Computer Software Assurance

Paradigm Shift

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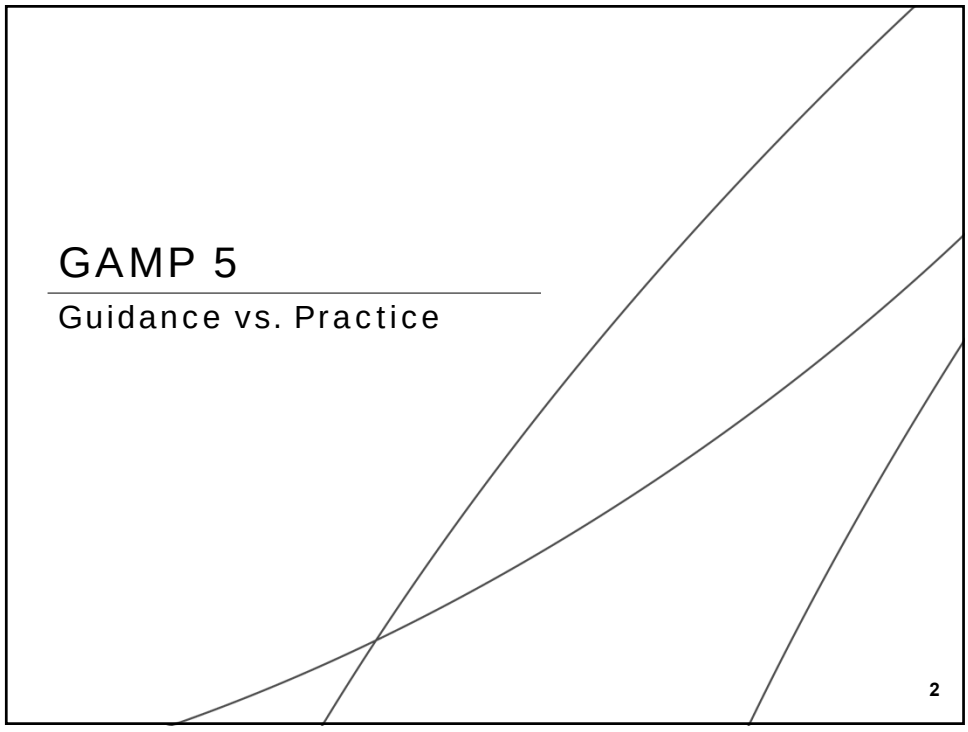
Guidance vs. Practice



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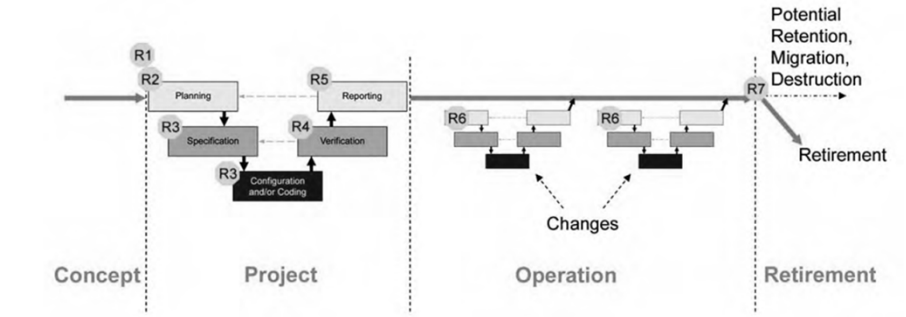
Risk-Based Guidance

Figure M3.3: Typical Use of Risk-Based Decision Making



R1 Initial risk assessment
R2 Risk-based decisions during planning
R3 Functional risk assessments
R4 Risk-based decisions during test planning
R5 Risk-based decisions during planning of operational activities
R6 Functional risk assessments in change control
R7 Risk-based decisions when planning system retirement

