



Computer System Validation Basics



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 v.23.05

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Your Facilitator

- Debra Bartel, MBA, CQA, PMP
- VP, Life Sciences QA
- 30 years' experience specializing in software quality assurance, validation and regulatory compliance, Information Systems project management, and process design.
- Previously held management positions in the pharmaceutical industry in both Quality Assurance and Information Systems organizations
- Active member of American Society for Quality (ASQ), Northeastern Illinois Section, Software Division


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CENTER




Computer System Validation



Computer System Compliance






Data Integrity




Training


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Target Audience

Industries


- Pharmaceutical & Biologics
- Medical Device
- Clinical Studies
- Blood Products

Regions


- Operating in the US
- Selling to the US Market

Personnel

- IT Personnel and Managers
- Quality Personnel and Managers
- Auditors and Audit Managers

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Webinar Outline

- 1 • CSV Regulatory Requirements
- 2 • CSV Purpose & Benefits
- 3 • CSV Methodology
- 4 • CSV Scope
- 5 • CSV Failure Consequences
- 6 • CSV Program Implementation

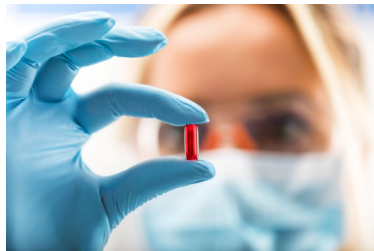


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CSV Regulatory Requirements

Part 1



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CSV Regulatory Requirements

Computer System Validation is required for companies that...

Activities

Design
Develop
Conduct clinical trials
Manufacture
Package
Label
Store
Distribute
Install
Service

Products

Pharmaceuticals
Biologicals
Medical Devices
Blood and Blood Components
Human Cell and Tissue Products
Infant Formula



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CSV Regulatory Requirements

USA



FDA 21 CFR 11 *Electronic Record; Electronic Signatures*

Subpart B--Electronic Records, Sec. 11.10

... procedures and controls **shall include** the following: (a) **Validation of systems**...

FDA 21 CFR 211 *cGMP for Finished Pharmaceuticals*

Subpart D--Equipment, Sec. 211.68(b)

Input to and output from the computer ... **shall be checked for accuracy.**

21 CFR 1271 *Human Cells, Tissues, and Cellular and Tissue-Based Products*

Subpart D Current Good Tissue Practice, Sec. 1271.160(d)

You must validate the performance of computer software for the intended use. ...

21 CFR 820 *Quality System Regulation*

Subpart C Design Controls, Sec. 820.30(g)

Design validation **shall include software validation**...

Subpart G Production and Process Controls, Sec. 820.70(i)

... the manufacturer shall **validate computer software for its intended use**....



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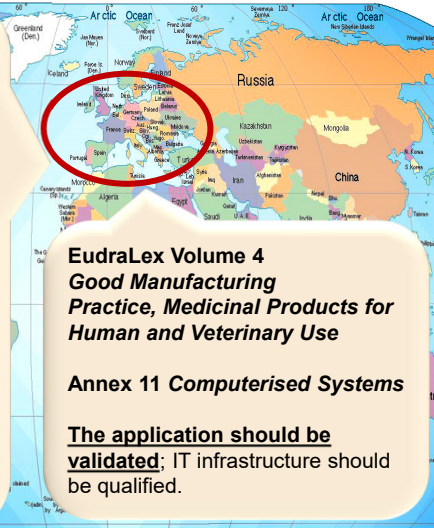
CSV Regulatory Requirements

European Union

**EC COUNCIL
DIRECTIVE 93/42/EEC**

**ANNEX I
ESSENTIAL
REQUIREMENTS**

12.1a For devices which incorporate software or which are medical software in themselves, **the software must be validated** according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.




**EudraLex Volume 4
Good Manufacturing
Practice, Medicinal Products for
Human and Veterinary Use**

Annex 11 Computerised Systems

**The application should be
validated; IT infrastructure should
be qualified.**

- Austria
- Belgium
- Bulgaria
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Ireland
- Italy
- Latvia
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden



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CSV Regulatory Requirements


Brazil, Japan...

**Brazilian ANVS
Good Practices
of
Medicament
Manufacturing**


... **computer systems .. must be qualified and / or validated.**


Validation shall be considered **part of the computer system's life cycle,**



**Japan's Guideline on
Management of
Computerized Systems
for Marketing
Authorization Holders
and Manufacturers of
Drugs and Quasi-drugs**

specifying the necessary matters during development of computerized systems, **the validation items to verify such systems, ...** in order to ensure such systems function as intended.





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CSV Regulatory Requirements

ICH






ICH Q7A, Good Manufacturing Practice for Active Pharmaceutical Ingredients

GMP related computerized systems should be validated. The depth and scope of validation depends on the diversity, complexity, and criticality of the computerized application.

ICH E6 Good Clinical Practice

When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:

Ensure and document that the electronic data processing system(s) conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation)

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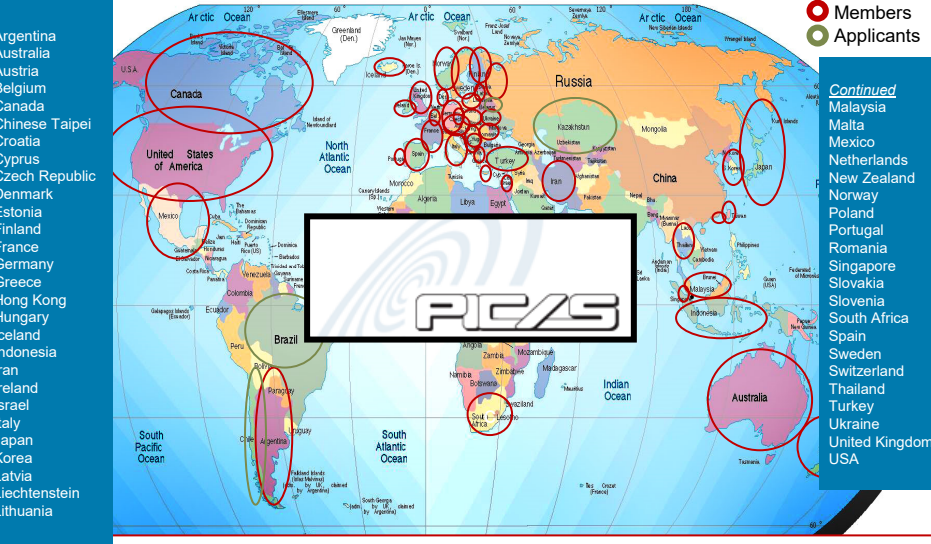
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CSV Regulatory Requirements

PIC/S






Members

Applicants

Argentina
Australia
Austria
Belgium
Canada
Chinese Taipei
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hong Kong
Hungary
Iceland
Indonesia
Iran
Ireland
Israel
Italy
Japan
Korea
Latvia
Liechtenstein
Lithuania

Continued
Malaysia
Malta
Mexico
Netherlands
New Zealand
Norway
Poland
Portugal
Romania
Singapore
Slovakia
Slovenia
South Africa
Spain
Sweden
Switzerland
Thailand
Turkey
Ukraine
United Kingdom
USA

