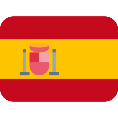
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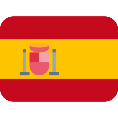
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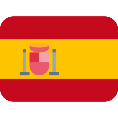
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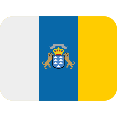
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# emoji-timeline General Glossary

## Regulations and Guidelines

**GAMP** = Good Automated Manufacturing Principles

**GMP** = **Good Manufacturing Practices (GMP)** are a set of regulations and guidelines that ensure that products are consistently produced and controlled according to quality standards. These guidelines are intended to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product. GMP covers all aspects of production, from the starting materials, premises, and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product.

Key aspects of GMP include: Patient safety, Manufacturing processes, Quality Management, Facilities and Equipment, Personnel, Validation and Qualification

**cGMP = Current Good Manufacturing Practices (cGMP)** are a refinement of the GMP guidelines. The "c" in cGMP stands for "current," emphasizing that manufacturers must employ up-to-date technologies and systems to comply with the regulations. This means that the practices should be not only in line with the foundational principles of GMP but also reflect the latest advancements and innovations in manufacturing processes, equipment, and quality systems.

Key aspects of cGMP include: Continuous Improvement, Risk Management, Modern Quality Systems, Regulatory Compliance

emoji-timeline **21 CFR** = Code of Federal Regulations, Chapter 21: Food and Drugs.

emoji-timeline [FDA 21 CFR 211](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211?toc=1) =  Current Good Manufacturing Practice for Finished Pharmaceuticals

emoji-timeline [FDA 21 CFR 210](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-210) =  Current Good Manufacturing Practice in Manufacturing, Processing, Packing, Or Holding of Drugs; General

emoji-timeline [FDA 21 CFR 11](https://www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm) =  Electronic Records and Electronic Signatures (ERES) for life science companies. It sets the criteria under which electronic records and signatures are considered trustworthy, reliable, and equivalent to paper records.

emoji-timeline [FDA 21 CFR 820](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820) = Software and Systems used in Manufacturing Medical Devices

FDA [Computer Software Assurance for Production and Software Systems](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/computer-software-assurance-production-and-quality-system-software) = FDA Draft guidance document (2022)



emoji-timeline [ASTM E2500](https://www.astm.org/e2500-20.html) =  American Society for Testing and Materials. Standard relating to the specification, design and verification of Pharmaceutical and Biotechnological manufacturing systems and equipment. It is applicable to equipment, systems/processes, utilities, laboratory systems, I.T. and automation systems that may affect product quality and patient safety.

**ISO** = International Organization for Standardization

**IEC** = International Electronical Commission

emoji-timeline[**ISO 13485**](https://www.iso.org/standard/59752.html) =  Quality Management System for Medical Device Manufacturing.

**ISO 14971** Medical devices = Application of risk management to medical devices

[**ISO 9001**](https://www.iso.org/standard/62085.html) = Quality Management Systems. ISO 9001 is a **globally recognized standard for quality management**. It helps organizations of all sizes and sectors to improve their performance, meet customer expectations and demonstrate their commitment to quality. Its requirements define how to establish, implement, maintain, and continually improve a quality management system (QMS).



Implementing ISO 9001 means your organization has put in place effective processes and trained staff to deliver flawless products or services time after time.

**ISO 14001** = Environmental Management Systems

**ISO 27001** = Information Security

**ISO 45001** = Occupational health and safety management systems

**IEC 62304** = Medical device software — Software life cycle processes

**IEC 62366-1** = Part 1: Application of usability engineering to medical devices

**TAPA TSR** = (Transported Asset Protection Association) Trucking Security Requirements

emoji-timeline[**WHO TRS 1052 – Annex 4: Good Practices for Pharmaceutical Quality Control Laboratories**](https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/quality-control/trs1052_annex4.pdf?sfvrsn=d3dfc0cc_4&download=true) **=** World Health Organisation guideline consistent with the requirements of the WHO good manufacturing practices for pharmaceutical products (1) and international standard ISO/IEC 17025:2017 (2), providing detailed guidance for laboratories performing quality control testing of medicines.

**Eudralex**

Eudralex is a compendium of all the legislative and regulatory texts of the European Union concerning medicinal products for human and veterinary use. It includes:

* Directives: These are European laws which must be transposed into the national law of each Member State. They establish objectives that Member States must achieve, but the way in which they do so may vary.
* Regulations: Unlike directives, regulations are directly applicable in all Member States without the need for transposition into national law.
* Decisions: These are binding on those affected by them.
* Recommendations and Opinions: These are non-binding instruments.

Eudralex is organised into different annexes covering various aspects of pharmaceutical regulation, such as good manufacturing practice (GMP), post-marketing surveillance and marketing authorisation procedures.

Twemoji 15.0.1 [EudraLex – Volume 4 – Good Manufacturing Practice](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en) =  guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use

Twemoji 15.0.1 [EudraLex – Volume 4 – Annex 11](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/annex11_01-2011_en.pdf) = ![A red square with white text

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Twemoji 15.0.1 [Eudralex – Volume 4 – Annex 15](https://health.ec.europa.eu/system/files/2016-11/2015-10_annex15_0.pdf) = ![A red square with white text

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Twemoji 15.0.1 **EudraLex volume 4 Annex 21** = This Annex summarizes the GMP requirements applicable to a MIA holder, when importing medicinal products (human, investigational and veterinary) from outside the EU/EEA.

Twemoji 15.0.1 [Directive (UE) 2017/1572](http://data.europa.eu/eli/dir/2017/1572/oj) =  Principles And Guidelines Of Good Manufacturing Practice For Medicinal Products For Human Use

[MDR 2017/745](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745) = Medical Device Regulation. Le nouveau règlement (UE) 2017/745 ou MDR (Medical Devices Regulation) est le règlement européen sur les dispositifs médicaux qui définit les réglementations et les contraintes que tous les fabricants et distributeurs doivent respecter pour mettre un dispositif médical (DM) sur le marché européen.



