Motto:
We trust God, everything
else must be validated
(an inspector)

Computer System Verification and Validation in the Pharmaceutical Industry

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Contents

- General Principles and Terminology
- V&V Elements and Ways
- Risk assessment in V&V
- Challenges and Responses

General Principles

- The purpose of the GxP quality guidelines:
  - to ensure a product is safe and meets its intended use,
  - fits current compliance and regulatory requirements and
  - built upon existing industry good practice in an efficient and effective manner.
- Key Aspects:
  - Safety (e.g. patients)
  - Quality of Products
  - Security, Reliability and Integrity
  - Traceability and Transparency (e.g Documented processes, evidence and activities)
  - Risks (mgt.)

GxP is a general term for Good (Anything...) Practice quality guidelines and regulations (e.g Good Manufacturing Practice)
Sources: General Principles of Software Validation; Final Guidance for Industry and FDA Staff January 11, 2002
FDA: Food and Drug Administration
US Food & Drug Administration - Code of Federal Regulations, Title 21, part 11: “Electronic Records; Electronic Signatures; Final Rule”

Definition and Terminology of V&V 1

„**Software verification** provides objective evidence that the design outputs of a particular phase of the software development life cycle meet all of the specified requirements for that phase.” It is a developer’s conceptual aspect and practice of verifying documents, design, code and program.

„**Software validation** 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.

Source: General Principles of Software Validation; Final Guidance for Industry and FDA Staff January 11, 2002
FDA: Food and Drug Administration

Definition of Validation

Evaluates the developed system, whether it meets the specified customer expectations and requirements and answers the questions:

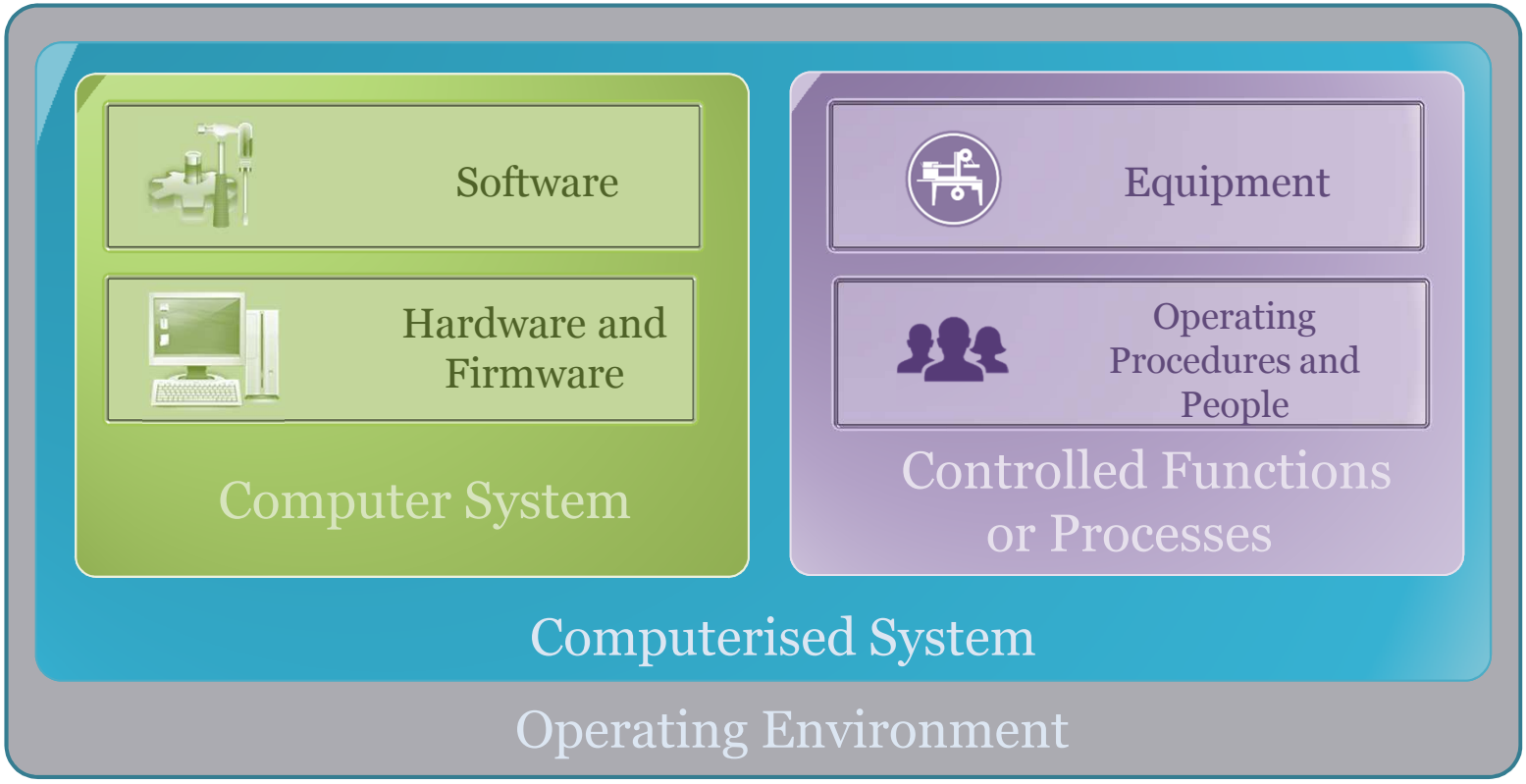
- Are we building the appropriate product?
- Does the software meet the user requirements and/or customer expectations?