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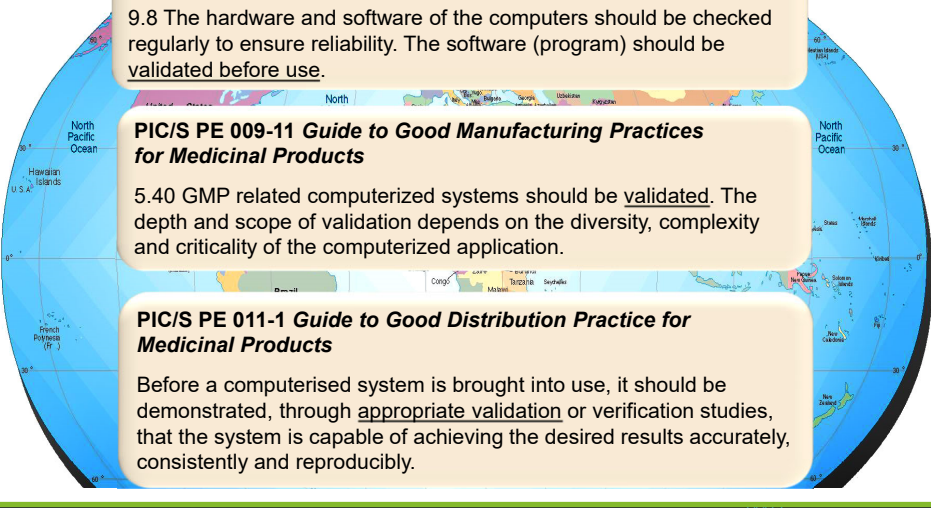
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CSV Regulatory Requirements

PIC/S



PIC/S PE 005-3 GMP Guide for Blood Establishments

9.8 The hardware and software of the computers should be checked regularly to ensure reliability. The software (program) should be validated before use.

PIC/S PE 009-11 Guide to Good Manufacturing Practices 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

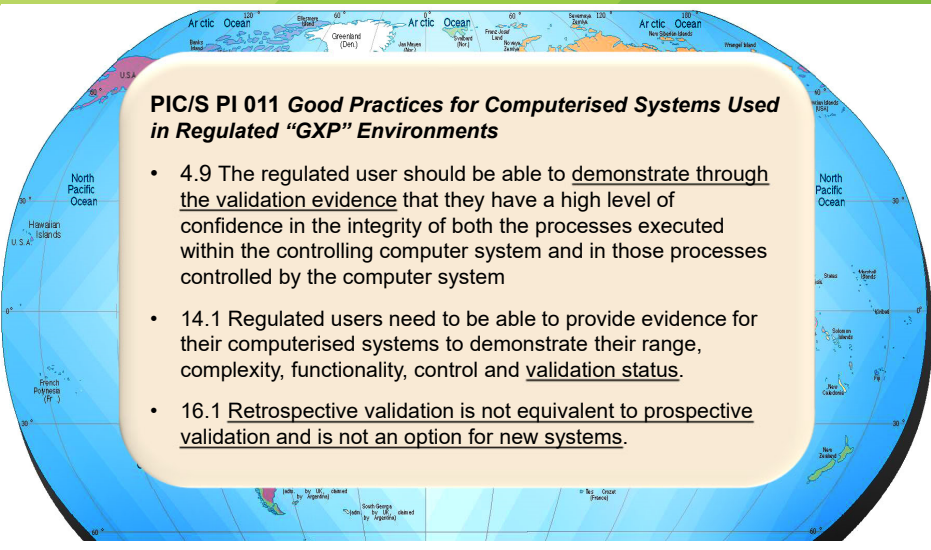
Before a computerised system is brought into use, it should be demonstrated, through appropriate validation or verification studies, that the system is capable of achieving the desired results accurately, consistently and reproducibly.

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CSV Regulatory Requirements

PIC/S



PIC/S PI 011 Good Practices for Computerised Systems Used in Regulated "GXP" Environments


- 4.9 The regulated user should be able to demonstrate through the validation evidence that they have a high level of confidence in the integrity of both the processes executed within the controlling computer system and in those processes controlled by the computer system
- 14.1 Regulated users need to be able to provide evidence for their computerised systems to demonstrate their range, complexity, functionality, control and validation status.
- 16.1 Retrospective validation is not equivalent to prospective validation and is not an option for new systems.


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CSV Regulatory Requirements


WHO





WHO Specifications for Pharmaceutical Preparations
6.3 Critical computerized systems should be validated before use.


WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles
4.11 Particular attention should be paid to the validation of analytical test methods, automated systems and cleaning procedures.

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CSV Purpose and Benefits

Part 2

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CSV Purpose and Benefits


Effectiveness

Safety


Integrity

Accuracy




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CSV Methodology

Part 3

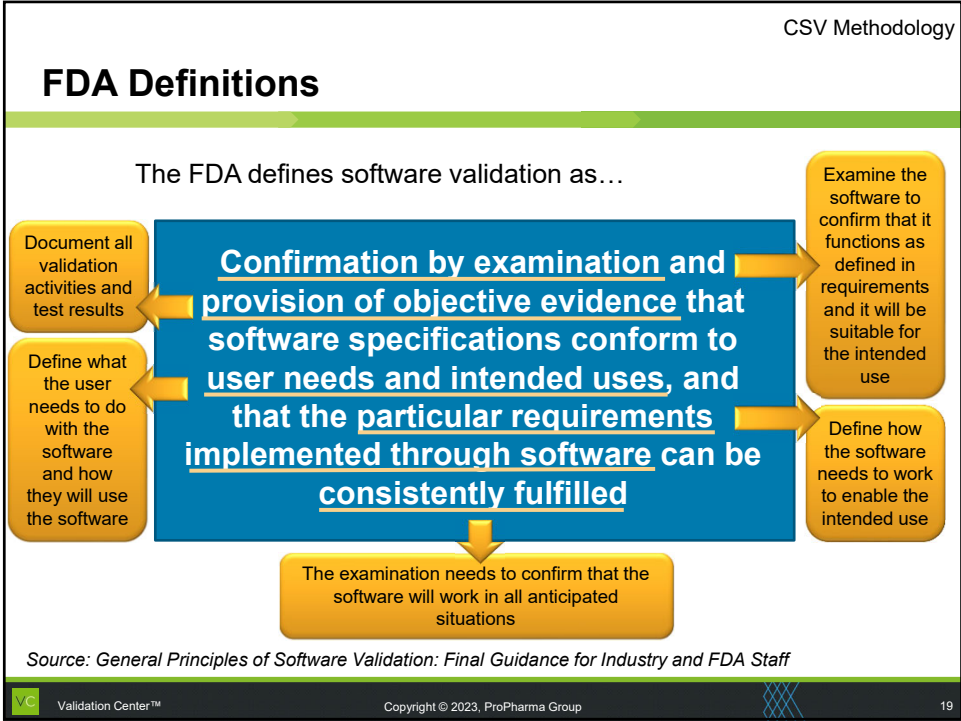
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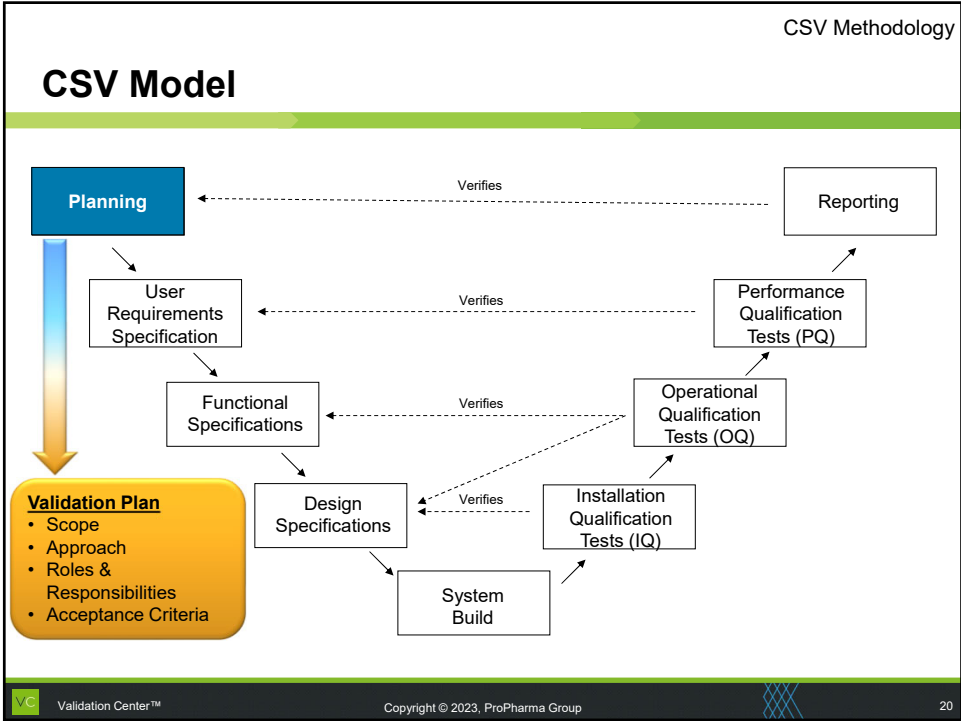