**MDD / MDR** = Medical Device Directive / Medical Device Regulation. <https://kobridgeconsulting.com/mdd-vs-mdr/>

There are many regulations in place that govern how medical device manufacturers can produce and supply their products. The EU has a few different regulatory requirements for medical devices. In Europe, there is the MDD (Medical Devices Directive) as well as MDR (Medical Device Regulation). Understanding the MDD vs MDR difference is vital for manufacturers to safely carry out their operations in European countries. The MDR is the successor of MDD and has been put in place to protect the health and safety of European Union citizens.

The purpose of this new regulation is to ensure that manufacturers produce safe products for Europeans. This includes the devices themselves as well as any medical device software (MDS). However, one major MDD and MDR difference is where they apply. **The MDD applies to medical devices that are used in the European Union**, and it includes all types of devices as well as software for those devices. This means any device marketed inside Europe is subject to strict MDD regulation standards such as complying with the regulatory requirements or meeting additional requirements. **The MDR applies to manufacturers of medical devices that are sold in Europe**.

emoji-timeline [Bonnes Pratiques de Fabrication de Médicaments à Usage Humain](https://ansm.sante.fr/documents/reference/bonnes-pratiques-de-fabrication-de-medicaments-a-usage-humain) =  Document presentation Website

emoji-timeline [Bonnes Pratiques de Fabrication de Médicaments à Usage Humain](https://ansm.sante.fr/uploads/2024/06/13/20240613-guide-bpf-2024-2.pdf) = ![A red square with white text

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[PICs Good Practices for Computerized Systems in Regulated GxP environments](https://picscheme.org/docview/3444) =  (2007)

[ICH guideline Q9](https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-ich-guideline-q9-quality-risk-management-step-5-first-version_en.pdf) = ![A red square with white text

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ISPE Baseline Guide Vol 5: Commissioning & Qualification 2nd Edition

ISPE Baseline Guide Vol 6 : Biopharmaceutical Manufacturing Facilities

ISPE Baseline Guide Vol 3 : Sterile Product Manufacturing Facilities

ISPE GAMP 5 (Good Automated manufacturing practices) : A Risk-Based Approach to Compliant GxP Computerized Systems (Second Edition)

**AMWHV** = German Ordinance for the Production of Medicinal Products and Active Substances

**AMG** = Medicinal Product Act - German Law on Pharmaceuticals

**SOX** = Sarbanes-Oxley Act, financial records keeping and reporting

**TPA** = Therapeutic Product Act (Swiss)

## Organisations

**ISPE** = International Society for Pharmaceutical Engineering

**ECA** = European Compliance Academy

**ECA Foundation** = Europe’s leading Association in the field of pharmaceutical Quality Regulation. The ECA Foundation is the legal entity and is headed by an Advisory Board. The Advisory Board (also called Foundation Board) consists of experts from industry and authorities. It is the aim of the Advisory Board to provide support to promote the move toward a harmonized set of GMP/GDP and Regulatory Guidelines.

**ECA Academy** = Educational organisation of the ECA Foundation. The Academy develops GMP training courses and conferences. In addition to the Academy the Foundation also initiated several Interest and Working Groups. It is the goal of the Foundation to further develop these groups and to set up new groups.

**EMA** = European Medicines Agency

**ASTM** = American Society for Testing and Materials

**FDA** = Food and Drugs Administration (USA)

**WHO** = World Health Organisation

**ICH** = International Council of Harmonisation of Technical Requirements of Pharmaceutical for Human Use

**MHRA** = Medicine and Healthcare products Regulatory Agency (UK)

**PIC** = Pharmaceutical Inspection Convention

**PIC/S** = Pharmaceutical Inspection Cooperation Scheme

**PDA** = Parenteral Drug Association

**ANSM =** Agence Nationale de la Sécurité du Médicament

## Miscellaneous

**The ISPE GAMP® 5 Guide**: A Risk-Based Approach to Compliant GxP Computerized Systems

**HSE** = Health Safety and Environment Protection

**GxP** = GLP – Laboratory, GCP – Clinical, GMP – Manufacturing, GDP – Distribution, GPvP – Pharmacovigilance, GLPMA – Laboratory Monitoring Activity,

**cGMP** = current Good Manufacturing Practice

**CMMI** = Capability Maturity Model Integrated

**PSO** = Public Service Obligation

**FMD** = Falsified Medicines Directives

**3PL** = Third-Party Logistics

**MIA** = Manufacturing Import Authorisation

**WDA** = Wholesale Distributor Authorisation

**MAH** = Marketing Authorisation Holder

**CMO - CDMO** = Contract Development Manufacturing Organization. The core business of pharmaceutical subcontractors, also known as CDMOs (Contract Development Manufacturing Organisations), is the manufacture and packaging of medicines on an industrial scale. They help pharmaceutical and biotechnology companies manufacture their innovative drug substances. Their offerings can include commercial production, drug development, formal stability, formulation development, method development, pre-formulation, and registration batches.

**CRO** = Contract Research Organisation

**OTC** = Over-the-counter. Refers to a medicine that can be bought without a prescription (doctor's order). Examples include analgesics (pain relievers), such as aspirin and acetaminophen. Also called nonprescription and over-the-counter.

**CMC** = Chemistry, manufacturing and controls; also referred to as pharmaceutical quality/CMC. The term covers the various procedures used to assess the physical and chemical characteristics of drug products, and to ensure their quality and consistency during manufacturing.

**IND** = An Investigational New Drug is a drug or biological drug that has not been approved for general use by the FDA.