Definition of Verification

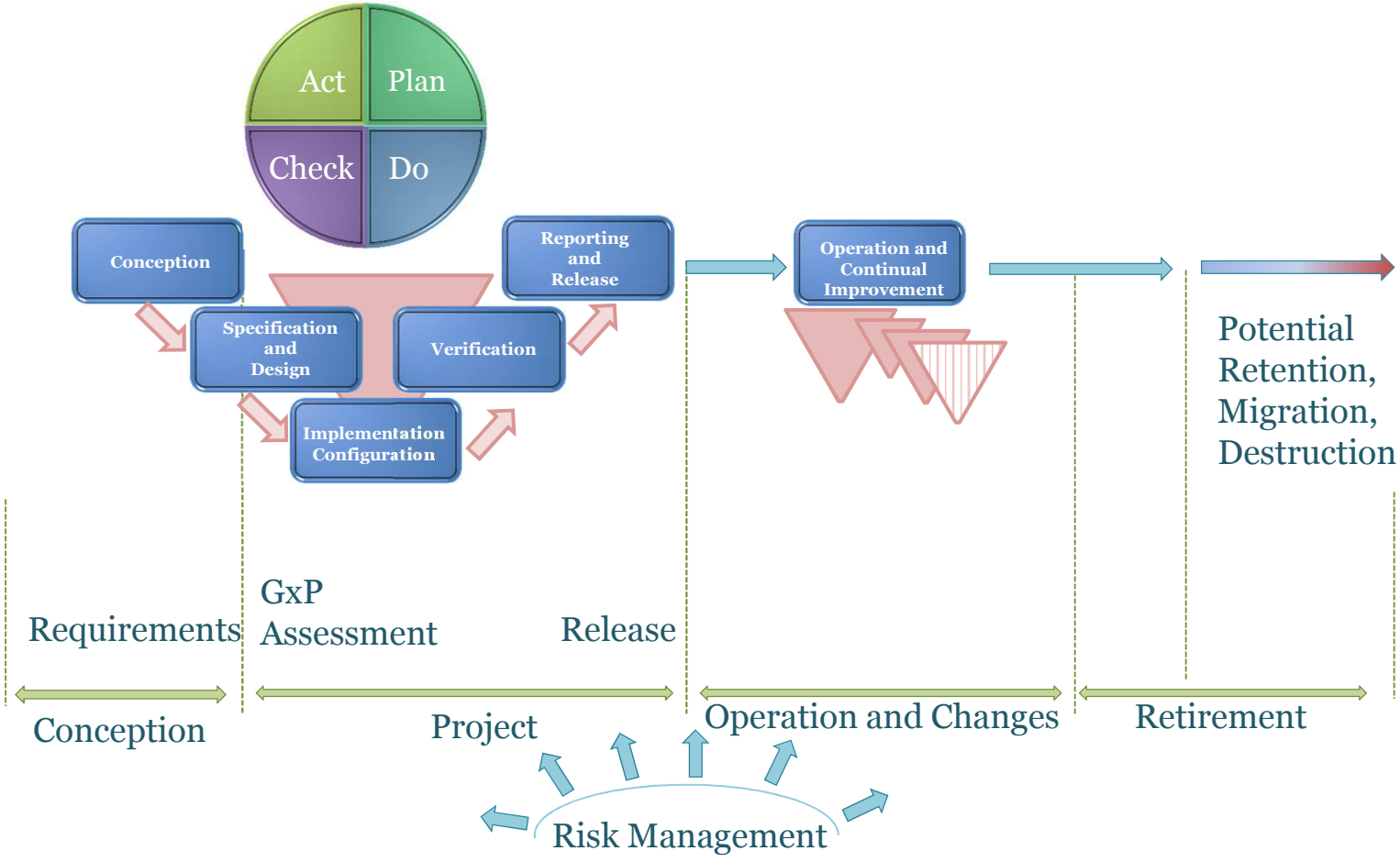
Determine whether the products of a particular development phase meet the specified requirements to start that phase (e.g specifications, code, app. function) and answers the questions:

- Are we building the product appropriately (in the right way)?
- Must the software conform to its specifications?

Elements of the Computerised System

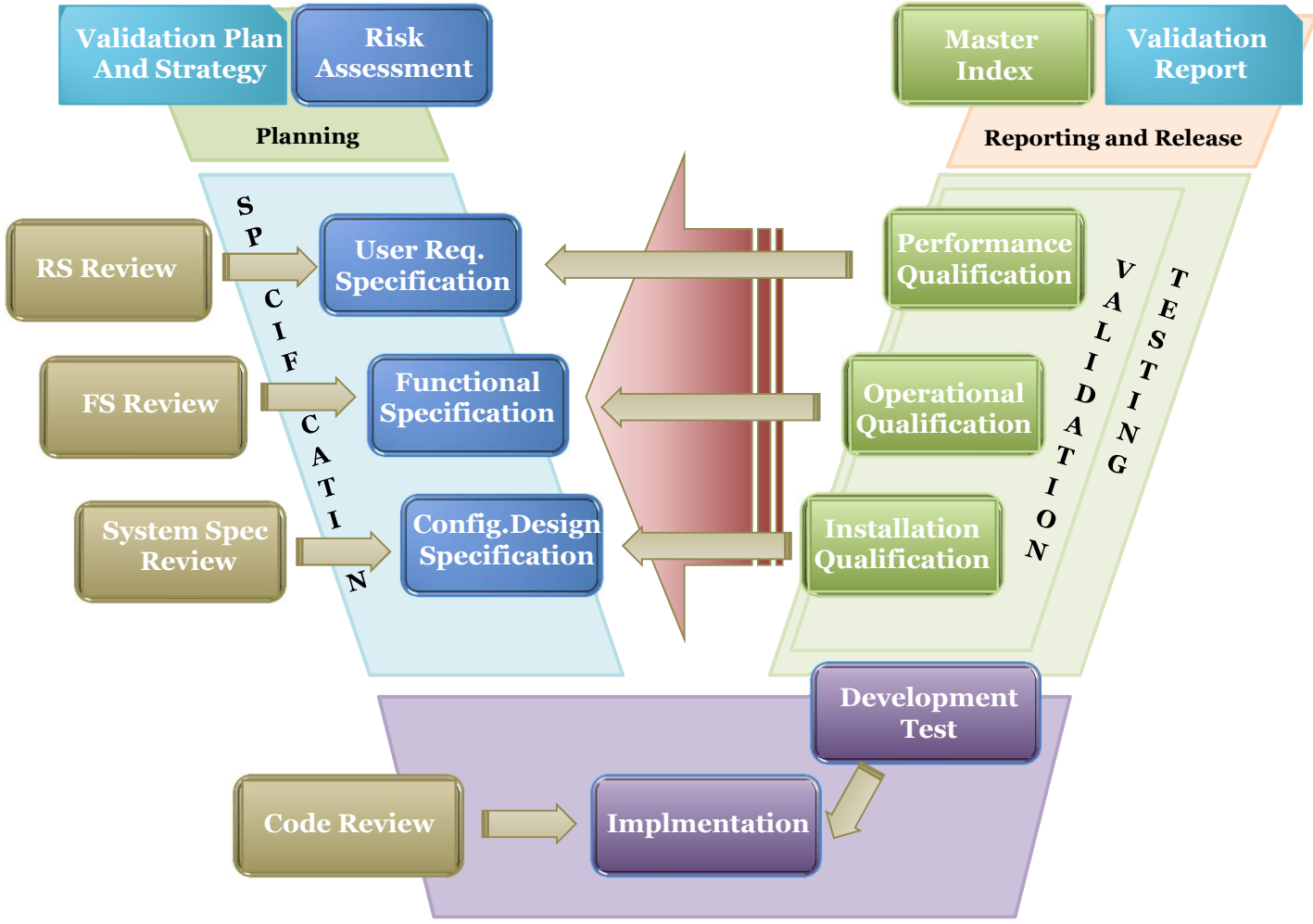


Computerised System Life Cycle



Source:
ISPE Headquarters GAMP 5 A Risk-based Approach to Compliant Gxp Computerized Systems 2008, Figure 3.2: Life Cycle Phases