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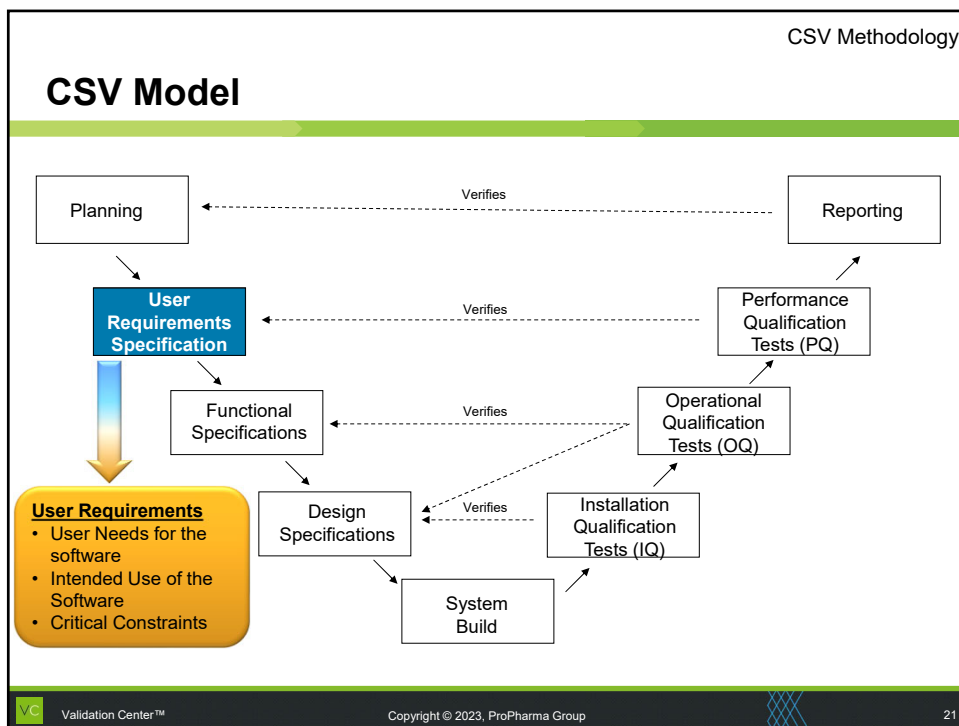
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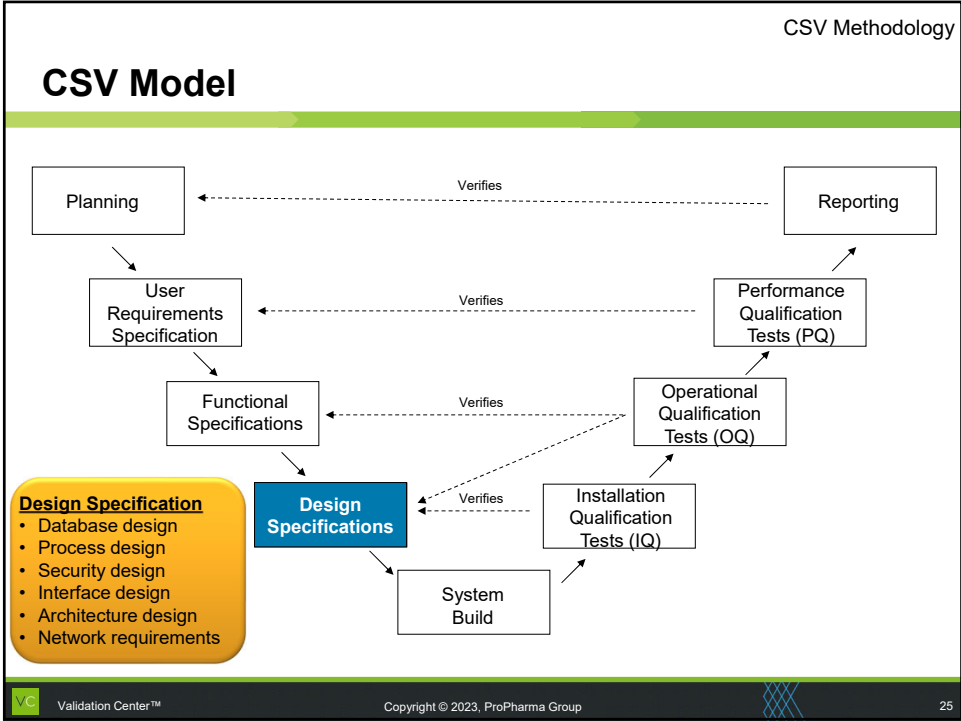
CSV Methodology

User Requirement, examples

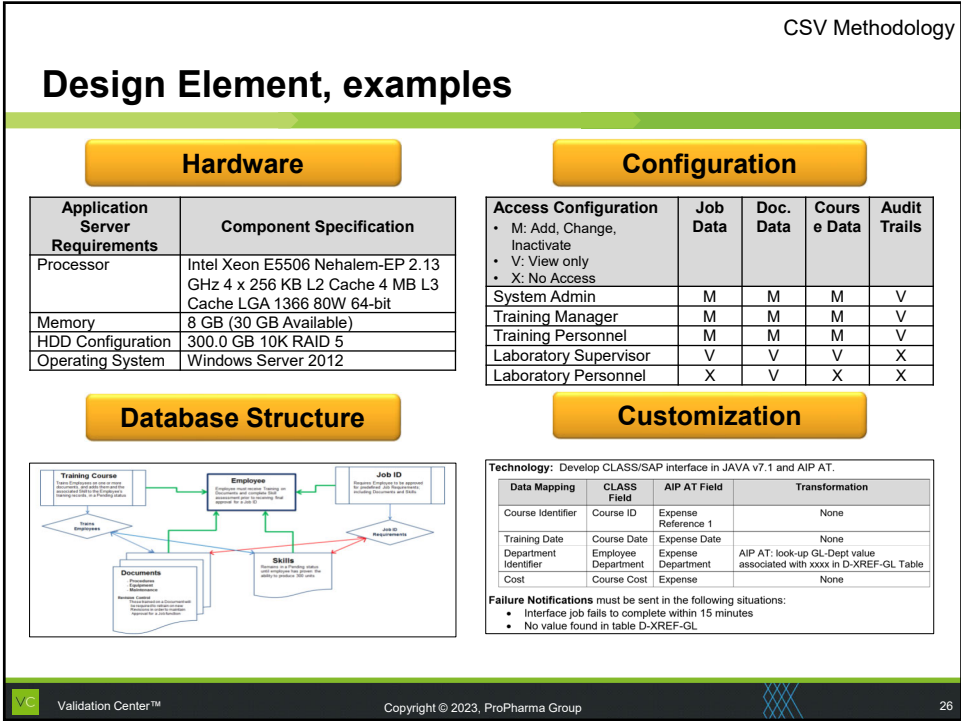
1.0 The system shall provide the capability for managing the training requirements for each job	2.0 The system shall provide the capability for managing the training for each employee	3.0 The system shall track completion of employee training
14.0 The system shall restrict user access to authorized personnel	15.0 The system shall require User IDs to be unique	16.0 The system shall require passwords that cannot be easily guessed
25.0. The system shall provide reports of employee training status	26.0. The system shall provide reports of training charges by department	32. The system shall provide an audit trail that complies with 21 CFR Part 11