**MVP** = Minimum Viable Product. Version of a product with just enough features to be usable by early customers who can then provide feedback for future product development.

**IVD** = InVitro Device

**QMS** = Quality Management System

**PQS** = Pharmaceutical Quality System (FDA)

**API** = Active Pharmaceutical Ingredient

**SOP** = Standard Operating Procedure

**ALCOA+** = Attributable, Legible, Contemporaneous, Original, Accurate, + (Complete, Consistent, Enduring, Available)

**CSV** = Computerised System Validation

**CAPA** = Corrective And Preventive Actions

**OOS** = Out of Specifications

**OOT** = Out Of Trend (Out Of Time?), Stability

**PQR** = Product Quality Review

**APR** = Annual Product Review

**HLRA** = High Level Risks Analysis

**DRA** = Detailed Risk Analysis

**RSI** = Reference Safety Information

**SAR** = Serious Adverse Reaction

**SUSAR** = Suspected Unexpected SAR

**SMF** = Site Master File

**EBR** = Electronic Batch Report

**RAS** = Rapid Alert System

**CQV** = Commissioning, Qualification and Validation

**FAT** = Factory Acceptance Test

**SAT** = Site Acceptance Test

**SME** = Subject Matter Expert

**QbD** = Quality by Design

**FMECA** = Failure Modes, Effects and Criticality Analysis.

**P FMEA** = Process Failure Mode Effects Analysis. Qualitative tool used with the intention of preventing failures. **AMDEC** (Analyse des modes de défaillance, de leurs effets et de leur criticité) in French

**KPI** = Key Performance Indicator

**KQI** = Key Quality Indicator

**FMCH** = Family Medicine and Community Health

**PAPP** = Production Part Approval Process is a process that manufacturers follow to ensure that the parts they produce conform to customer specifications and are of the highest quality. The PPAP allows suppliers to provide evidence of their processes that ensure their ability to consistently produce parts that meet customer specifications.

**SPC** = Statistical process control is defined as the use of statistical techniques to control a process or production method. SPC tools and procedures can help you monitor process behavior, discover issues in internal systems, and find solutions for production issues.

**PIL** = Package Information Leaflet

**SmPC** = Summary of products characteristics

**CCDS** = Company Core Data Sheet. It is an essential document prepared by the marketing authorization holder (usually a pharmaceutical company) that contains comprehensive information about a medical product, including safety information, indications, dosing, pharmacology, and other relevant details.

**CCSI** = Company Core Safety Information is the safety information contained in the CCDS. It is a term used in the field of pharmacovigilance and drug safety to refer to a standardized and comprehensive set of safety information that pharmaceutical companies are required to maintain and update for each of their marketed medicinal products.

**CTR** = The Clinical Trials Regulation harmonises the processes for assessment and supervision of clinical trials throughout the EU. The evaluation, authorisation and supervision of clinical trials are the responsibilities of EU Member States and European Economic Area (EEA) countries.

**CTA** = A Clinical Trials Application (CTA) is the application/submission to the competent National. Regulatory Authority(ies) for authorization to conduct a clinical trial in a specific country.

**CRA** = The main function of a clinical research associate is to monitor clinical trials. The CRA may work directly with the sponsor company of a clinical trial, as an independent freelancer or for a contract research organization (CRO).

# emoji-timeline Glosario Español

**PCD** = (GDP) Prácticas Correctas de Distribución o **BPD** = (GDP) Buenas Prácticas de Distribución

**SGA** = (WMS) Sistema de Gestión de Almacén

**PNT** = (SOP) = Procedimientos normalizados de trabajo

# Commissioning, Qualification, Validation

## Commissioning

Systematic approach to the start-up of a manufacturing system and covers all aspects of bringing a system or subsystem to a position where it is regarded as being ready for use in pharmaceutical (and other) manufacturing. Commissioning verifies that **what was specified was installed**, that it **functions properly**, and that it was **successfully turned over to the user**. The primary focus is placed on satisfying **engineering requirements** for the facility, defined earlier in the project.

## Qualification

Qualification extends beyond commissioning and is the action of proving that the facility, systems and equipment that have a direct impact on product quality and patient safety are correctly installed, work as expected and are fit for the intended use.

While commissioning can be viewed as primarily an engineering test and applies to all of the equipment in a manufacturing facility, **qualification only applies to systems** and equipment that have **direct or indirect impact on the quality of the product** and will be focused on by the regulatory authorities when they come to approve the medicines that are being manufactured in that facility.

emoji-timeline **Qualification**

La qualification porte sur les entrants du procédé / processus.

La qualification s’assure que l’équipement fonctionne correctement et est adapté à son utilisation prévue.

La qualification est une partie d’une validation

## Validation

A **broader** term and describes the process of creating an **evidence trail** to show that an action, process or system leads to a **consistent and reproducible result**. There are many other definitions of validation but the essence of all these definitions seems to be “documented scientific proof of consistent performance”.

Validation is a central part of the manufacturing process within the pharmaceutical and medical device industries. The products made must be the same every time and are tested at the end of the production process to ensure that this is the case, but final end-product testing isn’t enough.

In addition, the processes, systems, and equipment that lead to their manufacture are closely scrutinized too. This establishes that they meet predetermined specifications and always produce the same result.

emoji-timeline **Validation**

La validation porte sur le procédé / le processus

La validation s’assure que le procédé / la méthode / le processus atteint les objectifs de qualité et de performances fixés.

# emoji-timeline Computerised System Validation

## Specific Regulations, Guides and Recommendations

[FDA 21 CFR 211.68](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211/subpart-D/section-211.68) =  Computerized Systems are considered as equipment.



emoji-timeline [FDA 21 CFR 11](https://www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm) =  Electronic Records and Electronic Signatures

emoji-timeline [FDA 21 CFR 820](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820) =  Software and Systems used in Manufacturing Medical Devices

[EudraLex – Volume 4 – Annex 11](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/annex11_01-2011_en.pdf) = Computerized Systems (2011)



[PICs Good Practices for Computerized Systems in Regulated GxP environments](https://picscheme.org/docview/3444) = (2007)

[ISO 13485](https://www.iso.org/standard/59752.html) = Quality Management System for Medical Device Manufacturing.