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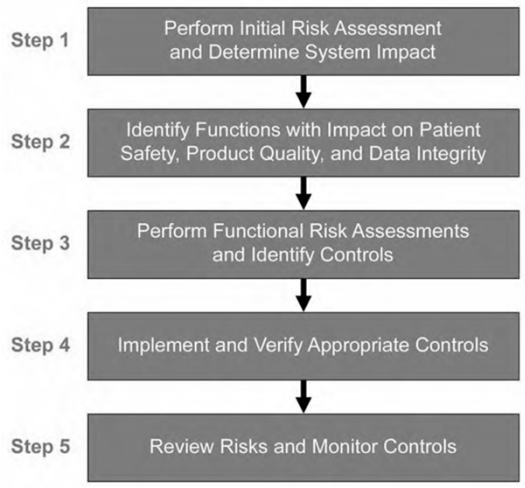
In Practice [Risk Management]

Figure M3.1: Quality Risk Management Process



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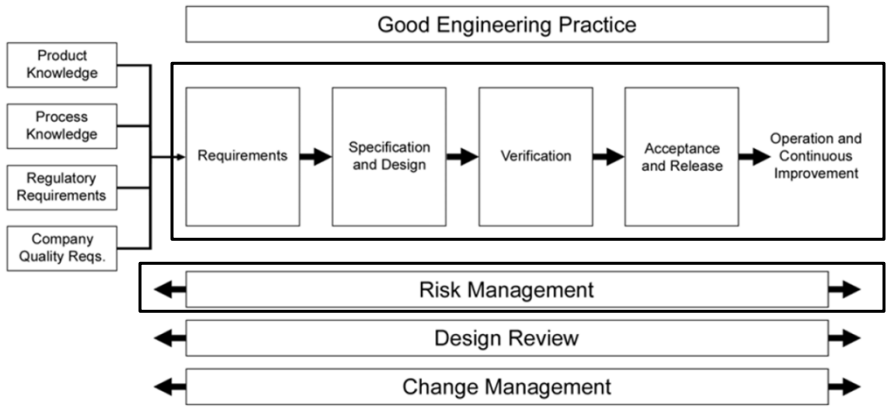
In Practice [Risk Management] *(continued)*

Figure 3.1: The Specification, Design, and Verification Process



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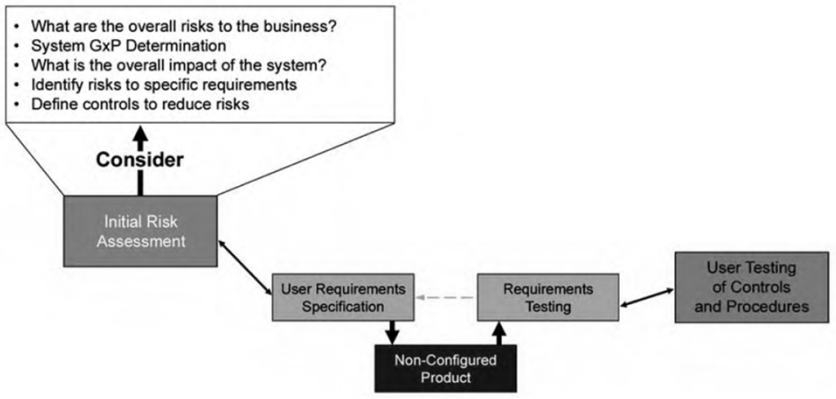
In Practice [Non-Configured Product V-Model]

Figure M3.6: Risk-Based Approach for Non-Configured Product (Category 3)



