm occurs
Risk Priority = Risk Class × Detectability

Commonly used methods and tools for risk assessment

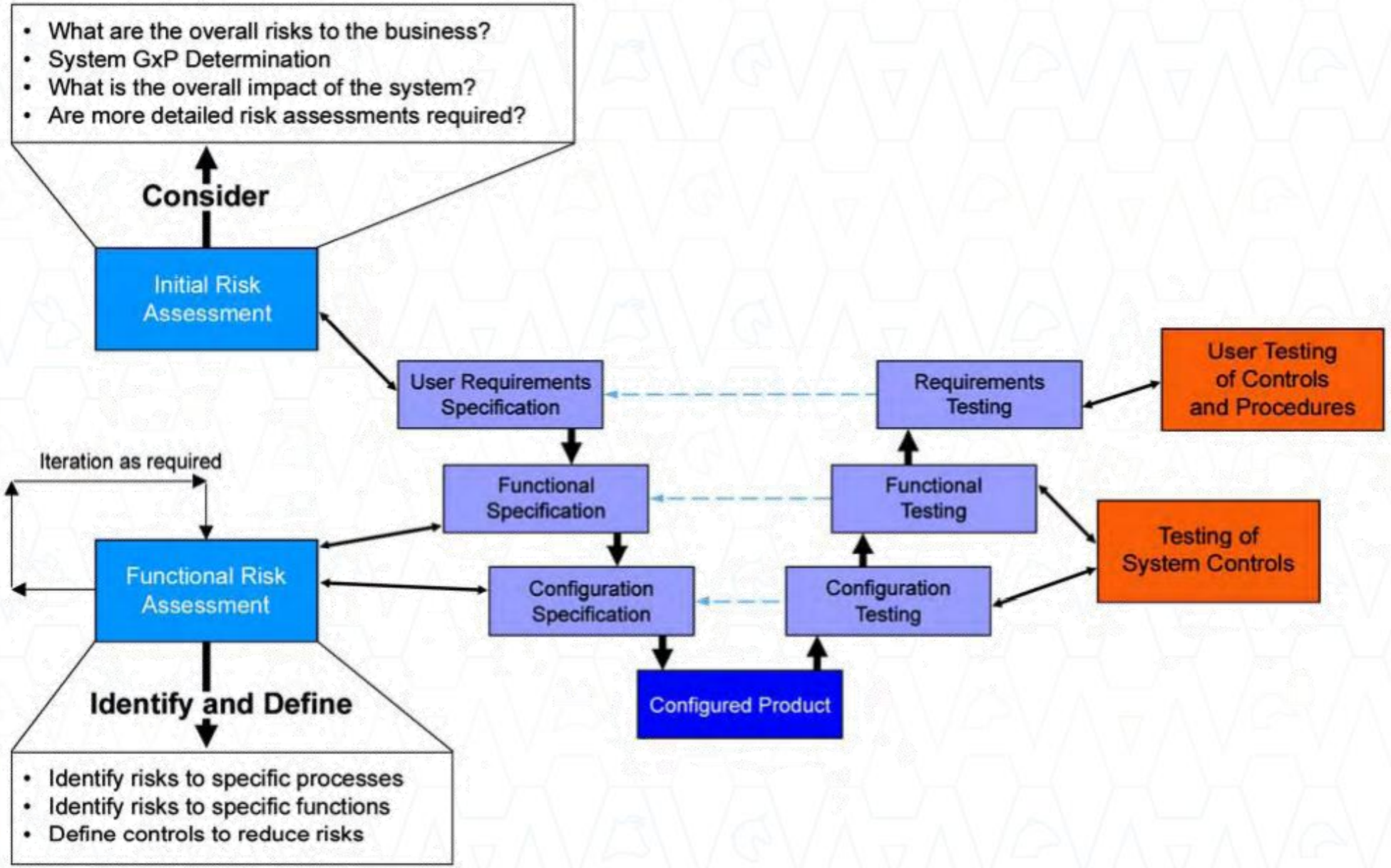
- Hazard and Operability Analysis (HAZOP)
- Computer Hazards and Operability Analysis (CHAZOP)
- Failure Mode and Effects Analysis (FMEA)
- Failure Mode, Effects, and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA)
- Hazard Analysis and Critical Control Points (HACCP)
- Basic Risk Management Facilitation Methods
- Preliminary Hazard Analysis (PHA)
- Risk Ranking and Filtering