[Computer Software Assurance for Production and Software Systems](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/computer-software-assurance-production-and-quality-system-software) = FDA Draft guidance document (2022)

ISPE GAMP 5 (Good Automated manufacturing practices) : A Risk-Based Approach to Compliant GxP Computerized Systems (Second Edition)

## V-Model documentation

### User Requirements:

**URS** = User Requirements Specifications. What the user needs from the system and how they will use it. It also contains any constraints such as regulations, safety requirements or operational requirements. Main goals: - to ensure a clear understanding of the user’s requirements, - to facilitate effective communication between stakeholders, - to serve as a reference throughout the project workflow. Computerised and automated system specific requirements: - UI descriptions, - Access control, Data management, - Audit trail management, - Backup management, - Electronic signature management, - Expected reports descriptions

**PQ** = Performance qualification (“user requirement testing”). Verifies that the system performs consistently under normal and stress conditions. Confirms that the software will meet the user’s needs (USR) and is suitable for their intended use.

**UAT** = User Acceptance Tests. Confirms that the system meets user’s needs and expectations.

### Functional Specifications:

**FS** = Functional Specifications. Detailed description of how the system will meet each of the requirements outlined in the URS. How the software works. What data needs to be captured. User interfaces.

**OQ** = Operational qualification (“functional testing”). Confirms that all functionality defined in the Functional Specification (FS) is present and working correctly.

### Technical Design:

**IS** = Installation Specifications. Documentation from an equipment manufacturer that describes how a product should be properly installed within a physical environment.

**DS** = Design Specifications. How each function is to be designed or configured. May contain configuration specifications or code – its intended audience is the system developer. Delve into the technical implementation details and architectural decisions:

* Focus on the "how" of the system. They describe how the system will be implemented, including the architecture, components, modules, interfaces, and technologies to be used.
* Delve into the technical details of the system's implementation, such as database design, integration points, data flow diagrams, and system behaviour under different scenarios.
* Created by system designers, architects, and developers to plan and guide the implementation phase of the project.
* Provide a detailed technical plan for building the system, ensuring that all team members understand how the system will be developed and integrated within the existing infrastructure.

**TS** = Technical Specifications. Focus on defining the requirements and functionality of the system:

* Outline the detailed requirements and functionality of the system to be developed. They describe what the system should do, its interfaces, data structures, algorithms, and other technical aspects.
* Typically focus on the "what" of the system, detailing the features, functions, and capabilities that the system must have.
* Created by business analysts and system architects in collaboration with stakeholders to ensure that the system meets the business requirements.
* Provide a roadmap for developers to implement the system according to the specified requirements, acting as a blueprint for development.

**DQ** = Design Qualification. A protocol defined as the documented verification of a proposed design’s ability to meet the requirements it needs to fulfil. Showing that a piece of technology – a device, apparatus, machine or system – has a GMP-compliant design

**IQ** = Installation Qualification (“configuration or integration testing”). Confirms that the software or system is installed and set up according to the Design Specification (DS). Showing it is set up, connected and installed as planned

## IT Glossary

**SDLC** = Software Development Life Cycle is used in technology to refer to the entire process of technology innovation and support.

**API** = Application Programming Interface

**RAD** = Rapid Application Development

**RUP** = Rational Unified Process

**RIM** = Regulatory Information Management

**PMO** = Project management Officer

**ERP** = Enterprise Resource Planning

**EHR** = An Electronic Health Record (EHR) is an electronic version of a patients medical history, that is maintained by the provider over time, and may include all of the key administrative clinical data relevant to that persons care under a particular provider, including demographics, progress notes, problems, medications, ...

**EPR** = Electronic Patient record. An EPR system is a digital platform that brings all your patient information, from medical history to results of investigations and medications prescribed, together in one place. Currently we hold your records in different places, such as paper-based notes and on several digital systems.

**EMR** = Electronic Medical Record. An electronic record of health-related information on an individual that can be created, gathered, managed, and consulted by authorized clinicians and staff within one health care organization. EMRs hold patient data within one practice, while EHRs offer a complete view of a patient's health history across various providers. For example, a medical practice can retrieve a patient's emergency contact information from the EMR but will need an EHR to view a total patient record.

**eDMS** = electronic Document Management System (Documents)

**eQms** = electronic Quality Management System (Processes)

**PAT** = Process Analytical Technology

**MES** = Manufacturing Execution System

**PLC** = Programmable Logic Controllers

**SPICE** = Software Process Improvement and Capability Determination

**ITIL** = IT Infrastructure Library

**COBIT** = Control Objectives for Information and Related Technologies

**SMART** (Requirements) = Specific, Measurable, Attainable, Relevant, Testable

**WAN** = Wide Area Network. WANs connect users and applications in geographically dispersed locations (across the globe).

**LAN** = Local Area Network. LANs connect users and applications in close geographical proximity (same building).

**ICT** = Information and Communication Technology is the infrastructure and components that enable modern computing. Among the goals of IC technologies, tools and systems is to improve the way humans create, process and share data or information with each other.

**SIA** = System Impact Analysis

**FCCA** = Factory Capability and Capacity Assessment. The purpose is to verify whether the production and production capacity of the plant meets the requirements.

**MDSW** = Medical Device Software

## emoji-timeline Glossaire

**DPI =** Dossier Patient Informatisé. (EPR – Electronic Patient Record or EHR – Electronic Health Record) Il a pour objectif d'améliorer la prise en charge des patients grâce au traitement numérique des informations en les rendant immédiatement accessible aux personnes et équipes concernées. Cela permet d'assurer la transversalité et la continuité des parcours de soins dans notre établissement et vers les autres.