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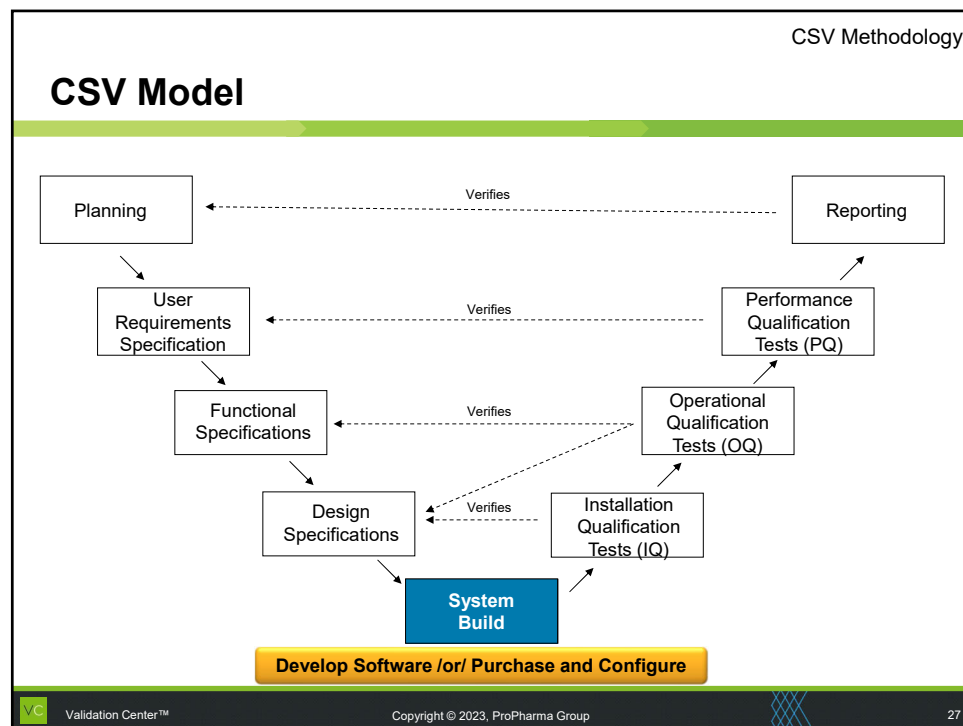
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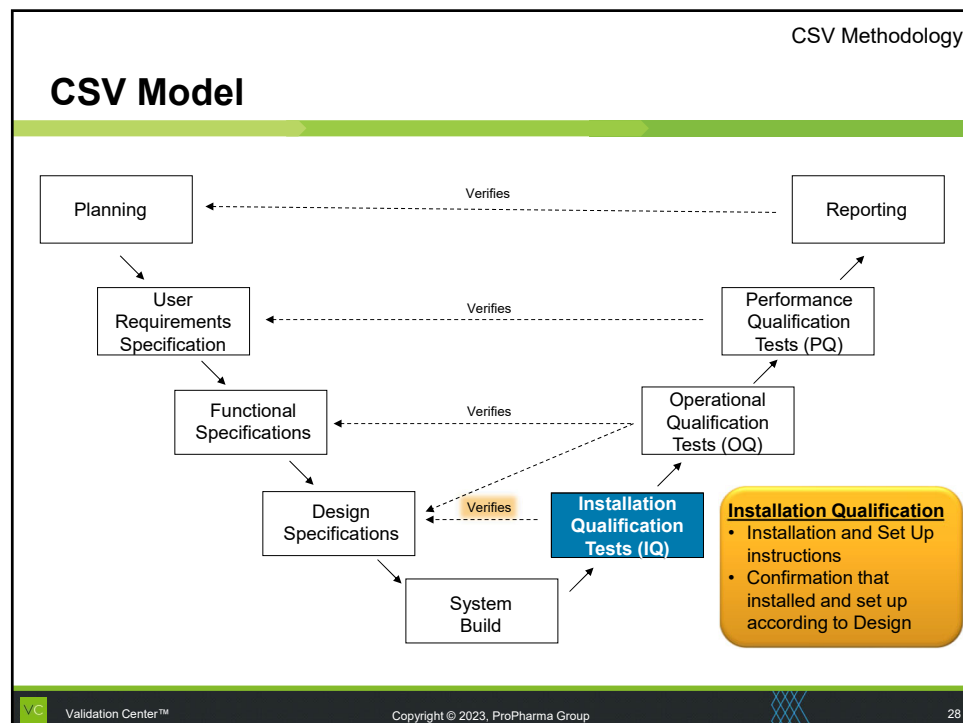
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CSV Methodology

IQ, examples

Hardware

Step	Element	Specification	Actual	Pass/Fail	Verified By
1	Processor	Intel Xeon E5506 Nehalem-EP 2.13 GHz 4 x 256 KB L2 Cache 4 MB L3 Cache LGA 1366 80W 64-bit			
2	Memory	8 GB (30 GB Available)			
3	HDD Configuration	300.0 GB 10K RAID 5			
4	Operating System	Windows Server 2012			

Customization

Section 1.0 Installation of CLASS/SAP Interface version 1

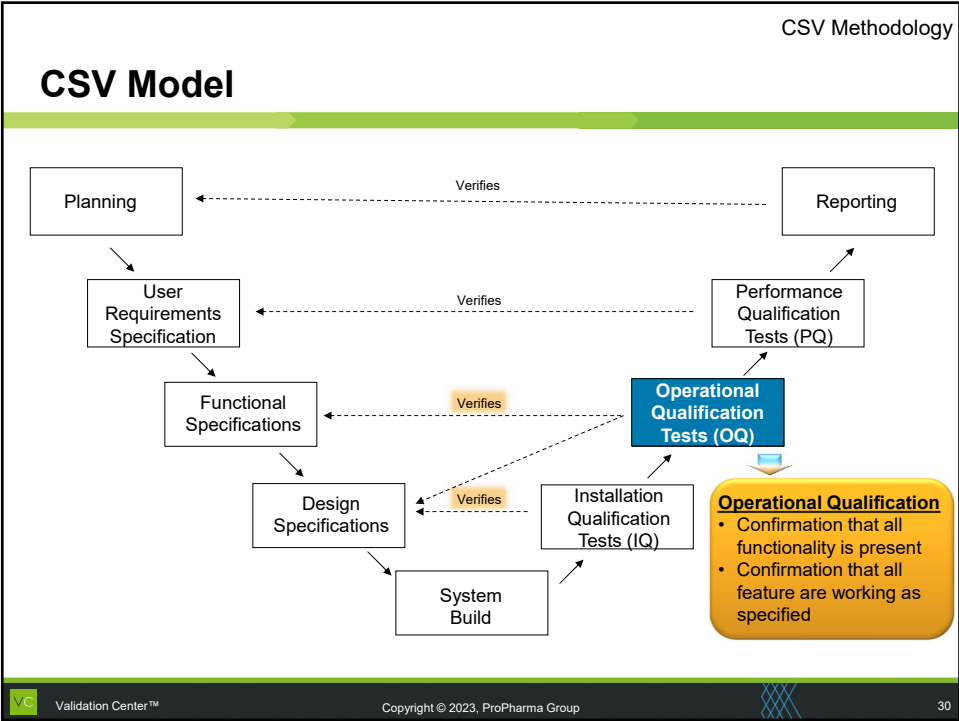
Step	Action	Expected Result	Actual Result	Pass/Fail	Executor Initial/Date
1.1	Move object "CL-SP-098-VS" to folder D:/Interface/Prod/Program	Object "CL-SP-098-VS" exists in folder D:/Interface/Prod/Program			
1.2	Set permission for object "CL-SP-098-VS" to Security Level ADMIN-ONLY	Permission for object "CL-SP-098-VS" is Security Level ADMIN-ONLY			
1.3	Move the following files to folder D:/Interface/Prod/Data <ul style="list-style-type: none">D-XREF-098MSG-098-V1	The following files are in folder D:/Interface/Prod/Data <ul style="list-style-type: none">D-XREF-098MSG-098-V1			