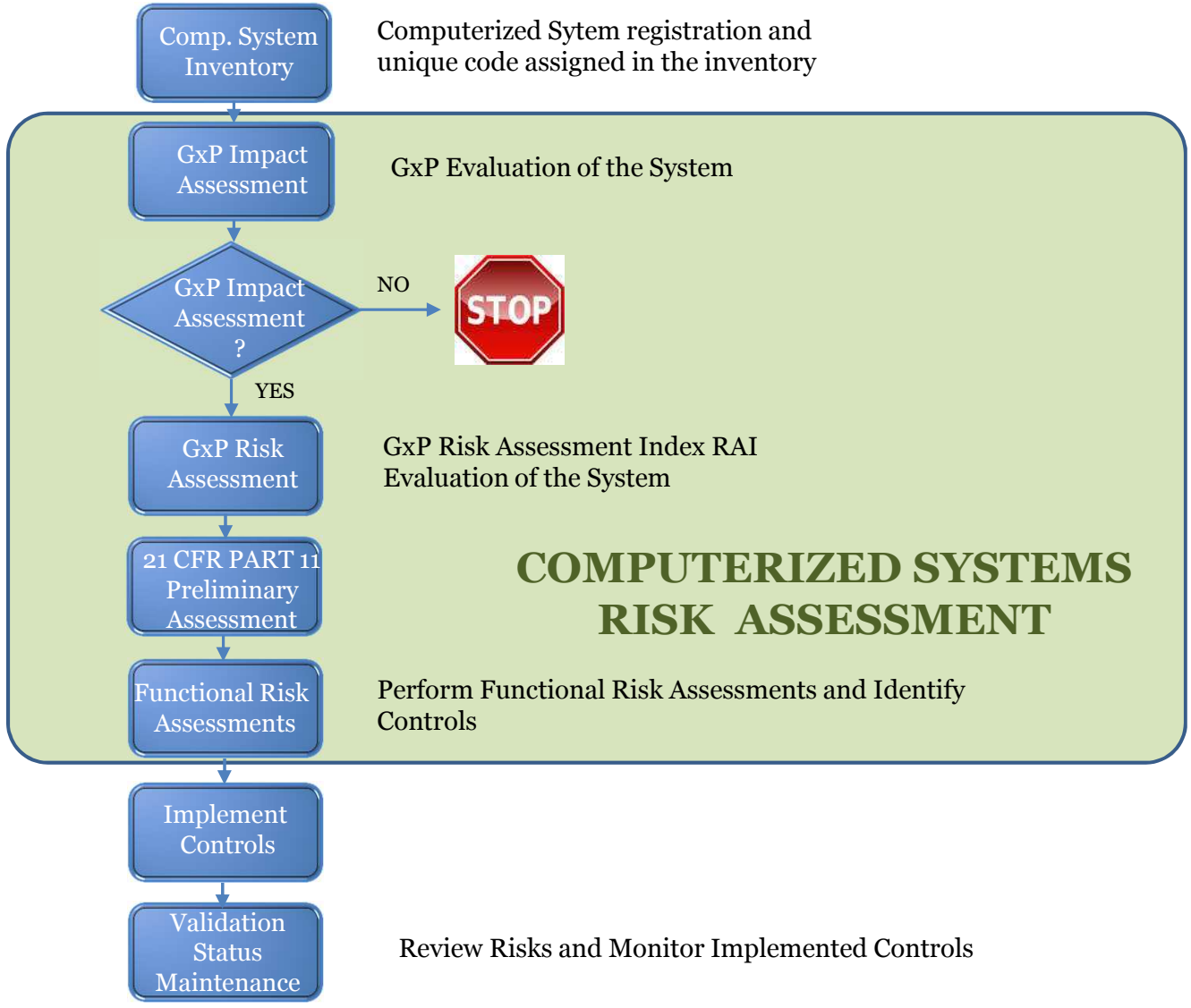
V Model Concept



Risk Management

- Goal of Risk Management
  - Identify potential problems before they occur
  - Manage risk-handling activities
- Scopes:
  - Project and Business
  - Business, Resources (HR, Financial, Technical etc.)
- GxP System Risk (Validation Risk mgt.)
  - Risk Impact Assessment
  - Detailed Risk Analysis (e.g Functional RAI)
- Risk Control Implementation and Monitoring

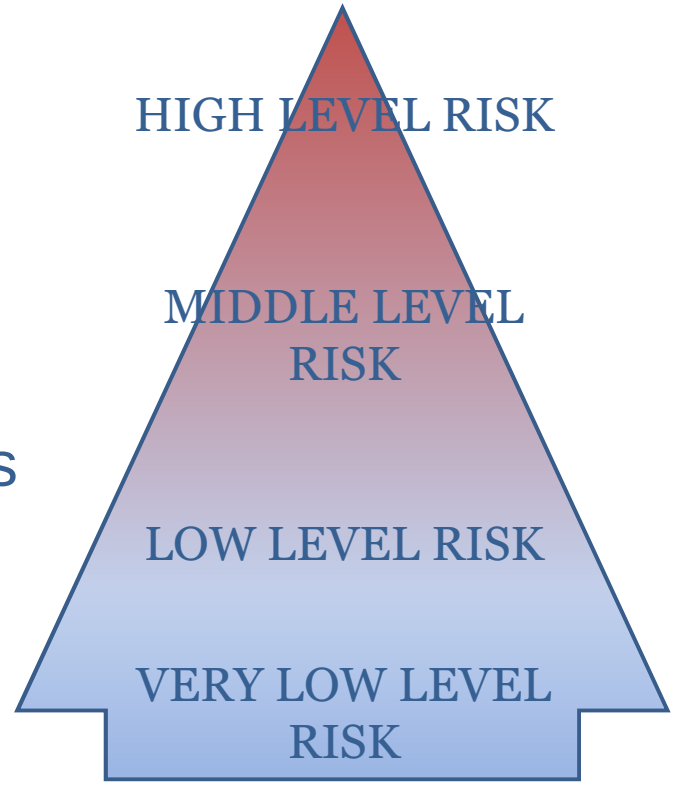
Key Steps of Validation Strategy



GAMP 5 Software Categories

Classification is a built-in risk assessment

- Category 5: Custom applications
  - Software custom designed and coded to suit the business process
- Category 4: Configured products
  - LIMS, EDMS, ERP, Spreadsheets, etc
- Category 3: Nonconfigured products
  - Firmware-based sw, Commercial-Off-the-Shelf (COTS) software
- Category 1: Infrastructure Software
  - Operating Systems, Network monitoring tools etc.