**SBU** = Spécification des Besoins Utilisateur ou **CCU** = Cahier des Charges Utilisateur (URS). Garantir la compréhension des besoins, Faciliter la communication entre les parties prenantes, Servir de référence pour les étapes ultérieures.

**AIS** = Analyse d’impact Système ou AC = Analyse de Criticité (SIA)

**QC** = Qualification de Conception (DQ)

**AR** = Analyse de Risque (HLRA, DRA)

**PDV** = Plan Directeur de Validation (VMP)

**QI** = Qualification d’Installation (IQ). Vérification documentée que l’équipement considéré est conforme à la conception approuvée et aux recommandations du fabricant. L’objet de cette qualification est de fournir les preuves documentées sur la conformité de l’équipement aux exigences du client (cahier des charges)

**QO** = Qualification Opérationnelle (OQ). Vérification documentée selon laquelle l’équipement fonctionne conformément aux spécifications établies dans les plages de fonctionnement représentatives de l’utilisation de l’équipement. Cette qualification a pour but de vérifier les paramètres de fonctionnement, les sécurités et protections, le contrôle de la précision des mesures selon les normes en vigueur.

**QP** = Qualification de Performance (PQ). Vérification documentée que l’équipement / système, mis en œuvre à l’intérieur des paramètres établis, peut fonctionner de manière efficace et reproductible pour fabriquer un produit conforme à ses spécifications et à ses caractéristiques de qualité préétablies. Qualification en conditions réelles. Tests de charge, tests aux limites

CQTP =

QSR =

**TAU** = Tests d’Acceptation Usine (FAT). Cette étape est requise, en particulier si l’équipement intègre une technologie nouvelle ou complexe.

**TAS** = Tests d’Acceptation sur Site (SAT). Les essais de SAT sont ceux réalisés chez le client final.

**AMDEC** = Analyse des Modes de Défaillance, de leurs Effets, et de leur Criticité (FMECA

## emoji-timeline CSV dentro de “Directrices sobre Prácticas Correctas de Distribución de medicamentos para uso humano” (05/11/2013)

3.2. Locales

“…

Cualquier sistema que sustituya a la separación física, como la separación electrónica basada en un sistema informatizado, debe proporcionar una seguridad equivalente y estar validado.

…”

3.3.1. Sistemas informáticos

“Antes de utilizar un sistema informático debe demostrarse, con una validación adecuada o con estudios de verificación, que puede lograr los resultados deseados de forma precisa, coherente y reproducible.

Una descripción escrita detallada del sistema (con gráficos, si procede) debe estar disponible. Dicha descripción debe actualizarse. El documento debe describir los principios, los objetivos, las medidas de seguridad, el alcance del sistema y las características principales, cómo se utiliza el sistema informático y la forma en que se relaciona con otros sistemas.

Los datos solo deben ser introducidos o modificados en el sistema informático por personas autorizadas para ello.

Los datos deben estar protegidos por medios físicos o electrónicos, así como contra las modificaciones accidentales o no autorizadas. Debe comprobarse periódicamente la accesibilidad de los datos almacenados. Hay que hacer periódicamente copias de seguridad de los datos, que deben conservarse durante el plazo previsto en la legislación nacional y, en cualquier caso, un mínimo de cinco años en un lugar aparte y seguro.

Deben definirse los procedimientos que deben seguirse en caso de que se produzca un fallo o una avería en el sistema. También deben existir sistemas de recuperación de datos.”

CAPÍTULO 4: DOCUMENTACIÓN

4.1. Principio

Una buena documentación es una parte esencial del sistema de calidad. La documentación escrita debe evitar errores que procedan de la comunicación oral y permitir el rastreo de las operaciones pertinentes durante la distribución de los medicamentos.

4.2. Información general

La documentación comprende todos los procedimientos, instrucciones, contratos, registros y datos, por escrito, en papel o en formato electrónico. La documentación debe estar disponible y ser fácil de recuperar.

En lo que respecta al tratamiento de los datos personales de los trabajadores, de los denunciantes o de cualquier otra persona física, se aplica la Directiva 95/46/CE, relativa a la protección de las personas físicas ( 1 ), para el tratamiento de los datos personales y la libre circulación de estos datos.

La documentación debe ser lo suficientemente completa respecto al alcance de las actividades de distribución al por mayor y estar redactada en una lengua que entienda el personal. Debe estar redactada en un lenguaje claro e inequívoco y no debe contener errores.

Los procedimientos deben ser aprobados, firmados y fechados por la persona responsable. En caso necesario, la documentación deberá ser aprobada, fechada y firmada por las personas competentes autorizadas. No debe estar manuscrita; si bien, cuando sea necesario debe proporcionarse espacio suficiente para hacer anotaciones a mano.

Cualquier modificación de la documentación debe firmarse y fecharse; la modificación debe permitir que se lea la información original. Cuando proceda, deben registrarse los motivos de la modificación.

Los documentos deben conservarse durante el plazo previsto en la legislación nacional y, en cualquier caso, cinco años como mínimo. Los datos personales deben suprimirse o hacerse anónimos en cuanto su conservación deje de ser necesaria para las actividades de distribución.

Cada trabajador debe tener fácil acceso a toda la documentación necesaria para las tareas realizadas.

Debe prestarse atención a que se utilicen procedimientos válidos y aprobados. Los documentos no deben contener ambigüedades; el título, la naturaleza y la finalidad deben indicarse claramente. Los documentos deben revisarse periódicamente y actualizarse. El control de las versiones debe aplicarse a los procedimientos. Tras la revisión de un documento, debe existir un sistema que evite el uso involuntario de la versión antigua. Los procedimientos reemplazados u obsoletos deben eliminarse de las estaciones de trabajo y archivarse.