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CSV Methodology

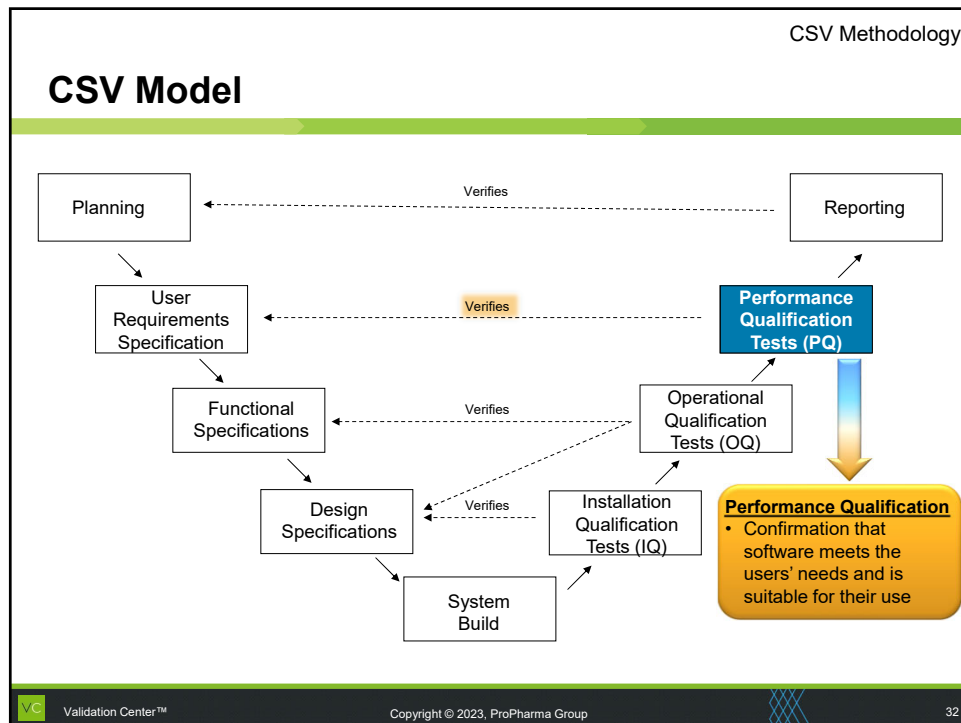
OQ, example

Data Setup					
Step	Description/Action	Verifier Initial/Date			
1.	Employees 3010, 3011, and 3012 are assigned to complete training on Document QLY-003				
2.	Employee 2010 is the supervisor for Employees 3010, 3011, and 3012				
3.	Employee 3012 has completed training on Document QLY-003				
Employees 3010 and 3011 have not completed training on Document QLY-003					
End of Data Setup					

Test Case 3					
Step	Description/Action	Expected Result	Actual Result	Pass/Fail	Tester Initial/Date
3.3	On the day after the Training Due Date recorded in step 1.9, launch email application for Employee 3010. - Capture Screen Shot of the Overdue Training email	An Overdue Training email notification for Document QLY-003 was received.			
3.4	On the day after the Training Due Date recorded in step 1.9, launch email application for Employee 2010. - Capture Screen Shot of the Overdue Training email	An Overdue Training email notification for Document QLY-003 was received for employee 3010			
3.5	On the day after the Training Due Date recorded in step 1.9, launch email application for Employee 3012...	No Overdue Training email notification for Document QLY-003 was received...			

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CSV Methodology

PQ, example

Data Setup					
Step	Description/Action				Verifier Initial/Date
1.	Employees 3010, 3011, and 3012 are assigned to complete training on Document QLY-003				
2.	Employee 2010 is the supervisor for Employees 3010, 3011, and 3012				
3.	Employee 3012 has completed training on Document QLY-003				
	Employees 3010 and 3011 have not completed training on Document QLY-003				
End of Data Setup					

Test Case 3					
Step	Description/Action	Expected Result	Actual Result	Pass/Fail	Tester Initial/Date
3.3	On the day after the Training Due Date recorded in step 1.9, launch email application for Employee 3010. - Capture Screen Shot of the Overdue Training email	An Overdue Training email notification for Document QLY-003 was received.			
3.4	On the day after the Training Due Date recorded in step 1.9, launch email application for Employee 2010. - Capture Screen Shot of the Overdue Training email	An Overdue Training email notification for Document QLY-003 was received for employee 3010			
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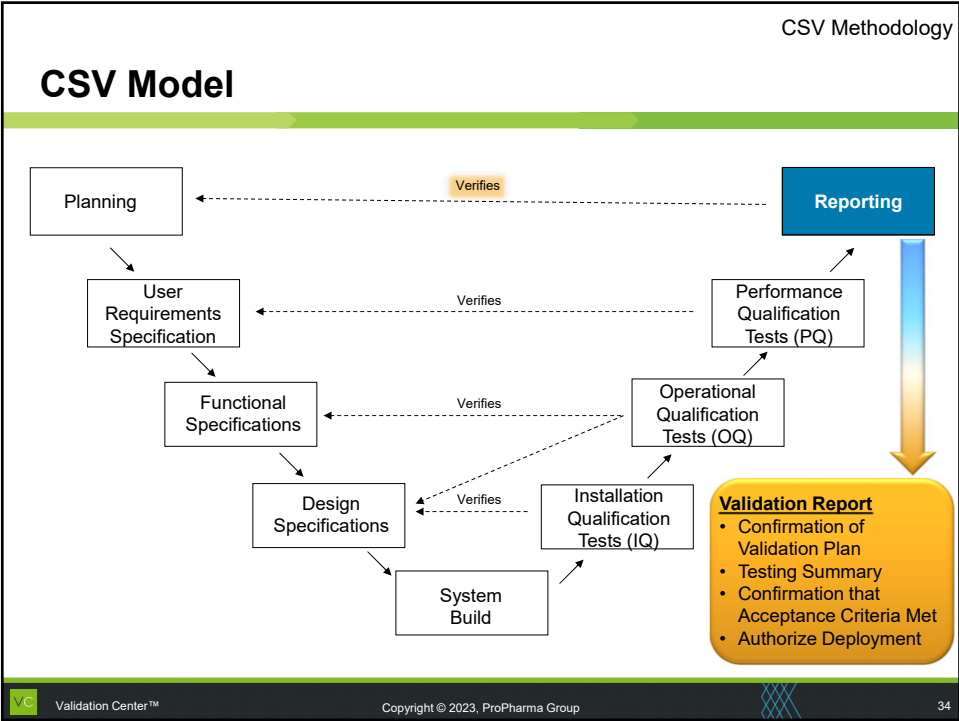
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CSV Methodology

Terminology

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.

VERIFICATION

...consistency, completeness, and correctness of the software and its supporting documentation,

URS Approval

Validation Report

FS Approval

Performance Qualification

Design Review

Operational Qualification

Code Walkthrough

Installation Qualification

Unit Testing

SOP Review

Trace Matrix

Training Review

QUALIFICATION

Formal testing to demonstrate that the software meets its specified requirements.


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CSV Scope

Part 4

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CSV Scope

What Software Requires Validation?

What Types of Computer Systems and Software Require Validation?