For further details see ICH Q9 Annex I: Risk Management Methods and Tools (Reference 10, Appendix G3).

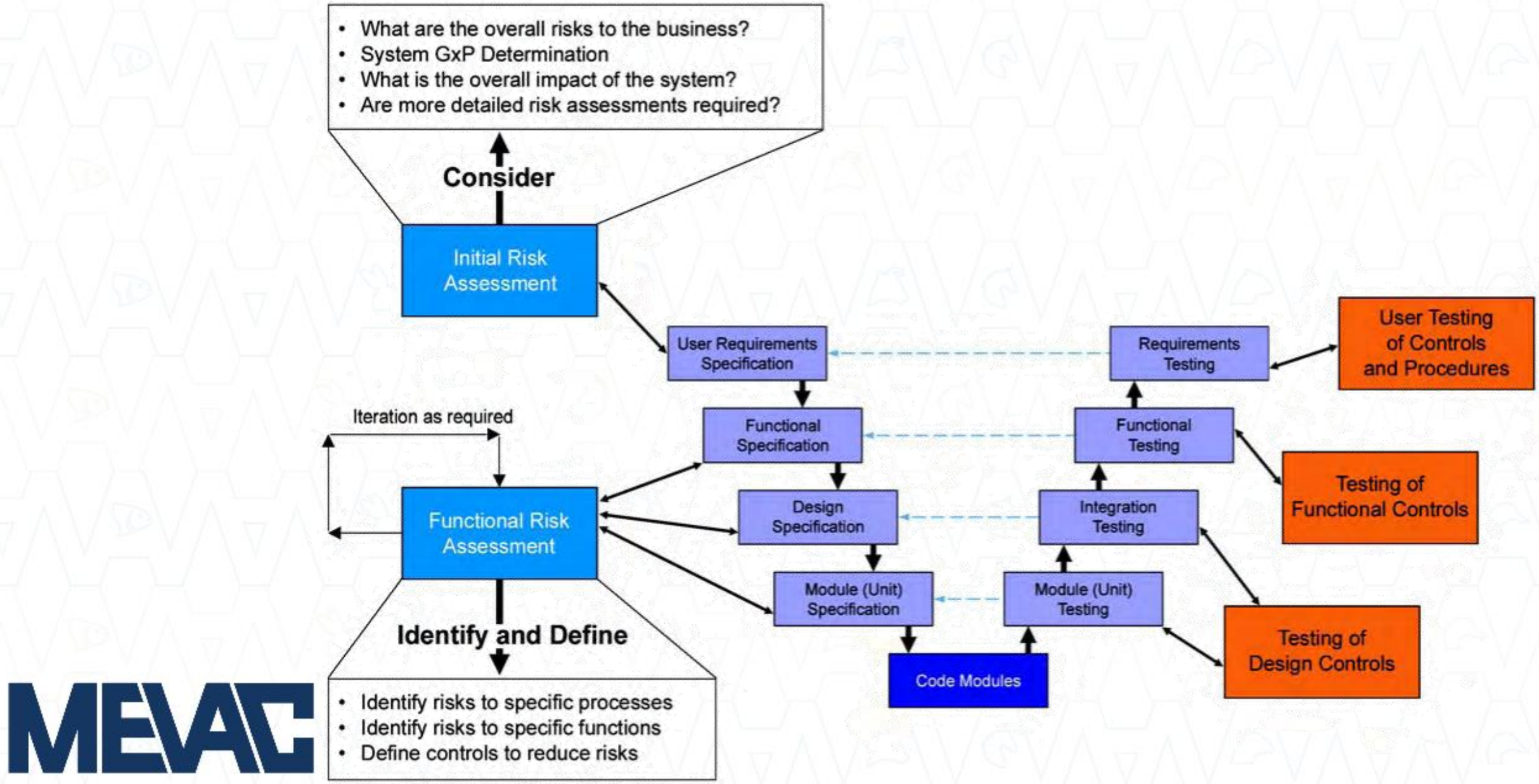
Risk-Based Approach for Non-Configured Product (Category 3)