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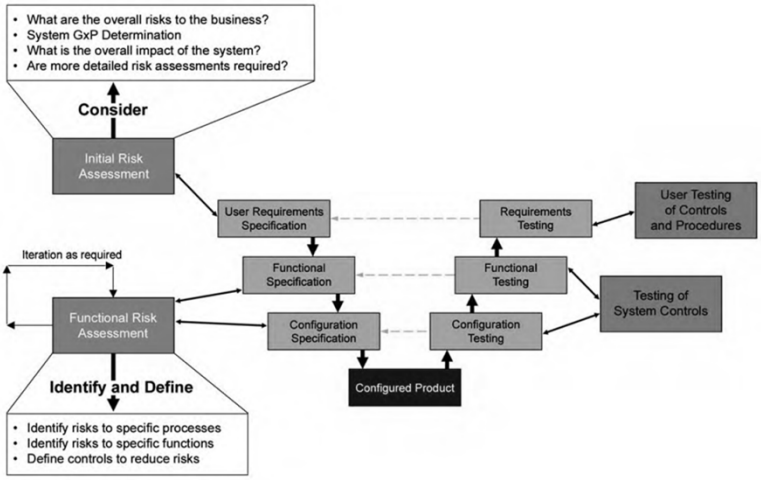
In Practice [Configured Product V-Model]

Figure M3.7: Risk-Based Approach for Configured Product (Category 4)



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Anticipated FDA Draft Guidance

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FDA CDRH
Case for Quality

"…the FDA is working with stakeholders—industry, health care providers, patients, payers, and investors—to build a strong Case for Quality."

https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/case-quality

Computer Systems Validation identified as a major pain point and barrier for moving to better, more efficient technology.

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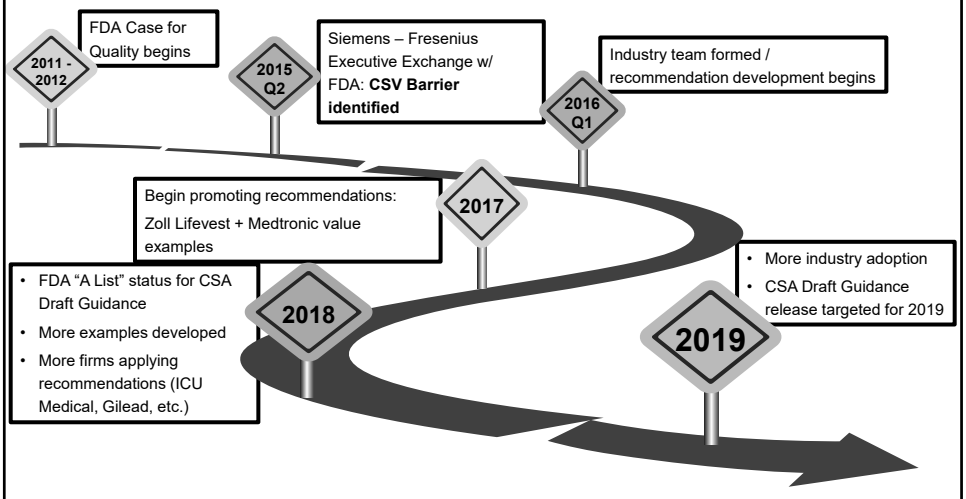
Journey of FDA CDRH CSV Team



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The Industry CSV Team

Company	Name
Baxter Healthcare	Tina Koepke
Boston Scientific	Damien McPhillips
Boston Scientific	Ray Murphy
Compliance Group	Khaled Moussally
Edwards Lifesciences	Penny Sangkhavichith
Edwards Lifesciences	Andy Lee
FDA	Cisco Vicenty
FDA	John Murray
Fresenius Medical Care	Bill D'Innocenzo
Fresenius Medical Care	Curt Curtis
Fresenius Medical Care	Marc Koetter
Gilead Sciences	Ken Shitamoto
Gilead Sciences	Senthil Gurumoorthi

Company	Name
Johnson and Johnson	Dana Guarnaccia
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Medtronic	Frankie Bill
Medtronic	Michael Branch
Medtronic	April Francis
NeuroVision Imaging	Pepe Davis
Ortho-Clinical Diagnostics	Des Chesterfield
Siemens PLM	Jason Spiegler
Siemens PLM	Greg Robino
Siemens PLM	Thorsten Ruehl
Zoll Lifevest	Frank Meledandri Sr.