Medical Device Software

- Software used as a component, part, or accessory of a medical device
- Software that is itself a medical device

Sources: General Principles of Software Validation: Final Guidance for Industry and FDA Staff
Guidance for Industry Part 11, Electronic Records; Electronic Signatures — Scope and Application

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CSV Scope

Examples: Medical Device Software

Medical Device Software

Software used as a component, part, or accessory of a medical device.
And, software that is itself a medical device.

Blood Supply Management Software

Radiation Treatment Control Software

Infusion Pump Software

Heart Arrhythmia Detection Software

Blood Donor Management Software

Defibrillator Software

Patient Monitoring Software

Injury Treatment Machine Software

Medical Imaging System Software

Laser Treatment Software

Robotic Surgery Software

Hospital Bed Software

Laboratory Diagnostics Software

Oxygen Regulating Software

Pacemaker Software

Wheelchair and Scooter Software

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CSV Scope

What Software Requires Validation?

What Types of Computer Systems and Software Require Validation?

Medical Device Software

- Software used as a component, part, or accessory of a medical device
- Software that is itself a medical device

Production Software

Software used in the production of the FDA regulated product

Sources: General Principles of Software Validation: Final Guidance for Industry and FDA Staff
Guidance for Industry Part 11, Electronic Records; Electronic Signatures — Scope and Application

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CSV Scope

Examples: Production Software

Production Software

Software used in the production of the FDA regulated product

Manufacturing Automation Software

Production Monitoring Software

Laboratory Instrument Software

Batch Release Software

Programmable Logic Controllers (PLCs)

Bill of Material Software

Laboratory Management Software

Product/Part Inspection Software

Computer Numerical Controls (CNCs)

Material Control Software

Laboratory Calculations (e.g., spreadsheets)

Product Testing Software

Building Management Systems

Work Order Management Software

Yield Calculations

Labeling Software

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What Software Requires Validation?

What Types of Computer Systems and Software Require Validation?

- Medical Device Software**
 - Software used as a component, part, or accessory of a medical device
 - Software that is itself a medical device
- Production Software**
 - Software used in the production of the FDA regulated product
- Quality Management Software**
 - Software used to implement the FDA-required quality management system

Sources: General Principles of Software Validation: Final Guidance for Industry and FDA Staff
Guidance for Industry Part 11, Electronic Records; Electronic Signatures — Scope and Application

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CSV Scope

Examples: Quality Management Systems

Quality Management Software
Software used to implement the FDA-required quality management system

Complaints Software	Calibration Software	Document Management Software	Non-Conformance Tracking Software
Inventory Control Software (e.g., ERPs)	Preventive Maintenance Management	Internal Audit Software	Deviation Tracking Software
Product Returns Management Software	Quality Trending Software	Specification Management Software	CAPA Software
Product Recall Management Software	Device History Software	Specification Setting Software	Change Control Software

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CSV Scope

What Software Requires Validation?

What Types of Computer Systems and Software Require Validation?

Medical Device Software

- Software used as a component, part, or accessory of a medical device
- Software that is itself a medical device

Production Software

- Software used in the production of the FDA regulated product

Quality Management Software

- Software used to implement the FDA-required quality management system

➔

Software for FDA-Regulated Records

- Software used to create, modify, maintain, archive, retrieve, or transmit FDA-required records. And electronic records submitted, per FDA requirement.

Sources: General Principles of Software Validation: Final Guidance for Industry and FDA Staff
Guidance for Industry Part 11, Electronic Records; Electronic Signatures — Scope and Application

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CSV Scope

Examples: Records Software

Software for FDA-Regulated Records
 Any software used to create, modify, maintain, archive, retrieve, or transmit FDA-required records. And, electronic records submitted, per FDA requirement.

Electronic Submissions Software	IRB Records Software	Training Records Software	Prescription Order Fulfillment Software
Adverse Event Reporting Software	Clinical Trial Records Software	Learning Management Software	Distribution Records
MDR Reporting Software	Service Records Software	Supplier Approval Records	Warehouse Management Software
Organ / Tissue Donor Records	Call Center Records Software	Validation Records	Product Rework Records

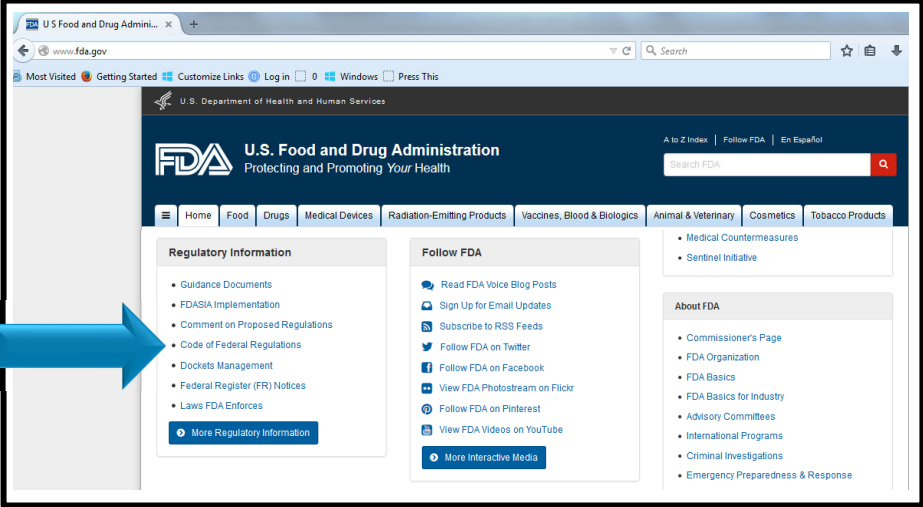
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CSV Scope

FDA Regulations



The screenshot shows the FDA website with the 'Regulatory Information' section highlighted. The section includes links to Guidance Documents, FDASIA Implementation, Comment on Proposed Regulations, Code of Federal Regulations, Dockets Management, Federal Register (FR) Notices, and Laws FDA Enforces. A blue arrow points to this section from the left.




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CSV Scope

FDA Regulations

Topic	Part	Title
Clinical Trials	21 CFR 50	Protection of Human Subjects
Clinical Trials	21 CFR 56	Institutional Review Boards
Nonclinical Lab Studies	21 CFR 58	Good Laboratory Practice for Nonclinical Laboratory Studies
Drugs	21 CFR 210	Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General
Finished Pharmaceuticals	21 CFR 211	Current Good Manufacturing Practice for Finished Pharmaceuticals
Drugs	21 CFR 312	Investigational New Drug Application
Drugs	21 CFR 314	Application for FDA Approval to Market a New Drug
Biological Products	21 CFR 600	Biological Products: General
Blood & Components	21 CFR 606	Current Good Manufacturing Practice for Blood and Blood Components
Medical Devices	21 CFR 803	Medical Device Reporting
Medical Devices	21 CFR 806	Medical Devices: Reports of Corrections and Removals
Medical Devices	21 CFR 820	Quality System Regulation
Cells and Tissue Products	21 CFR 1271	Human Cells, Tissues, and Cellular and Tissue-Based Products


