Update on FDA/Industry Collaboration on Non-Product CSV + Success Stories

CBI 4th Annual Medical Device Validation Week

Presenters:

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March 12, 2019

What Does Success Look Like?

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On Non-Product CSV:

- Create awareness to accelerate improvement and innovation
- Share success stories
- Inspire action so you can begin to realize value

Agenda

- Overview/Business Case
- Recommendations and examples
- Value - Success Stories
  - Compliance Group Customers
  - Medtronic, Global IT
- Next Steps

Spoiler Alert…

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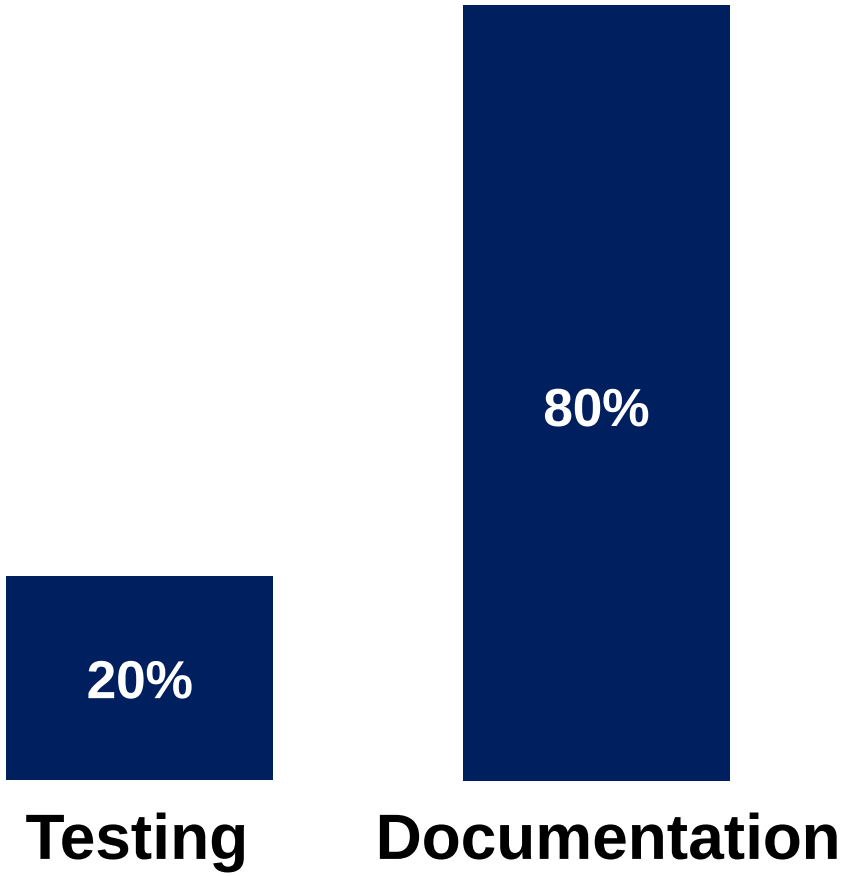
Current State of % Time Spent



Spoiler Alert…

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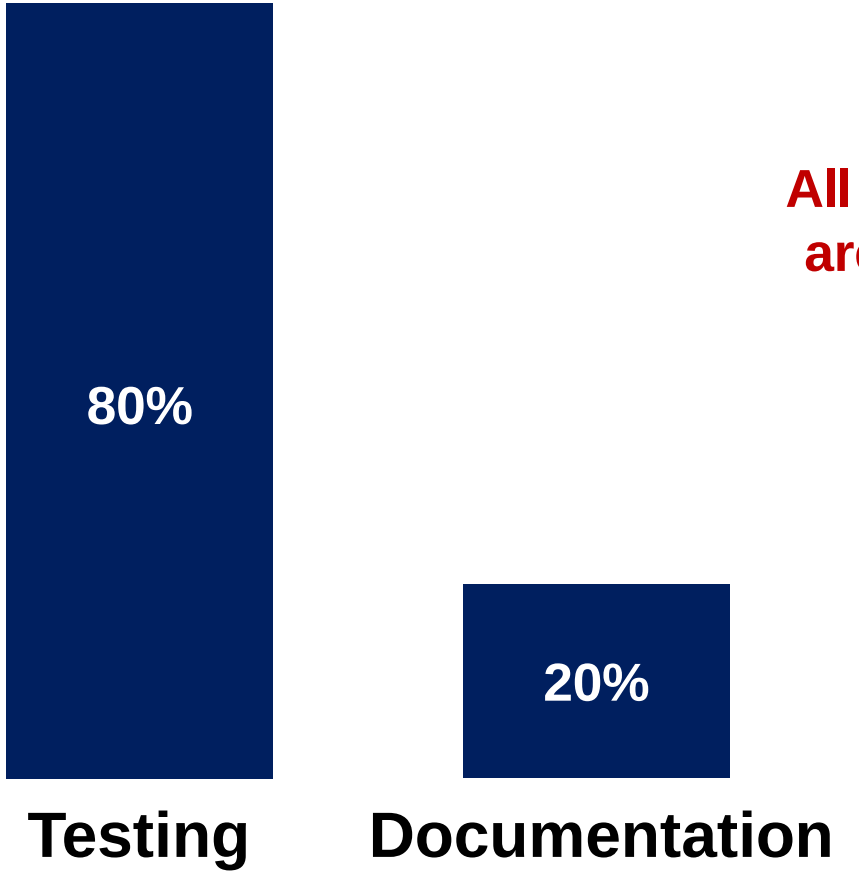
Future State of % Time Spent



All of these Recommendations are within FDA Regulations!!!