Contributions also provided by past team members:
Stacey Allen, Jason Aurich, Sean Benedik, Laura Clayton, Bill Hargrave, Joe Hens , Scott Moeller & Mark Willis

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Computer Software Assurance Considerations and Approach

The Quality System regulations allow for a manufacturer to apply a critical risk-based approach to their assurance activities. ***Establishing the intended use of the system, software, or feature is the foundation for determining the direct impact to device safety, device quality, or quality system integrity***. Furthermore, FDA is interested in the situations when a failure to fulfill the intended use of the system, software, or feature, directly impacting device safety and device quality, results in direct patient safety risk.

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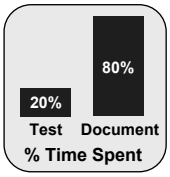
Key Take Aways

Why Now?

Med Dev lags other industries

- Lack of clarity
- Outdated compliance approach
- Perceived regulatory burden
- Reduces manufacturer's capability to learn, react, & improve



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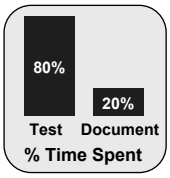
Key Take Aways

Why Now?

Create a Paradigm Shift…

- Streamline with value-driven, patient focused approaches
- Critical thinking & risk-based agile approaches
- Improve manufacturer's capabilities with automation



Defining Risk

- **Clearly define "intended use".**
- **Focus on the "direct impact on device safety and device quality", and does it result in "patient/user safety risk?" See examples.**
  - LMS vs Manufacturing Equipment Software
- ***For PMA Products, CDRH is exploring using risk determination to make implementation of systems an annually reportable change no 30-Day Notice***

Risk Based Assurance Strategies

- **Take credit for work already done**
  - Leverage existing activities and *trusted supplier data*
- **Use *Agile test methods* (e.g. unscripted testing) when appropriate**
- **Mitigate risk with *downstream process controls***
- **Leverage continuous data and information for monitoring and assurance**

Assurance Evidence Capture

- **Use *CSV tools to automate* assurance activities**

  Note: FDA does not intend to review validation of support tools.
- **Use *electronic data capture* & record creation vs paper documentation, screen shots, etc.**

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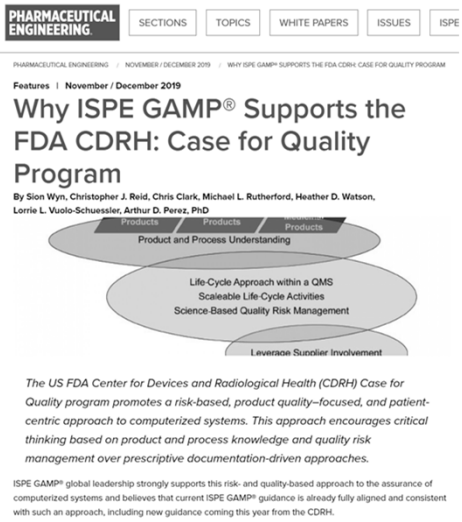
Supports Case for Quality



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PHARMACEUTICAL ENGINEERING / NOVEMBER / DECEMBER 2019 / WHY ISPE GAMP® SUPPORTS THE FDA CDRH CASE FOR QUALITY PROGRAM

Features | November / December 2019

Why ISPE GAMP® Supports the FDA CDRH: Case for Quality Program

By Sion Wyn, Christopher J. Reid, Chris Clark, Michael L. Rutherford, Heather D. Watson, Lorrie L. Vuolo-Schuessler, Arthur D. Perez, PhD

The US FDA Center for Devices and Radiological Health (CDRH) Case for Quality program promotes a risk-based, product quality–focused, and patient-centric approach to computerized systems. This approach encourages critical thinking based on product and process knowledge and quality risk management over prescriptive documentation-driven approaches.