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CSV Scope

FDA Regulations

Topic	Part	Title
Clinical Trials		TITLE 21—FOOD AND DRUGS
Clinical Trials		CHAPTER I—FOOD AND DRUG ADMINISTRATION
Clinical Trials		DEPARTMENT OF HEALTH AND HUMAN SERVICES
Clinical Trials		SUBCHAPTER H—MEDICAL DEVICES
Nonclinical Lab Studies		PART 820 QUALITY SYSTEM REGULATION
Drugs	2	Subpart A—General Provisions
Drugs	2	§ 820.1 - Scope.
Drugs	2	§ 820.3 - Definitions.
Drugs	2	§ 820.5 - Quality system.
Finished Pharmaceuticals	2	Subpart B—Quality System Requirements
Finished Pharmaceuticals	2	§ 820.20 - Management responsibility.
Finished Pharmaceuticals	2	§ 820.22 - Quality audit.
Finished Pharmaceuticals	2	§ 820.25 - Personnel.
Drugs	2	Subpart C—Design Controls
Drugs	2	§ 820.30 - Design controls.
Drugs	2	Subpart D—Document Controls
Drugs	2	§ 820.40 - Document controls.
Biological Products	2	Subpart E—Purchasing Controls
Biological Products	2	§ 820.50 - Purchasing controls.
Blood & Components	2	Subpart F—Identification and Traceability
Blood & Components	2	§ 820.60 - Identification.
Blood & Components	2	§ 820.65 - Traceability.
Medical Devices	2	Subpart G—Production and Process Controls
Medical Devices	2	§ 820.70 - Production and process controls.
Medical Devices	2	§ 820.72 - Inspection, measuring, and test equipment.
Medical Devices	2	§ 820.75 - Process validation.
Cells and Tissue Products	2	Subpart H—Acceptance Activities
Cells and Tissue Products	2	§ 820.80 - Receiving, in-process, and finished device acceptance.
Cells and Tissue Products	2	§ 820.85 - Acceptance status.
		Subpart I—Nonconforming Product
		§ 820.90 - Nonconforming product.
		Subpart J—Corrective and Preventive Action
		§ 820.100 - Corrective and preventive action.
		Subpart K—Labeling and Packaging Control
		§ 820.120 - Device labeling.
		§ 820.130 - Device packaging.
		Subpart L—Handling, Storage, Distribution, and Installation
		§ 820.140 - Handling.
		§ 820.150 - Storage.
		§ 820.160 - Distribution.
		§ 820.170 - Installation.
		Subpart M—Records
		§ 820.180 - General requirements.
		§ 820.181 - Device master record.
		§ 820.184 - Device history record.
		§ 820.186 - Quality system record.
		§ 820.198 - Complaint files.
		Subpart N—Servicing
		§ 820.200 - Servicing.
		Subpart O—Statistical Techniques
		§ 820.250 - Statistical techniques.

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CSV Scope

FDA Regulations

Topic	Part	Title
Clinical Trials		TITLE 21—FOOD AND DRUGS
Clinical Trials		CHAPTER I—FOOD AND DRUG ADMINISTRATION
Clinical Trials		DEPARTMENT OF HEALTH AND HUMAN SERVICES
Clinical Trials		SUBCHAPTER C—DRUGS: GENERAL
Nonclinical Lab Studies		PART 211 CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS
Drugs	2	Subpart A—General Provisions
Drugs	2	§ 211.1 - Scope.
Drugs	2	§ 211.3 - Definitions.
Finished Pharmaceuticals	2	Subpart B—Organization and Personnel
Finished Pharmaceuticals	2	§ 211.22 - Responsibilities of quality control unit.
Finished Pharmaceuticals	2	§ 211.25 - Personnel qualifications.
Finished Pharmaceuticals	2	§ 211.28 - Personnel responsibilities.
Finished Pharmaceuticals	2	§ 211.34 - Consultants.
Drugs	2	Subpart C—Buildings and Facilities
Drugs	2	§ 211.42 - Design and construction features.
Drugs	2	§ 211.44 - Lighting.
Finished Pharmaceuticals	2	§ 211.46 - Ventilation, air filtration, air heating and cooling.
Finished Pharmaceuticals	2	§ 211.48 - Plumbing.
Finished Pharmaceuticals	2	§ 211.50 - Sewage and refuse.
Drugs	2	§ 211.52 - Washing and toilet facilities.
Drugs	2	§ 211.56 - Sanitation.
Drugs	2	§ 211.58 - Maintenance.
Biological Products	2	Subpart D—Equipment
Biological Products	2	§ 211.63 - Equipment design, size, and location.
Biological Products	2	§ 211.65 - Equipment construction.
Blood & Components	2	§ 211.67 - Equipment cleaning and maintenance.
Blood & Components	2	§ 211.68 - Automatic, mechanical, and electronic equipment.
Blood & Components	2	§ 211.72 - Filters.
Medical Devices	2	Subpart E—Control of Components and Drug Product Containers and Closures
Medical Devices	2	§ 211.80 - General requirements.
Medical Devices	2	§ 211.82 - Receipt and storage of untested components, drug product containers, and
Medical Devices	2	§ 211.84 - Testing and approval or rejection of components, drug product containers, and
Medical Devices	2	§ 211.86 - Use of approved components, drug product containers, and closures.
Cells and Tissue Products	2	§ 211.87 - Retesting of approved components, drug product containers, and closures.
Cells and Tissue Products	2	§ 211.89 - Rejected components, drug product containers, and closures.
Cells and Tissue Products	2	§ 211.94 - Drug product containers and closures.
		Subpart F—Production and Process Controls
		§ 211.100 - Written procedures; deviations.
		§ 211.101 - Charge-in of components.
		§ 211.103 - Calculation of yield.
		§ 211.105 - Equipment identification.
		§ 211.110 - Sampling and testing of in-process materials and drug products.
		§ 211.111 - Time limitations on production.
		§ 211.113 - Control of microbiological contamination.
		§ 211.115 - Reprocessing.
		Subpart G—Packaging and Labeling Control
		§ 211.122 - Materials examination and usage criteria.
		§ 211.125 - Labeling issuance.
		§ 211.130 - Packaging and labeling operations.
		§ 211.132 - Tamper-evident packaging requirements for over-the-counter (OTC) human d
		§ 211.134 - Drug product inspection.
		§ 211.137 - Expiration dating.
		Subpart H—Holding and Distribution
		§ 211.142 - Warehousing procedures.
		§ 211.150 - Distribution procedures.
		Subpart I—Laboratory Controls
		§ 211.160 - General requirements.
		§ 211.165 - Testing and release for distribution.
		§ 211.166 - Stability testing.
		§ 211.167 - Special testing requirements.
		§ 211.170 - Reserve samples.
		§ 211.173 - Laboratory animals.
		§ 211.176 - Penicillin contamination.
		Subpart J—Records and Reports
		§ 211.180 - General requirements.
		§ 211.182 - Equipment cleaning and use log.
		§ 211.184 - Component, drug product container, closure, and labeling records.
		§ 211.186 - Master production and control records.
		§ 211.188 - Batch production and control records.
		§ 211.192 - Production record review.
		§ 211.194 - Laboratory records.
		§ 211.196 - Distribution records.
		§ 211.198 - Complaint files.

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CSV Scope

What About ...


- **Off-The-Shelf (OTS) Software?**
- **Configured Applications?**
- **Software as a Service (SaaS) Applications?**
- **Systems in the Cloud?**

1

Validation scope can be limited to the features that will be used by the regulated company

For example, a device manufacturer who chooses not to use all the vendor-supplied capabilities of the software only needs to validate those functions that will be used and for which the device manufacturer is dependent upon the software results as part of production or the quality system

FDA, *General Principles of Software Validation*

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CSV Scope

What About ...


- **Off-The-Shelf (OTS) Software?**
- **Configured Applications?**
- **Software as a Service (SaaS) Applications?**
- **Systems in the Cloud?**

2

Validation must be specific to the regulated company's planned and documented use of the application

The acceptance of vendor-supplied validation data in isolation of system configuration and intended use is not acceptable. In isolation from the intended process or end user IT infrastructure, vendor testing is likely to be limited to functional verification only, and may not fulfil the requirements for performance qualification.

MHRA, *GMP Data Integrity Definitions and Guidance*

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CSV Scope

What About ...

- Off-The-Shelf (OTS) Software?
- Configured Applications?
- Software as a Service (SaaS) Applications?
- Systems in the Cloud?