Risk-Based Approach for Configured Product (Category 4)



Risk-Based Approach for Custom Application (Category 5)



Project Phase Deliverables

S.No.	Deliverables	GAMP Category-1	GAMP Category-3	GAMP Category -4	GAMP Category -5
1.	User Requirement Specification	×	✓	✓	✓
2.	Vendor Assessment	×	×	✓	✓
3.	Initial Risk Assessment	✓	✓	✓	✓
4.	Project Validation plan	✓	×	✓	✓
5.	Functional Specification	×	×	✓	✓
6.	Functional Risk Assessment	✓	✓	✓	✓
7.	Configuration Specification	×	×	✓	✓
8.	Design Specification	×	×	✓	✓
9.	Setup, Configuration& Testing in validation Environment	×	×	✓	✓
10.	Installation Qualification	✓	✓	✓	✓
11.	Operational Qualification	×	✓	✓	✓
12.	PerformanceQualification-1	×	✓	✓	✓
13.	Setup, Configuration& Testing in Production Environment	×	×	✓	✓
14.	PerformanceQualification-2	×	×	✓	✓
15.	Traceability Matrix	×	✓	✓	✓
16.	Project Validation Report	✓	✓	✓	✓

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Computer Software Assurance

Five Things You Need To Know

Computer Software Assurance (CSA) comes from a multi-year collaboration between FDA and industry. It identifies common pain points, FDA's current thinking and puts patient safety and product quality ay the heart of the risk assessment process.

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New Computer Software Assurance