ISPE GAMP® global leadership strongly supports this risk- and quality-based approach to the assurance of computerized systems and believes that current ISPE GAMP® guidance is already fully aligned and consistent with such an approach, including new guidance coming this year from the CDRH.

https://ispe.org/pharmaceutical-engineering/why-ispe-gamp-supports-fda-cdrh-case-quality-program

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In Real Life

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What Kind of Elephant Are You?

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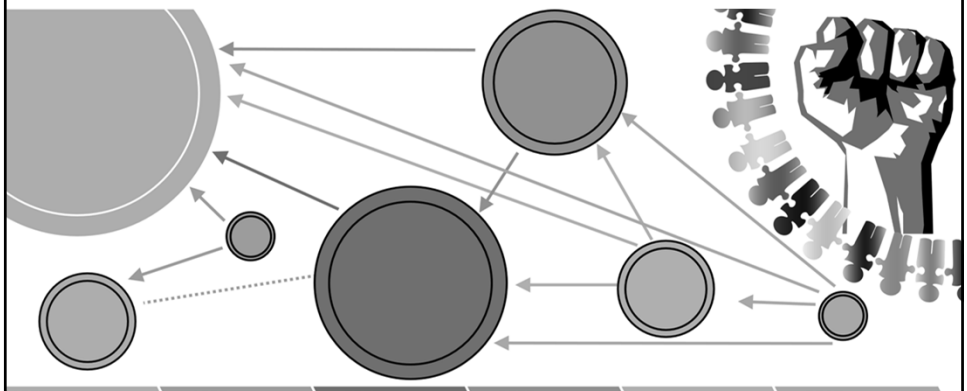

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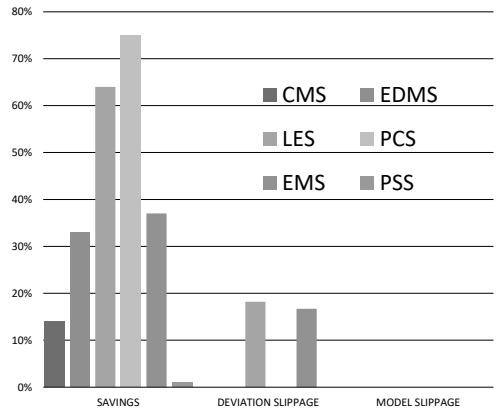
Empirical Analysis

Validation Effort Comparison of Traditional vs. New Models and Their Potential Savings



System Name
Change Management System* (Jan 2014)
Electronic Document Management System (Dec 2014)
Laboratory Execution System (May 2015)
Process Control System* (May 2016)
Environmental Monitoring System (Jul 2016)
Product Serialization System (Aug 2018)

* Bold = favorable audit

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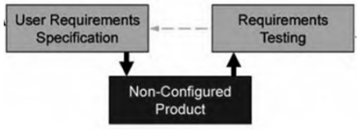
Example: Learning Management System

Determine Impact of System *(Direct / Indirect / None)*

Indirect Impact

Determine Category *(Non-Configured / Configured / Custom)*

Non-Configured



Determine Type of Testing Required *(Ad Hoc / Unscripted / Scripted)*

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Risk Based CSV Example: Learning Management System (LMS)

Streamlined Risk-Based CSV

A medical device firm applies Risk Based Validation to an off the shelf LMS. Qualifying the vendor then applying risk to the feature level allows for much less documented verification activities.