How did we get started?

- Case for Quality. Develop new engagement and regulatory tools that enhance and incentivize the adoption of practices and behaviors to improve medical safety, responsiveness, and how patients experience devices.
- FDA engaged with stakeholders to learn what barriers exist and best practices for high quality medical device manufacturing.
- We discovered fundamental barriers that FDA could work with industry to address, outside of the Case for Quality.

CSV identified as a barrier for the FDA…

For your technology investments, what are the barriers for Realizing Value?

CSV!!!

The Industry CSV Team

Streamlined Risk-Based CSV

FDA

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
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FDA	John Murray
Fresenius Medical Care	Bill D'Innocenzo
Fresenius Medical Care	Curt Curtis
Fresenius Medical Care	Marc Koetter

Company	Name
Johnson and Johnson	Dana Guarnaccia
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Medtronic	Frankie Bill
Medtronic	Michael Branch
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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

Streamline Non-Product Computer System Validations

Why

- ***Medical device industry lags*** in implementation of ***automated systems*** and new technologies due to ***lack of clarity***, ***outdated compliance approaches***, and ***perceived regulatory burden***.
- This reduces a firm's capability to learn, react to issues, and improve product quality.

What

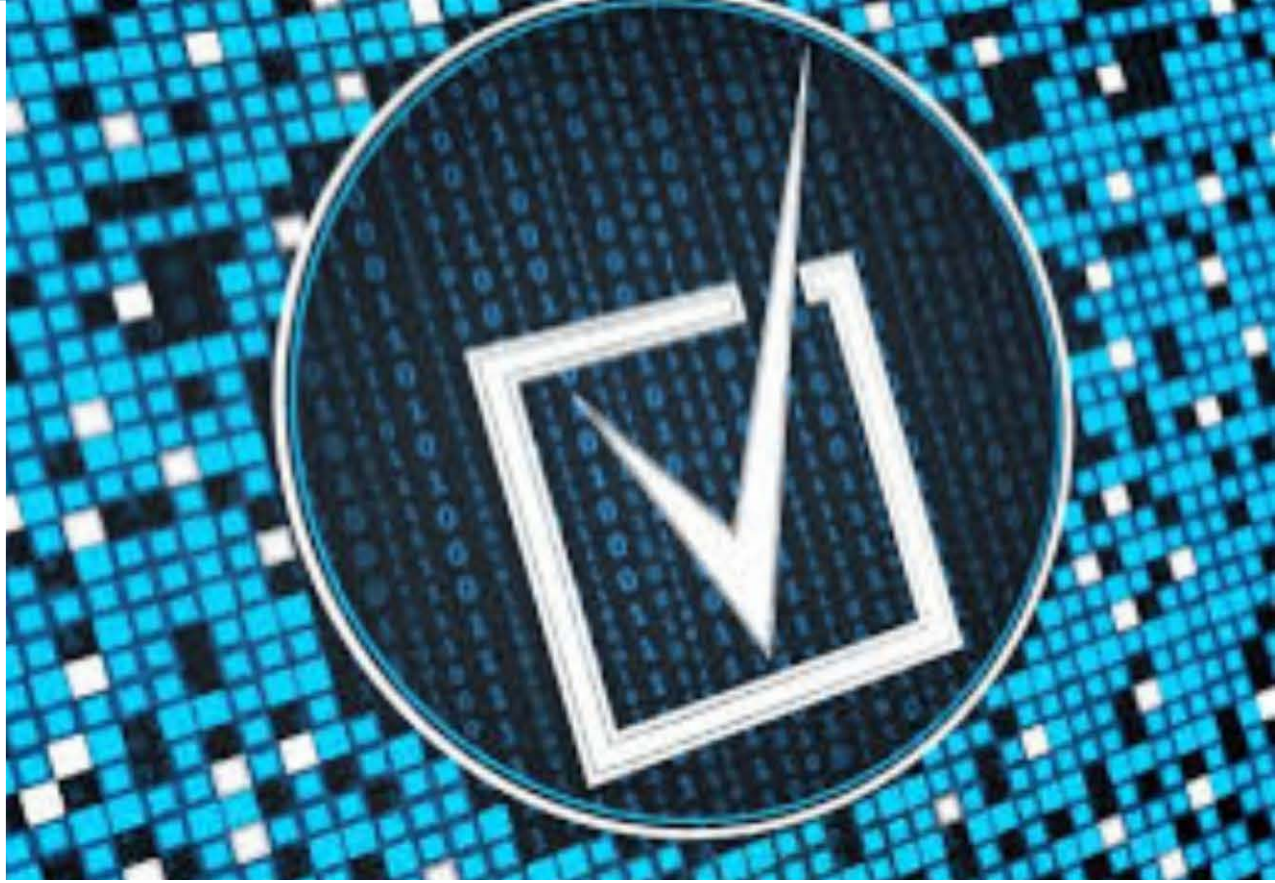
- Drive a paradigm shift in applying ***value-driven and patient-focused approaches*** to ***streamline non-product software CSV***.
- Use ***critical thinking and risk-based agile*** approaches to streamline assurance activity and evidence capture.