01

A more flexible, less burdensome, and faster risk-based approach

02

Various assurance approaches depending on the system/feature risk

03

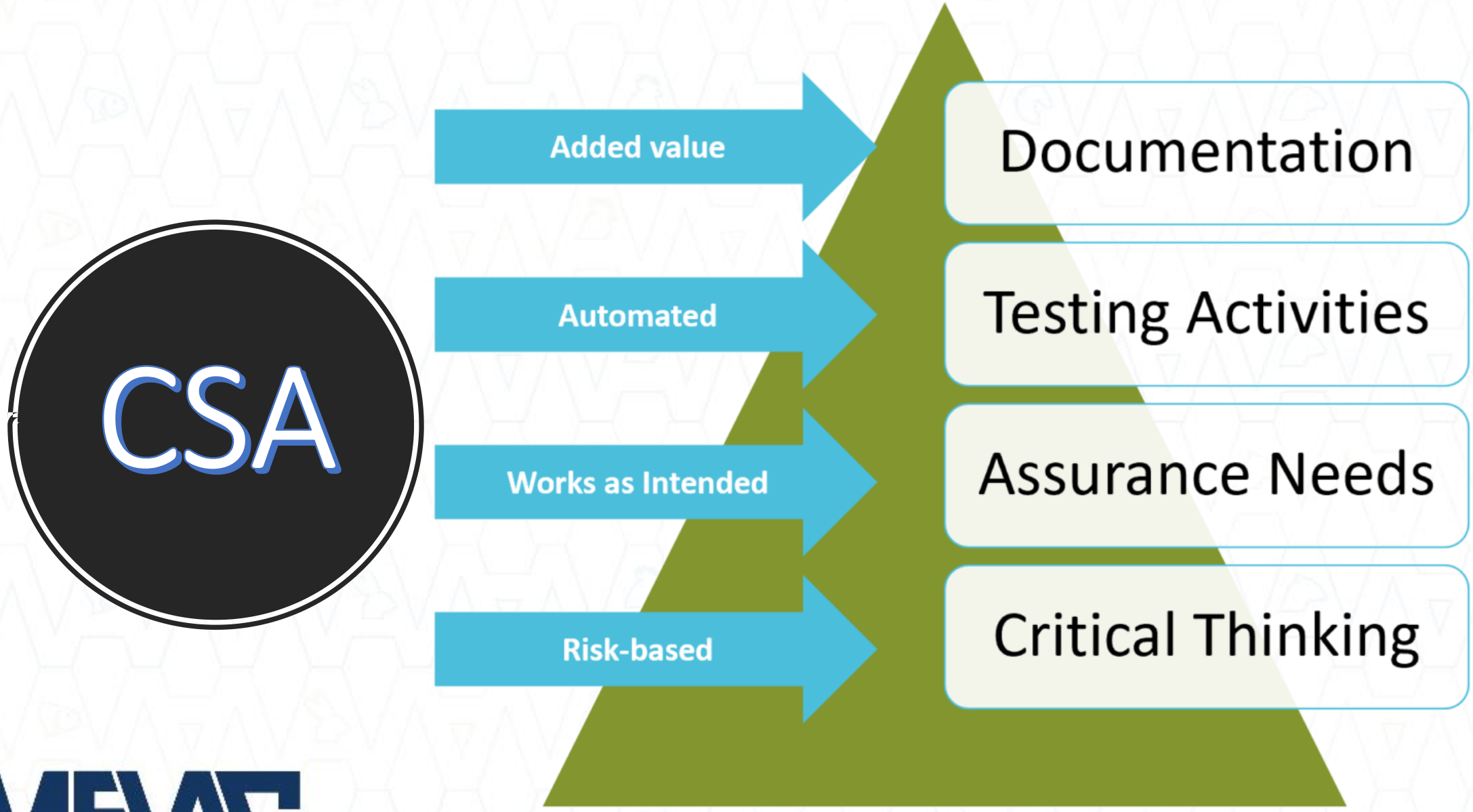
Apply critical thinking to ensure the software is safe and meet its intended use