Basic Assurance / Low Risk Features	Ex: Usability Features – training notifications, overdue training lists, curricula assignments.	Ad Hoc Testing 80%
Medium Risk Features	Ex: Capture evidence of training completion by entering username & password.	Unscripted Testing 20%
High Risk Features	No High Risk Features	Scripted Testing 0%

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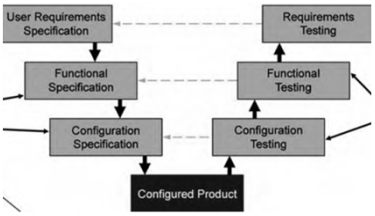
Example: NCR / CAPA System

Determine Impact of System *(Direct / Indirect / None)*

Direct Impact

Determine Category *(Non-Configured / Configured / Custom)*

Configured



Determine Type of Testing Required *(Ad Hoc / Unscripted / Scripted)*

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Risk Based CSV Example: Non-Conformance & CAPA Process

Streamlined Risk-Based CSV

A medical device firm applies Risk Based Validation to an off the shelf CAPA System. Qualifying the vendor then applying risk to the feature level allows for much less documented verification activities.

Basic Assurance / Low Risk Features	Ex: Usability Features – required data entry from optional data entry, attachments of objects, system workflow, non conformance initiation.	Ad Hoc Testing 30%
Medium Risk Features	Ex: Electronic Signature Features – audit trail, meaning of signature (review, approval).	Unscripted Testing 50%
High Risk Features	Ex: Product Containment – NC is initiated for product outside of the company's control, then the system prompts the user to identify if a product recall is then needed.	Scripted Testing 20%

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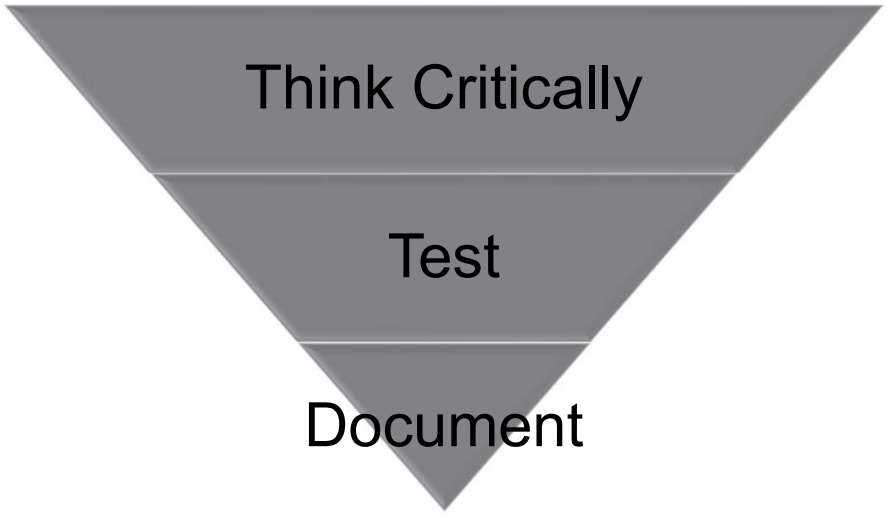
Time Spent



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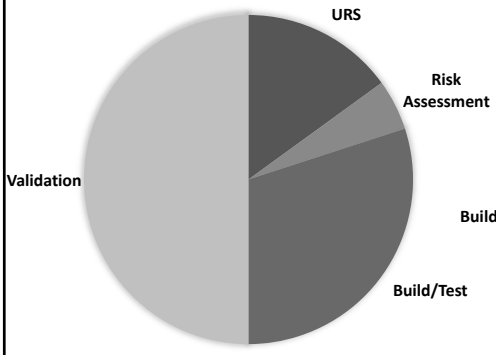
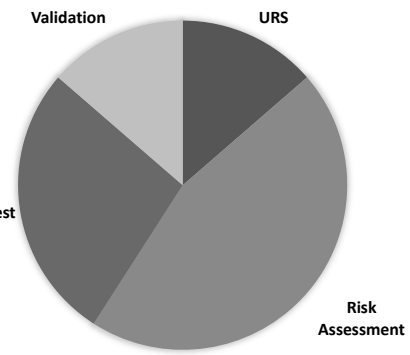
Same Regulations: A Different Perspective

RGNX: GAMP 5



Resulted in **numerous** deviations related to documentation and testing errors with **minimal** bugs found.