How

- Developing ***streamlined practice recommendations*** and pilots.
- ***Modifications to the 820.70(i) and 820.50*** regulatory language.
- ***Guidance development*** centered on this software category.

The Meat - “CSV Recommendations”

Note: All of these recommendations are within FDA Regulations!



FDA’s View of Automation

The FDA supports and encourages the use of automation, information technology, and data solutions throughout the product lifecycle in the design, manufacturing, service, and support of medical devices. Automated systems provide manufacturers advantages for reducing or eliminating errors, increasing business value, optimizing resources, and reducing patient risk. Is based on learning from other industries where automation has already shown significant benefits in enhancing product quality and safety, which in turn reduces Risk, compared with non-automation.

www.fda.gov

Focus on Assurance

Shift the discussion

(Unique) Clarifications and Recommendations

Intended Use

- What is the intended use?
- Does feature, operation, or function directly impact
  - device safety
  - device quality or
  - quality system integrity?

Risk Based Approaches

- Do automation features, operations, or functions directly impact device safety or device quality?
  - High-risk areas may require the most rigorous assurance effort to ensure they perform as intended.
- FDA intends focus on areas that ***Directly*** impact device safety or device quality. FDA does not intend to focus on ***Indirect*** impact areas. Ex: MES or LIMS compared with an LMS.

Assurance (Testing) Approaches

- Provide confidence that the system, feature, or function performs as expected and meets intended use.
- Assurance Activities driven by the Risk associated with the system, feature, or function, depending on how you approach it (e.g. Direct vs Indirect).
- Traditional IQ/OQ/PQ is not necessary for CSV.
- Next slides will include examples of assurance activities, including numerous Agile testing methods.

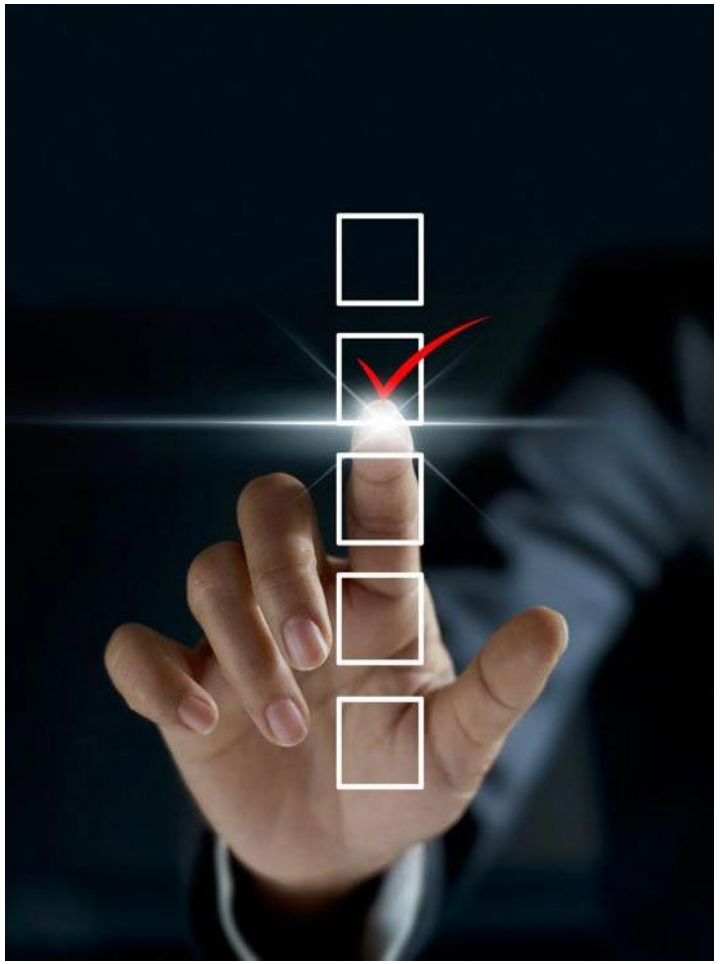
Evidence Capture Methods

- Least-burdensome record (see next slides). Record needs to be of value to the Manufacturer, not the Investigator or Auditor.
- CSV tools encouraged to automate assurance activity. **Use electronic data capture and record creation** (vs paper documentation, screen shots, etc).
  - 21 CFR 820.70(i) is applied only when software part of production or quality system. FDA does ***Not Intend*** to review validation of support tools. Manufacturer responsible for determining assurance.
  - Part 11 narrowly scoped & under enforcement discretion (**apply appropriately**)