3


Vendor documentation can be used as the starting point for validation

If the vendor can provide information about their system requirements, software requirements, validation process, and the results of their validation, the medical device manufacturer can use that information as a beginning point for their required validation documentation.

FDA, General Principles of Software Validation

Documentation supplied with commercial off-the-shelf products should be reviewed by regulated users to check that user requirements are fulfilled

Eudralex Annex 11, Computerised Systems

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CSV Scope

What About ...

- Off-The-Shelf (OTS) Software?
- Configured Applications?
- Software as a Service (SaaS) Applications?
- Systems in the Cloud?

4


The regulated company needs to audit the vendors of critical applications and services – depending on risk

The audit should demonstrate that the vendor's procedures for and results of the verification and validation activities performed for the OTS software are appropriate and sufficient for the safety and effectiveness requirements ...

FDA, General Principles of Software Validation

The competence and reliability of a supplier are key factors when selecting a product or service provider. The need for an audit should be based on a risk assessment.

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CSV Scope

What About ...


- Off-The-Shelf (OTS) Software?
- Configured Applications?
- Software as a Service (SaaS) Applications?
- Systems in the Cloud?

5


Formal agreements are required to document responsibilities

When third parties (e.g. suppliers, service providers) are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerised system or related service or for data processing, formal agreements must exist between the manufacturer and any third parties, and these agreements should include clear statements of the responsibilities of the third party.

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CSV Failure Consequences

Part 5

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Consequences

FDA Enforcement Tools

- Warning Letter
- Injunction
- Product seizure
- Import restrictions
- Clinical hold
- Delay in approval of new products or facilities
- Consent decree
- Rejection of application data
- Disqualification of clinical investigators
- Debarment
- Criminal prosecution

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Consequences

Warning Letter Statistics

Over 100 Warning Letter citations in a 3 years period (2019-2021) for software and computer system issues

Nearly 1/4 of these were for validation issues

A majority of the validation issues were for simply failing to validate the software or computer system

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Consequences

Warning Letter Example

Company	German manufacturer of endoscopic grasping/cutting instruments
System	Purchased, configured ERP used for production planning and quality records. NOTE: Software vendor performed installation and upgrades
Warning Letter Excepts	<ul style="list-style-type: none"> • There are no procedures that describe the qualification and maintenance of the Majesty Enterprise Resource Planning (ERP) software for production planning and maintenance of quality records. • There are no records documenting that the Majesty system is validated or meets user needs and intended uses. • There are no documents that define the system's features and functions, operating environment, or hardware requirements. • The procedure which addresses vendor selection qualification and requalification of suppliers, has not been not implemented. There is no documentation that the supplier of Majesty software, was qualified or re-qualified as a supplier.



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Consequences

Warning Letter Example

Company	California manufacturer of wound bio-engineered alternative tissue devices
System	Spreadsheet used for calculations
Warning Except	<ul style="list-style-type: none"> • Your firm did not validate use of an Excel spreadsheet used to calculate the Moisture Vapor Transmission Rate (MVTR)
Company	New Jersey manufacturer of medical devices
System	SharePoint used for document management
Warning Excepts	<ul style="list-style-type: none"> • Off-the-shelf software (Microsoft SharePoint) is being used to manage quality system documents for document control and approval. However, firm has failed to adequately validate this software to ensure that it meets your needs and intended uses. • There were two different versions of your CAPA & Customer Complaint procedure; however, no revision history was provided on the SharePoint document history. Your firm has failed to validate the SharePoint software to meet your needs for maintaining document control and versioning.

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Consequences

Warning Letter Example

Company

Idaho manufacturer of radiopharmaceuticals

System

Custom developed system for batch records, calculations, and label generation

Warning Letter Except

Firm's custom software for Master Batch Production record has not been validated. This software is responsible for generating the batch production record, performing calculations to produce varying concentrations of drug product, and generating label information for customer vials and lead pigs.

Company

Italian manufacturer of laser devices

System

Custom developed system for tech calls, complaints, and service records

Warning Letter Excepts

The software developed by your firm to record, evaluate, investigate, correct and repair incoming technical assistance calls, complaints, and service records was implemented and has not been validated.

No validation documentation was available for an established protocol, any testing data, or a finished report for the validation of this system.

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Consequences

Warning Letter Example

Company

German manufacturer of sterile and non-sterile needles and sutures

System

Software controlling the machinery making needles

Warning Letter Except

Your firm uses custom automatic machines in the needle production process. Your firm stated that it performed software validation for the automatic machines and that the software protocol was tested, but these validation activities were not documented.

Company

Kentucky medical center

System

Blood management

Warning Letter Except

Your firm went live with version 2.0.0 of the Hemocare Lifeline (HCLL) Donor Module; however, the validation of Module 15, Product Labeling, was incomplete in that it was not reviewed, accepted, or signed off by a responsible individual.

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CSV Program Implementation

Part 6

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CSV Program Implementation

Procedure Examples

- How to validate
- How to perform risk assessment
- How to audit vendors

CAPA (if out of compliance)
Validation Master Plan

- Policies, Procedures
- Inventory
- Validation Timeline

Define Policies

Develop SOPs and Templates

Train Staff

Inventory Systems and Software

Assess and Prioritize Systems and Software

Document Plan


Validate!

Policy Examples


- Which systems and software require validation?
- When does validation occur?
- When do vendors need to be qualified? Audited?

Example

- Which systems and software require validation?
- What is the risk level of each?
- What is the priority for validating each system?

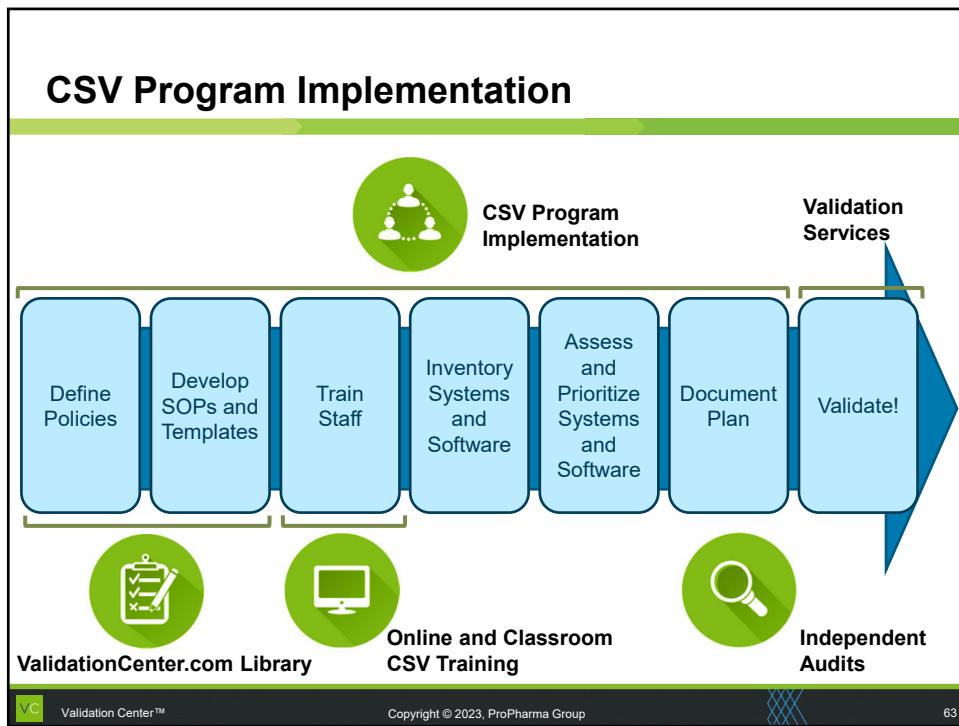
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Thank You!




Thanks for your interest in Computer System Validation

Any questions about what we have discussed today?
Please, feel free to contact me:

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