Deben llevarse registros, ya sea en forma de facturas de compra o de venta, albaranes, en forma informatizada o en cualquier otra forma, respecto a todas las transacciones de medicamentos recibidos, suministrados, o que hayan sido objeto de intermediación.

En los registros debe constar, como mínimo, la información siguiente: fecha; denominación del medicamento; cantidad recibida, suministrada u objeto de intermediación; nombre y dirección del proveedor, el cliente, el intermediario o el destinatario, según proceda; y número del lote, por lo menos para los medicamentos que lleven los dispositivos de seguridad ( 2 ).

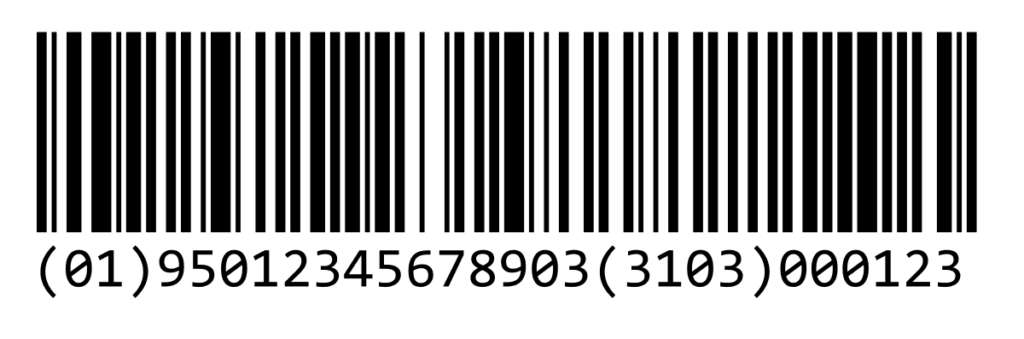
Los registros deben efectuarse en el momento en que se realiza cada operación.

# emoji-timeline Venta al por mayor, Logística

EAN 13



EAN 128



* Lote
* Código seriado de la unidad de envío
* Código de articulo/agrupación
* Fecha de caducidad
* Fecha de producción
* Fecha de envasado
* Fecha de consumo preferente

SEVeM: Sistema Español de Verificación de Medicamentos

CGCOF: Consejo General de Colegios Farmacéuticos

AEMPS: Agencia Española de Medicamentos y Productos Sanitarios

# Computerized Systems Examples



A diagram of a software system

Description automatically generated

Process Control Software

* PLC = Programmable Logic Controllers for Controlled Packaging Equipment
* SCADA = Supervisory Control and Data Acquisition
* DCS = Distributed Control System

CTOS (Commercial off-the-shelf) or SasS (Software as a service) Software

* **LIMS** = Laboratory Information Management System
* Clinical Trial Monitoring Systems
* CDS = Chromatography Data System
* **ERP** = Enterprise Resource Planning Systems
* MES = Manufacturing Execution System
* Batch Record System
* **BMS** = **(Building Management Systems):** Focuses on the overall management of the facility's mechanical, electrical, and environmental control systems to ensure a safe and efficient working environment.
* **EMS** = **(Environmental Monitoring System)**: Specifically targets the monitoring and control of environmental conditions in critical areas to ensure product quality and regulatory compliance.
* **WMS** = Warehouse Management System
* **SGA** = Sistema de Gestión de Almacenes
* Cloud base software services
* Spreadsheets

WMS = Warehouse Management System

Electronic records with electronic signatures

## Pharmaceutical ERP software

Pharmaceutical ERP software refers to any digital tool that manages enterprise resource planning (ERP) within a pharmaceutical business context.

Pharma ERP software provides an integrated and connected view of your key business processes and databases, such as your manufacturing capacity, finished drug lots and batches, raw materials, cash, purchase orders, payrolls and so on.

Pharmaceutical ERP software is a great way to keep track of your inventory, stock, active pharmaceutical ingredients (APIs) and packaging as it flows into and out of your business.

Examples:

**SAP Business ByDesign**,

**SAP S/4HANA** = 4th generation SAP Business Suite for High-performance ANalytic Appliance

**SAP Information Collaboration Hub (ICH)** = cloud-based solution that allows pharmaceutical partners to exchange serialization information in a secure and easy manner.

**Microsoft Navision** = Microsoft Navision is the old name for Dynamics NAV (which is now known as Dynamics 365 Business Central!), an ERP system that provides businesses with an end-to-end solution for connecting and managing all processes (such as sales, purchasing, accounting, plus general reporting).

**Medtracker** = data management software solution for pharma applications that enables users to comply with legal requirements for serialising products.

Oracle NetSuite

Infor CloudSuite

QAD Systems

## Interfaces

**Lobster Data** = Lobster\_data is an intuitively operated data integration platform. It simplifies the development and monitoring of interfaces as well as the onboarding of partners via EDI (Electronic Data Interchange).

## Supply Chain Management

## Warehouse Management System

Sistema para la gestión de almacenes (SGA)

## Workforce Management

## Pharmaceutical manufacturing software

Pharmaceutical manufacturing software is a broad category of software tools which support the manufacture of pharmaceutical product.

**Process Analytical Technology, or PAT**, is a crucial subset of pharma manufacturing software which makes both c(current)GMP and ICH Q8 quality by design easier to embed.

Since QbD works by the setting and measuring of critical quality and performance attributes connected to your product, PAT pharma manufacturing software helps you design, analyze and control your pharma manufacturing by measuring, tracking, trending and reporting on those attributes.

PAT pharma manufacturing software tools include real-time monitoring and analysis tools like imaging systems, spectroscopic platforms and chromatography.