GAMP: Good Automated Manufacturing Practice Forum was founded in 1991 and partnered with the International Society for Pharmaceutical Engineering (ISPE) to publish the GAMP guidelines
GAMP guide version 5, that was released in March 2008 and
Category 2 (Firmware) discontinued

GxP System Risk Assessment 1

- GxP Impact Assessment
  - evaluating the potential impact of the System on the GxP processes on key areas (e.g. MES, LAS etc.)
- GxP System Risk Assessment
  - Effort should be focused on high risks
  - The risks identified and documented on three levels in two dimensions (e.g. Criticality and Complexity)
  - Detailed Risk Assessment
    - Process and/or Functional Risk Analysis
    - Through the Specification and Design phases
- Risk control recommendations are needed

GxP System Risk Assessment 2

RAI vs. Deliverable Documents

GxP Impact Assessment

GxP System

ID	Verify if the Computeri… the following…

CRITICALITY	COMPLEXITY		
	HIGH	MEDIUM	LOW
HIGH	HIGH	HIGH	MEDIUM
MEDIUM	HIGH	MEDIUM	LOW
LOW	MEDIUM	LOW	LOW

	Questions	Answers YES/NO
Criticality	Does the sys… that may hav…	
	Does the sys… or reject proc…	
	Does the Co… regulated Ele… Record)?	
	Does the Co… Regulated El…	
	Has the cont… perform oper…	
	Has the cont… perform oper…	
Complexity	The System … checks	
	Does the Co… external critic…	
	Does the Co… calculations/…	
	Is the Compu… regulated en…	
	Can be the C… user require…	
	Does the Co… components…	

Does the system includes … to have documented evide…

N

ss?

GxP I…

NUMBER OF POSITIVE ANSWERS	CRITICALITY/ COMPLEXITY
0-2	Low
3-4	Medium
5-6	High

#	DELIVERABLES	RAI LOW	RAI MEDIUM	RAI HIGH
	PREPARATION			
1	Supplier Evaluation	○	●	●
2	Validation Plan	●	●	●
3	Risk Analysis	●	●	●
	SPECIFICATION			
4	User Requirements …	●	●	●
5	Functional Specifications	○	○	●
6	Configuration Specifications	○	●	●
7	Design Specifications	○	○	●
	TESTING			
8	Functional Risk Analysis	○	●	●
10	Installation Qualification	●	●	●
11	Operational Qualification	○	●	●
12	Performance Qualification	●	●	●
	ACCEPTANCE			
13	Traceability Matrix	●	●	●
14	Validation Report	●	●	●
15	…	○	○	●
	ON GOING			
16	SOP Security	●	●	●
17	SOP Change Control	●	●	●
18	SOP Backup and Recovery	●	●	●
19	SOP Periodic Review	●	●	●

Challenges

- High standards and expectations of business and authorities
- Reducing Risks
- Reducing validation time, cost and effort
- Be green (GMP =<> Giant Mass of Paper)
- Change Control
- Application of new technologies and techniques

Response to the Challenges

- Low Hanging Fruits
  - Cover-all Risk-based approach
  - Off-the-shelf solutions with customisation possibilities and applied preconfigured industry best practices
  - Predefined processes and templates
  - Industry best practices
  - Tools
- Cloud-based services (e.g SaaS, IaaS)
- Combined-techniques (e.g. Prototyping + Waterfall)
- New paradigms (e.g. RAD, AGILE)

Source: Gartner Hype Cycle for Life Sciences, 2015

Conclusion

- The V&V:
  - Much more than testing
  - Improves quality assurance
  - The risk-based approach is crucial
  - Team-oriented, documented activities
  - New trends and paradigms can be seen for improvement

Thank you very much for your attention!

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