What does FDA care about? Risk Considerations

- Direct impact to device quality and device safety that also has a direct patient safety risk
  - Directly impacts physical properties of the product or manufacturing process identified as essential to device safety or device quality by the manufacturer
  - Measures, inspects, analyzes, and or dispositions the product or process
  - Determines acceptability or performs process corrections without human intervention, awareness, or review
  - Directly impacts labeling, instructions for use, or direct alerts or communications to the user
  - Automates surveillance, trending, or tracking of product quality or patient safety issues identified as essential by the manufacturer

Appropriate methods and activities for software assurance



- Take a least-burdensome approach – focus on value for the Manufacturer, not the Investigator.
- Leverage existing activities and supplier data. Do not reinvent the wheel; take credit for work already done
- Leverage use of process controls to mitigate risk
- Use Computer System Validation tools to automate assurance activities
  - Scope of 21 CFR 820.70(i) is applied *when computers or automated data processing systems are used as part of production or quality system.*
  - **FDA does not intend to review validation of support tools**. Manufacturer determines assurance activity of these tools for their intended use.
  - Part 11 narrowly scoped and is under enforcement discretion **apply appropriately**
- Use Agile testing methods and unscripted testing as appropriate
- Use electronic data capture and record creation, as opposed to paper documentation, screen shots, etc
- Leverage continuous data and information for monitoring and assurance

Acceptable record of results

Assurance Approach	Test Plan	Test Results	Record (Digital Acceptable)
Unscripted Testing: Ad-hoc (with least-burdensome documentation)	• Testing of features and functions with no test plan	• Details regarding any failures/deviations found	• Summary description of features and functions tested • Issues found and disposition • Conclusion statement • Record of who performed testing and date
Unscripted Testing: Error guessing	• Testing of feature and function fail-modes with no test plan	• Details regarding any failures/deviations found	• Summary description of fail-modes tested • Issues found and disposition • Conclusion statement • Record of who performed testing and date
Unscripted Testing: Exploratory Testing	• Establish high level test plan objectives for features and functions **(no step-by-step procedure is necessary)**	• Pass/fail for each test plan objective • Details regarding any failures/deviations found	• Summary description of features and functions tested • Result for each test plan objective – only indication of pass/fail • Issues found and disposition • Conclusion statement • Record of who performed testing and date
Scripted Testing: Limited	• Limited Test cases (step-by-step procedure) identified • Expected results for the test cases • Identify unscripted testing applied • Independent review and approval of test plan.	• Pass/fail for test case identified • Details regarding any failures/deviations found and disposition regarding fails	• Summary description of features and functions tested • Result for each test case - only indication of pass/fail • Issues found and disposition • Conclusion statement • Record of who performed testing and date • Signature and date of appropriate signatory authority
Scripted Testing: Robust	• Test objectives • Test cases (step-by-step procedure) • Expected results • Independent review and approval of test cases.	• Pass/fail for test case • Details regarding any failures/deviations found and disposition regarding fails	• Detailed report of assurance activity • Result for each test case - only indication of pass/fail • Issues found and disposition • Conclusion statement • Record of who performed testing and date • Signature and date of appropriate signatory authority

Examples

Automated Computer System Validation Tools

Function	Intended Use	Examples
Software testing tool measuring system behavior and performance under load	Used for testing the performance of new manufacturing automations under load	*Loadrunner, Apache JMeter
Automated functional graphical user interface (GUI) testing tool that allows a user to record and play back user interface (UI) interactions as test scripts.	Used for developing a test script based on user interactions to automate future testing of UI modifications	*Winrunner, Ranorex
Bug tracking, issue tracking, and project management systems.	Used for rapidly capturing issues and bugs found during assurance testing	*Jira, Confluence
Manage and track the application lifecycle development process. Includes, risk, test, and the respective change control/approval of applications	Used for tracking and monitoring all stages of new IT system implementations, throughout the lifecycle.	*Polarion ALM, PTC Integrity
Dynamic web performance evaluation tool.	Used for testing the performance of web-based User Interfaces	*Dynatrace AJAX Edition, New Relic APM
***All product trademarks, registered trademarks or service marks belong to their respective holders.**		

Manufacturer is using these tools to automate and supplement tracking and assurance testing for non-product systems. These intended uses of these tools do not have a direct impact on device quality and device safety.