04

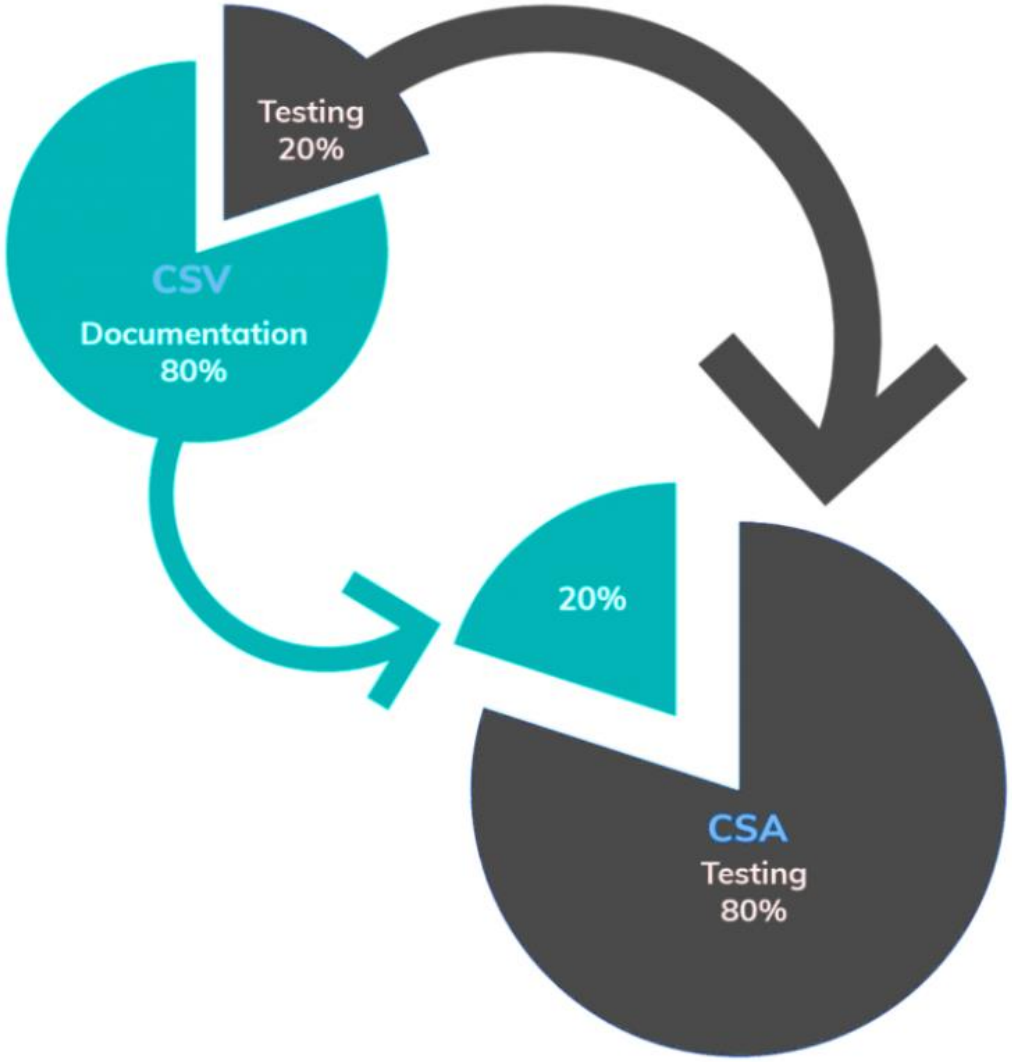
Reduced testing activities resulting from better supplier qualification and collaboration

05

Reduced number of deviations due to tester error


CSA
Added value
Automated
Works as Intended
Risk-based
Documentation
Testing Activities
Assurance Needs
Critical Thinking

Shifting from CSV to CSA



Spreadsheet to Analyze and Graph Non-conformances

The manufacturer developed a spreadsheet used to analyze, and graph non-conformances stored in a controlled system. Intended use of the spreadsheet has a low patient risk.

Test Assurance Report

- **Intended Use**: Analyze and graph non-conformances data stored in a controlled system
- **Risk Assessment**: The intended use of the spreadsheet is for analyzing process quality outcomes and is identified as a high-risk function. The manufacturing process includes additional changes and inspections that assure non-conformances do not escape therefore the patient risk is low.
- **Tested**: Spreadsheet X, Version 1.2
- **Test type**: Unscripted testing – exploratory testing
- **Goal**: Ensure that analyses can be Created/Read/Updated/Deleted
- **When/Who**: July 9, 2019, by John Smith
- **Testing activities**: Created, updated, and deleted analyses and observed that all calculated fields were correctly updated
- **Conclusion**: No errors observed

Vs

- **1 page vs 25 pages**
- **1 hour vs 5 days**
- **Product quality is equivalent or better**
- **Focus on the right level of assurance on the right things, eliminate redundancy**

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Conclusion

- This presentation provides a review of the CSV as a requirement od GMP and CSA as a new approach for more practical software acceptance. It highlights the common elements of CSV and CSA, explains their differences, explains the main focus of CSA, and highlights how to achieve both, quality and compliance.

- We assume attendees are already aware with concepts like CSV and data integrity.

Recommendations

1. There are many benefits to implement the CSV.

2. Companies must invest in improve the staff awareness with the CSV and CSA.

3. CSA will replace CSV approach very soon.

THANK YOU

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