Another pharmaceutical manufacturing software subset is the **Manufacturing Execution System, or MES.**

MES platforms form a kind of bridge between your pharmaceutical ERP software system, which operates at a high-level strategic resource focus, and something like a supervisory control and data acquisition (SCADA) platform, which supervises on a more tactical level how your machines and processes work and mesh in real time.

The MES, in short, tracks and monitors the flow of APIs through your manufacturing system into their finished dosage forms (FDFs). For this reason, it's a key example of software for pharma companies looking to optimize the quality and integrity of their outputted product.

By analysing and monitoring your manufacturing execution, MES pharmaceutical manufacturing software allows resource scheduling, equipment and product quality analysis, production and downtime measurements, and drug lifecycle tracking. Since MES platforms typically generate electronic manufacturing histories, they're particularly valuable for outputting electronic batch records - a crucial pharmaceutical cGMP requirement.

## emoji-timeline Computerized Systems

**Soluciones de Gestión Empresarial (ERP):**

**OSR**: Order Storage & Retrieval sistema de almacenamiento y distribución de productos semiautomático que se encarga diariamente de ordenar y movilizar más de 30.000 productos identificados por su referencia. Su disposición en diferentes niveles y su gran envergadura le aporta la apariencia de un gran almacén gestionado por un amplio abanico de “pequeños robots” que identifican y transportan cada uno de los productos.

**SDA**: sistema diseñado para seleccionar y desplazar rápidamente una gran cantidad de productos, pero a diferencia del OSR, este permite a los operarios añadirlos manualmente al sistema. Complementando el uso de ambos sistemas se cubren las necesidades específicas en función de la demanda o manejabilidad de cada uno de los productos.

**Reconocimiento por imágenes**: técnica que han desarrollado a medida en COFARTE usando tecnología Open Source para mantener el control y realizar un seguimiento exhaustivo, tanto de los productos mientras son transportados por toda la línea de almacenamiento, como de las cubetas una vez se organizan para su envío. Además, es de gran utilidad para comprobar el estado de las cubetas antes de hacer los envíos, de manera que, si algún lote no cumple con los estándares de calidad de envío, se gestiona de manera eficiente.

**Etiquetadora y Flejadora**: cumplen funciones más simples que las anteriores, no obstante, permiten garantizar que cada una de las partidas de productos sean identificadas y aseguradas correctamente antes de salir de los almacenes para ser enviados a su destino final. También cuentan con sistemas que comprueban automáticamente que tanto el etiquetado como el flejado se han completado con éxito.

Picking por radiofrecuencia:

## emoji-timeline Ejemplos en Canarias

Cofarca: ERP SAP HANA, Qlik (Business Intelligence – Inteligencia de Negocio), KNAPP (OSR, SDA Fast Mover Picking Machine, Radiofrecuencia)

Cofarte: ERP SAP, OSR, SDA, Unycop (gestión de farmacias)

(Cofares) – Peninsula: Farmavenix

Pedro Duque: <https://pedroduquecanarias.com/farma/>

Coalca SA: <http://www.coalca.com/>

Farmavenix: <https://www.farmavenix.es/calidad>

# What is meant by Computer System Validation?



By: Gerry Creaner B.Chem Eng and Donagh Fitzgerald B.Prod Eng. Last Updated: January 2024

https://www.getreskilled.com/what-is-computer-systems-validation-csv/

## What is Computer System Validation (CSV)?

Computer Systems Validation (CSV) – is a process used to test, validate and formally document that a regulated computer-based system does exactly what it is designed to do in a consistent and accurate manner that is secure, reliable and traceable.

These sectors use computer systems to operate and record a range of processes and activities from clinical trials, manufacturing, product testing, distribution, storage, logistics, etc so it’s critical that these systems can be relied upon to:

* produce data accurately and consistently
* create an indelible electronic data trail that is transparent, traceable and tamper-proof
* store those electronic data records in a way that is safe, secure and can stand the test of time

And that the standard operating procedures (SOPs) and processes are put in place to manage these systems.

In addition, the CSV process is used when replacing paper records and handwritten signatures with electronic data records and electronic signatures in highly regulated environments that impact public health and safety such as the pharmaceutical and medical device industries.

## Where is Computer System Validation Used?

Computer System Validation (CSV) is applied to GxP computerized system applications used at any point in the research, clinical testing, manufacturing, distribution and storage processes. Examples might include:

* Process Control Software
  + PLC for Controlled Packaging Equipment
  + Supervisory Control and Data Acquisition (SCADA)
  + Distributed Control System (DCS)
* Commercial off-the-shelf (CTOS) or Software as a service (SasS) Software
  + Laboratory Information Management System (LIMS)
  + Clinical Trial Monitoring Systems
  + Chromatography Data System (CDS)
  + Enterprise Resource Planning (ERP) Systems
  + Manufacturing Execution System (MES)
  + Batch Record System
  + Building Management Systems (BMS)
  + Cloud base software services
  + Spreadsheets

## Why Do We Need CSV?

The pharmaceutical and medical device industries are regulated, meaning that what goes on inside the factory walls is subject to the law of the land. We have to be confident that the computer system generates and stores data accurately and reliably and doesn’t do anything that could harm the patient. In addition, in the 90s, the regulatory authorities for these industries took the decision to replace paper records and handwritten signatures with electronic records.

CSV is a process that creates an indelible electronic data trail that allows us to treat the regulated data and electronic signatures captured in drug discovery, drug trials, manufacturing, distribution and storage as the legal equivalent of paper records and handwritten signatures and have the equivalent level of confidence in their accuracy, reliability and data integrity.