Industry Team Recommendations

Streamlined Risk-Based CSV

Risk	Patient/Product	Quality System	Assurance Approach
	From failure, event, or consequence with potential to cause:	Software that supports the:	
Low	• Minor harm to a patient.	• Implementation of a quality system activity but is not in a regulation	Ad-Hoc Testing
Medium	• Significant but temporary harm or reversible damage to a patient	• Indirect implementation of a quality system activity, defined in a regulation.	Unscripted Testing
High	• Death, life-threatening harm, or irreversible damage to a patient.	• Direct implementation of a quality system activity, defined in a regulation.	Scripted Testing

Implementation Definitions	
Out of the Box	Feature works simply by installing the software and adding necessary master data (e.g. products, BOM, routes, etc.).
Configured	Feature is enabled through the setting of parameters without changing the code of the software
Custom	Feature requires programming or change to software code

Risk Rating	Assurance Activities
5	Requirement validated through robust scripted testing
4	Requirement validated through limited scripted testing
3	Requirement validated through unscripted testing
2	Requirement validated through ad-hoc testing
1	Relies on vendor audit and base-line assurance

		Implementation Method		
		Out of the Box	Configured	Custom
Patient Risk	High	3	4	5
	Medium	2	3	4
	Low	1	2	3
	None	1	1	1

Risk Based CSV Example: COTS Manufacturing Execution System

Streamlined Risk-Based CSV

A medical device firm replaces custom, “home grown” Manufacturing Execution System (MES) with a purchased Configurable Off the Shelf (COTS) solution. Vendor qualification takes into account vendor’s long track record in the Medical Device industry, mature and transparent SDLC processes, CMMI level, ISO certification, etc.

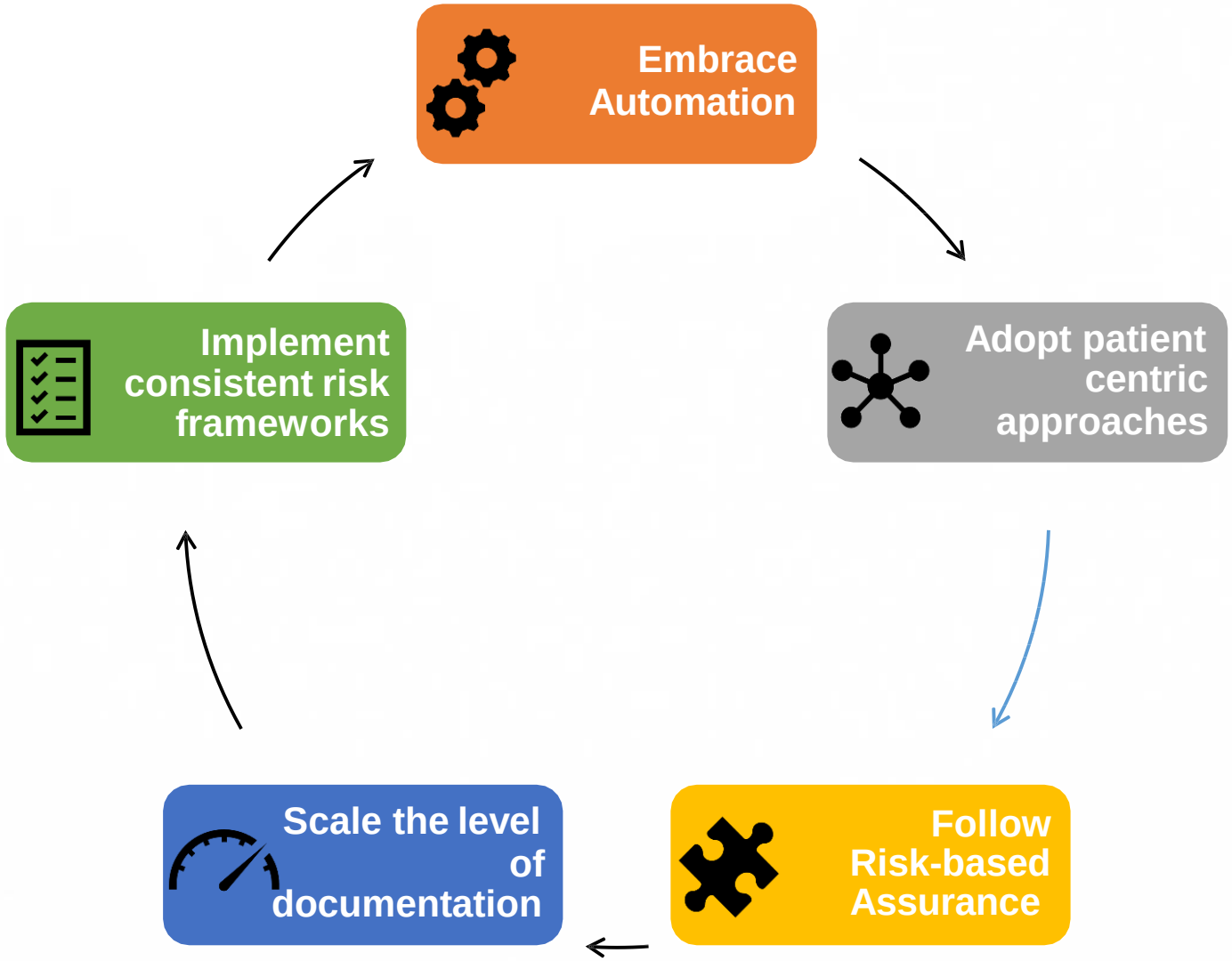
Applying risk to the feature level and type of implementation allows for much less documented verification activities. Configuration of features is enabled through the setting of parameters.