RGNX: CSA



Resulted in **zero** deviations related to documentation and testing errors with **more** bugs found.

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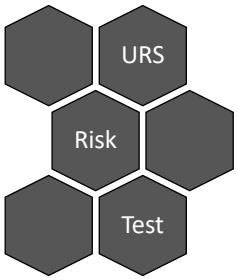
Same Regulations: A Different Perspective

RGNX: GAMP 5

- Require Risk Assessment for all GxP systems.
- Require step by step IQ/OQ/PQ for all GxP systems.



RGNX: CSA

- Conduct System Level impact assessments (Direct/Indirect/None)
- Require Risk Assessment for Direct impact systems only.
- Require step by step protocols for Direct impact systems and only those URS items that are custom/direct impact.

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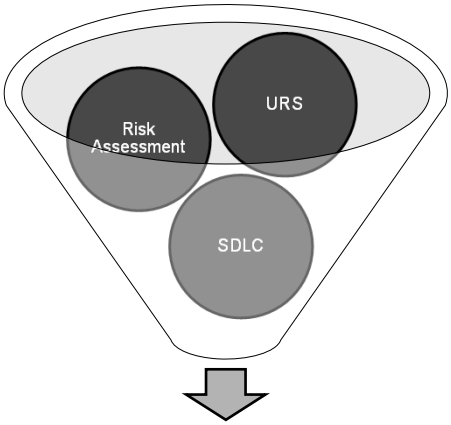
Computer Software Assurance
Inputs / Outputs



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Questions / Discussion

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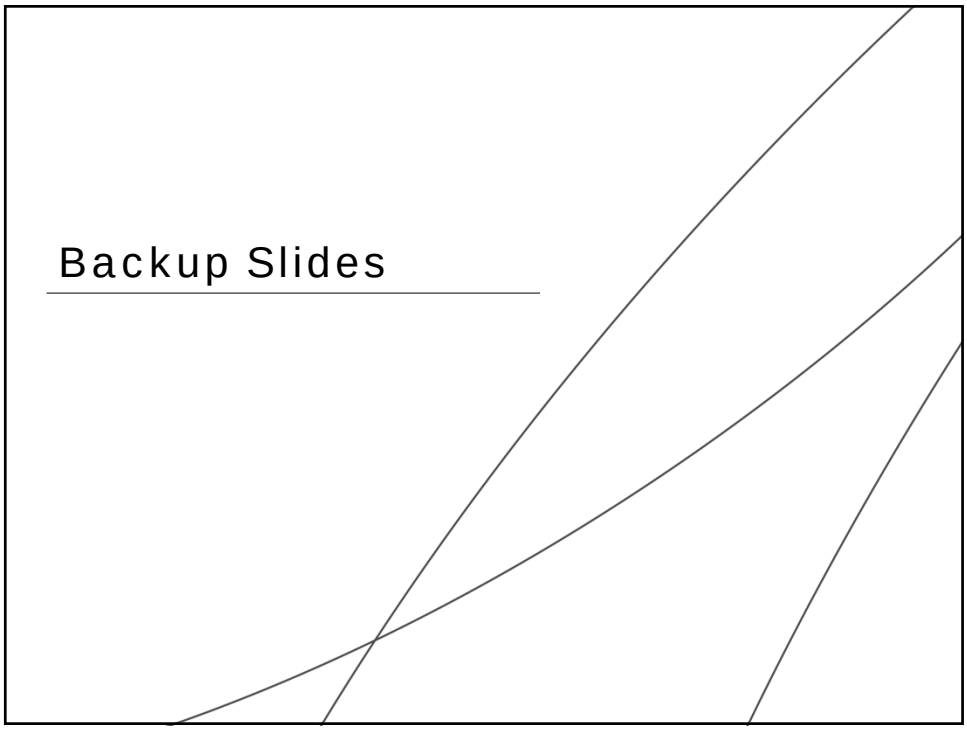
Backup Slides



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