Feature	The systems need to:	Patient Risk Level	Assurance Activity	
			Prior Custom MES	*New COTS MES
Training Enforcement	Enforce that operator is trained on latest SOP revision.	Low (Since product quality is inspected at multiple steps in process)	**Unscripted Testing**	**Vendor Audit**
Material Expiration Enforcement	Enforce that raw materials are not expired.	Medium	**Level 4 Scripted Testing**	**Ad-hoc Testing**
Label Printing	Print correct P/N, description, L/N, quantity, UDI and barcodes in customer’s language	High	**Level 5 Scripted Testing**	**Unscripted Testing**

*Out of the Box implementation

Case Studies

FDA CSV Team Recommendations – Case Study Themes



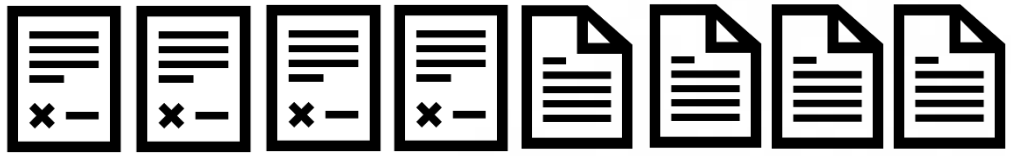
Embrace Automation

- *Automation needs to be seen as an enabler.*
- *Automation doesn't need to involve complex tools.*

Case Study Examples – Embrace Automation – Infrastructure Qualification

FDA CSV Team Recommendation	• Use **electronic** data capture and record creation, vs **paper** documentation, screen shots, etc. • Leverage continuous data and information for monitoring and assurance
Success Story Brief Description	• Replaced **manual, paper based** test evidence capture with an **automated** approach. • Replaced **manual, error-prone** specification maintenance with an **automated, error-free** specification generation approach.

Before



- **Manual** screen shots of evidence of server's hardware and software specifications.
- Manual and **reactive** maintenance of infrastructure specifications – specifications are often not in sync with the actual infrastructure as infrastructure is so dynamic.
- Time taken – **10X**

After

- **Automated** reports of server's hardware and software specifications by installing monitoring tools on servers.
- Automated, **proactive** generation of infrastructure specifications with the click of a button. Continuous data monitoring and assurance.
- Time taken – **1X**

Case Study Examples – Embrace Automation – Smart Glasses

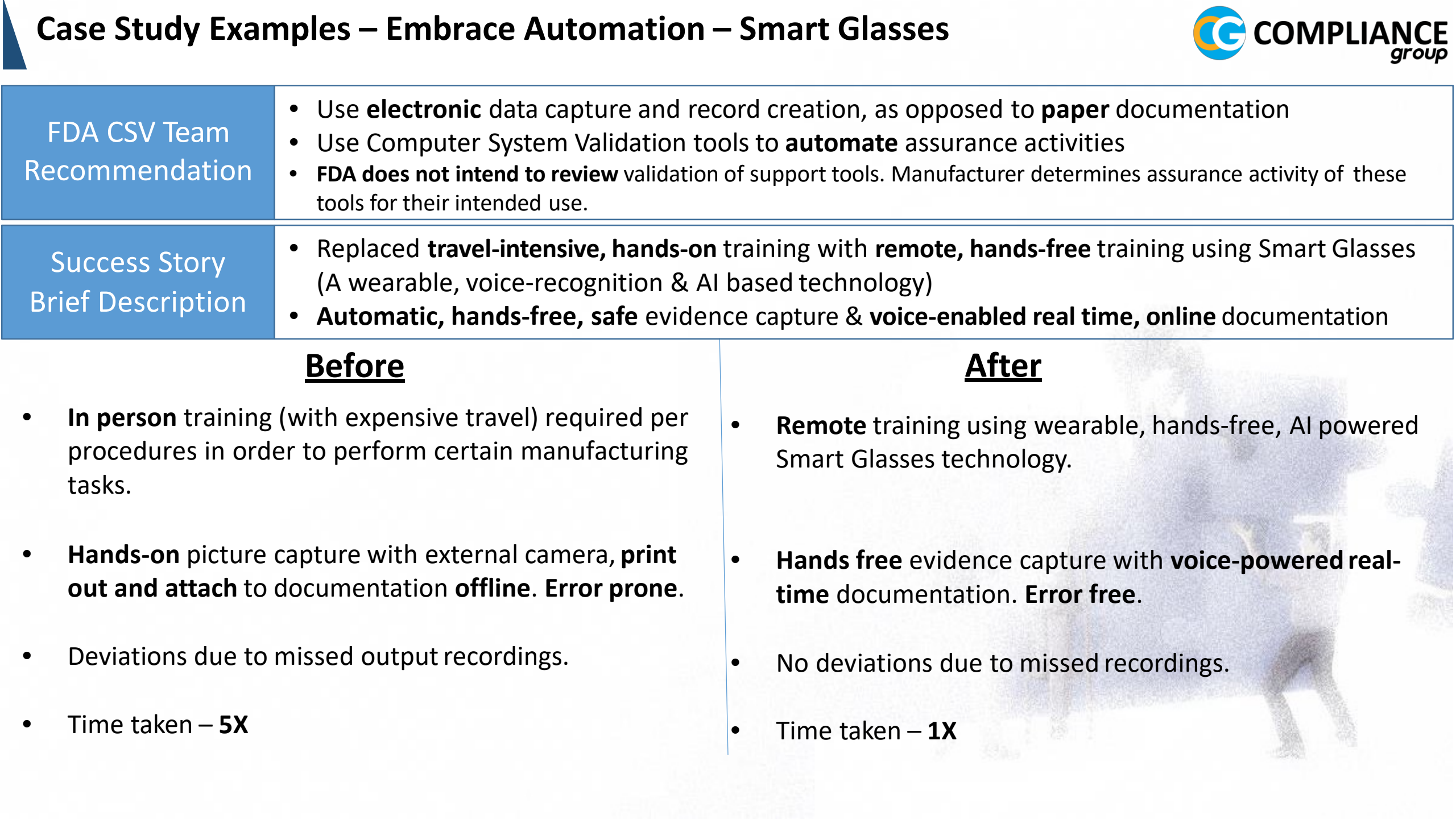
FDA CSV Team Recommendation	• Use **electronic** data capture and record creation, as opposed to **paper** documentation • Use Computer System Validation tools to **automate** assurance activities • **FDA does not intend to review** validation of support tools. Manufacturer determines assurance activity of these tools for their intended use.
Success Story Brief Description	• Replaced **travel-intensive, hands-on** training with **remote, hands-free** training using Smart Glasses (A wearable, voice-recognition & AI based technology) • **Automatic, hands-free, safe** evidence capture & **voice-enabled real time, online** documentation

Before

- **In person** training (with expensive travel) required per procedures in order to perform certain manufacturing tasks.
- **Hands-on** picture capture with external camera, **print out and attach** to documentation **offline**. **Error prone**.
- Deviations due to missed output recordings.
- Time taken – **5X**

After

- **Remote** training using wearable, hands-free, AI powered Smart Glasses technology.
- **Hands free** evidence capture with **voice-powered real-time** documentation. **Error free**.
- No deviations due to missed recordings.
- Time taken – **1X**



Case Study Examples – Risk based Assurance – ERP System Validation

FDA CSV Team Recommendation	• Use **Agile testing methods and unscripted testing** as appropriate • Take a least-burdensome approach – focus on value for the Manufacturer, not the Investigator. • **Traditional IQ/OQ/PQ is not necessary** for CSV.
Success Story Brief Description	• Leveraged FDA CSV Team's Risk-based assurance to retrospectively **validate an entire ERP system in less than 3 months**. • Leveraged FDA CSV Team's agile Unscripted testing approach to test the system.

Before

- Focus on **scripting**.
- **80% of test defects** were test script issues.
- Leveraged traditional IQ/OQ/PQ.
- 100% step by step scripted testing.
- Time taken – **3X**

After

- **Focus on testing – not on scripting**.
- **No test script issues.**
- **50% reduction** in validation budget by leveraging IQ & Agile Unscripted Testing.
- 10% scripted testing for High Risk functions, 50% Unscripted – Exploratory Testing, 40% Ad Hoc Testing
- Time taken – **1X**

Case Study Examples – Risk based Assurance – Consistent Frameworks

FDA CSV Team Recommendation	• 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.
Success Story Brief Description	• Deployed a patient centric risk framework across Software life-cycle – i.e. Validation, Change Management & Periodic Reviews. • Leveraged FDA CSV Team's risk assurance framework.

Before

- Siloed risk frameworks across processes – frameworks that don't talk to each other
- Confusion among implementing teams with risk definitions that don't align with each other
- Redundant work efforts due to misalignment

After

- Consistent, simplified risk framework across processes that drive a common risk based assurance approach
- Consistent implementation of harmonized risk assurance framework
- Reduced cycle times from consistent interpretations across processes

Case Study Examples – Risk based Assurance – Deliverable Scalability

FDA CSV Team Recommendation	• 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.
Success Story Brief Description	• Deployed a software validation framework in which deliverables are scaled based on risk level of the software. • Leveraged FDA CSV Team's risk assurance framework.

Before

- One-size-fits-all list of validation documentation for all types of software
- Creation of documentation – not assurance
- Time consuming validation cycles

After

- Deliverables scaled (both quantity & quality) by using a risk assurance framework included in FDA CSV Team's recommendations
- Creation of "assurance" – not just documentation
- At least 25% improvement in validation cycles

PAVING WAY FOR A NEW QUALITY CULTURE

RISK BASED TESTING FOR IT SOFTWARE

System Level

A software system is:

Validated – part of the IT quality processes impact per Val plan

Non-Validated – not part of the IT quality process per scope doc

Change Level Risk HIGH	Change Level Risk MEDIUM	Change Level Risk LOW
• Add traceability from Requirements to Design to Test case • Test all new requirements • Execute formal regression testing	• Standard traceability Requirements to Test cases • Formal testing of all new requirement for IT system testing • Informal execution of regression testing • Informal execution of UAT	• Standard traceability Requirements to Test cases • Informal testing for IT system • Informal testing for UAT

CSV RISK MANAGEMENT AUTOMATION

POLARION

WHAT IS IT ?

An **application lifecycle** tool that **manages** software development **projects**

GLOBAL IT QUALITY PAIN POINTS & SOLUTIONS

REPEAT ISSUES	POLARION SOLUTIONS
Missing Quality deliverables	Workflow **auto-populates** required quality **deliverables** based on project type
Can't find Quality deliverables	Deliverables **organized by system** >> project/change
Project resources missing RBT evidence	User Access **requires RBT completion**
Quality deliverable sequence issues	Workflow **enforces sequence**
Incorrect template version used	**Auto-populates** current version and **highlights delta changes** if using previous approved deliverable
Deliverables have imbedded files or links	**Automatically removes** imbedded files or links in rendering deliverable
Incorrect or missing approvals	**Auto-populates** minimum required roles per deliverables type

QUALITY BEGINS WITH ME

POLARION
USE IN MEDTRONIC NON-PRODUCT SOFTWARE

BENIFITS

- √ **Reduce CAPAs, Audits** and **time** needed to reconcile these issues
- √ **Automate** Global IT's validation processes while **supporting** a **unified** and **consistent** Global IT demand **process**

USER FRIENDLY

- Easy to adopt, use and support
- Flexible process for validated and non-validated applications/projects
- Repeatable process execution across the Global IT organization

IMPROVED DOCUMENTATION

- Central repository for living validation documentation
- Real time template updates applied to new documents
- Eliminate paper execution of methodology
- Migration of existing data (documents, QC)

TRACEABILITY END-TO-END

- Electronic signatures 21CFR part 11 compliant
- System of record for validation status
- Ability to support on-demand IT audits
- Cross-functional reporting

Medtronic

POLARION PHASE 3: RISK BASE TESTING

CSV Approach on Risk Rating

		Implementation Method		
		Out of the Box	Configured	Custom
Probability of Patient or User Safety Issue	High	3	4	5
	Medium	2	3	4
	Low	1	2	3
	None	1	1	1

Risk Rating	Assurance Activities
5	Requirement validated through robust scripted testing
4	Requirement validated through limited scripted testing
3	Requirement validated through unscripted testing
2	Requirement validated through ad-hoc testing (with record)
1	Requirement validated vendor data, installation test, and operation test

(Proposed) MDT Approach on Risk Rating

Patient Risk	OTS	OTS w/ configured	Custom
High	3	4	5
Medium	2	3	4
Low	1	2	3

Risk	Test Standard
5	Robust
4	Limited
3	Unscripted
2	Unscripted
1	Unscripted

POLARION PHASE 3: RISK BASE TESTING

Logic for "Test Standard" Custom Field:

CSV Industry Partner “Quote”

“…….sitting here with DQS-MED auditor for our 13485-2016 audit.. just talked software application validation for the last hour. Our auditor was impressed with everything we have set up, loved the risk based approach. Told us that other companies get into lots of arguments with him over this and it was refreshing to talk with us. He personally was about a defined OQ verbiage, however how I explained we do our test cases in test and live environments and he agreed it was just a wording thing on his part. We also talked a lot about the difference between verification activities vs validation activities and effectively setting up test cases. He was impressed with everything we had……”

“……It was awesome finally going through a validation and being assured that things were good from the EU perspective as well...

- Frank M.

Next Steps

Next Steps

- Continue developing Use Cases and new recommendations
- Encourage manufacturers to start using recommendations
  - Capture value - measure better, faster, and less expensive CSV activity and…
  - Provide FDA with input on what is working vs not working, barriers, etc
- FDA 2019 “A List” - new Non-Product CSV FDA Guidance to encourage automation and clarify expectations for risk-based CSV.

  Your assignment: Provide comments to the Docket!
- Review and possibly modify 820.70(i) – improve clarity on automated processes
- Promoting recommendations through recorded Webinar: https://www.plm.automation.siemens.com/country/en-us/webinar/fda-non-product-csv/29180/index.html

For Additional Questions

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