## What Are Examples of Computer System Validation Regulation?

The Food and Drug Administration (FDA) considers computer systems as equipment 21 CFR 211.68 and thus needs to be validated. It also provides detailed controls for electronic records and electronic signatures in the Code of Federal Regulations (CFR) under FDA 21 CFR 11. Part 11 mandates the requirements for electronic records and signatures to be accurate, reliable, readily retrievable, and secure and to be able to legally replace paper records and handwritten signatures. This code applies to (bio)pharmaceutical and medical device manufacturers, biotechnology companies and other FDA-regulated industries. Some examples of the controls required are:

1. Data should be stored in electronic format and can be archived. Electronic records should be as trustworthy as paper records.
2. The system must ensure that electronic signatures are as trustworthy and secure as handwritten signatures. Controls on electronic signatures should include:
   1. the name of the singing user
   2. the day/time the signature was executed
   3. and the meaning of the signature
3. Signed records cannot be altered by users. The system can determine when a record was created, altered, or deleted by a user of the system.
4. Password masking facility should be available in the system.
5. Password complexity should be required i.e. password should be of minimum character length, etc. Previous passwords can’t be re-used.
6. Screen lock should trigger after a defined period of time.
7. Only authorised people can use the system.
8. The system should have different access levels based on the criticality of the system.
9. The system must be able to generate an audit trail. i.e. every activity should be stored in the system such as who, when, what, etc should be captured.

For medical device makers, the FDA requires them to validate the software and systems used in manufacturing medical devices using 21 CFR 820.

Within the EU, EudraLex – Volume 4 – Good Manufacturing Practice (GMP) provides guidance on the validation of Computerised Systems under Annex 11: Computerised Systems.

The Pharmaceutical Inspection Co-Operation Scheme (PICs) provides guidance with its document on Good Practices for Computerised Systems in Regulated GxP Environments.

Computer System Validation is also required in ISO 13485 standard 2016 – For Medical Devices.

In late 2022, the FDA released a draft guidance document on Computer Software Assurance for Production and Software Systems. This document states that it is “Not for implementation. Contains non-binding recommendations” so it is unclear what impact it will have on the approach to software validation. So we have not referred to it throughout this post.

## What are GAMP Guidelines and How Do They Work Together With the Regulations?

Good Automated Manufacturing Practice (GAMP) is a set of guidelines and procedures that pharmaceutical manufacturers and users of automated systems use to validate the computer systems and achieve compliance with the above regulations such as FDA 21 CFR 11

Think of the controls outlined in FDA 21 CFR 11 as what the regulators want to see the computer system be able to do. Think of GAMP as the approach taken to achieve those controls.

GAMP has enjoyed the support of numerous regulatory authorities and is now a recognized good practice worldwide.

However, GAMP is not regulation. You don’t comply with GAMP

This is a widespread misconception, but GAMP is not a regulation or law that pharmaceutical and medical device companies are legally bound to comply with.

## How do you Validate a Computer System?

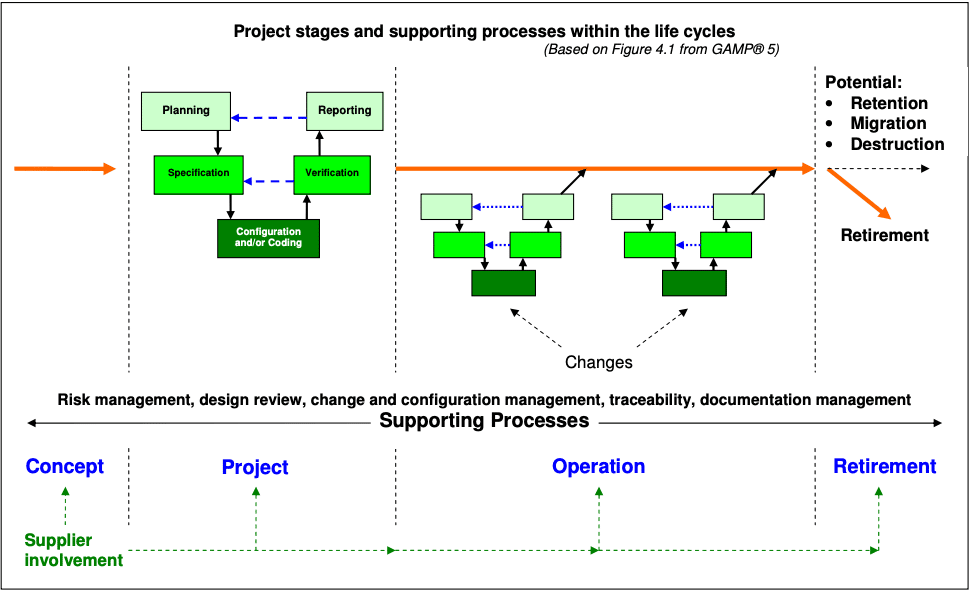
In the pharmaceutical and medical device sector, the most widely used method is to follow the GAMP® 5 guidelines and break the process down into its life cycle phases. According to GAMP, there are four life cycle phases in a computer system and each phase contains a number of individual activities. (See diagram below)

In order, these phases are:

1. **Concept** – a high-level overview of the system and design considerations
2. **Project** – detailed description of the system and objectives
3. **Operation** – how the system will be managed during operations
4. **Retirement** – how to retire the system

In addition, there are a lot of supporting processes or activities that take place across the phases of the life cycle such as risk management, document management, repair activity, security management, etc and you should include them when visualizing the CSV process. You will often use various suppliers across different phases of the lifecycle, and you should leverage their expertise as much as possible.

Process stages and supporting processes within the life cycle



Now, let’s take a look at the individual activities in each of the four phases as well as the relevant supporting processes of each phase viewed through the project life cycle.

### 1. Concept Phase

The concept phase is where the idea for a system is conceived. At this point, there is a general idea of what the system should do. This phase would include data gathering (i.e. vendors, costs, high-level project plan, resources, timelines, benefits, restrictions and justification of the requirement for the system). The first risk assessment should take place at this point and should ask questions such as, what are the risks to the business of implementing or not implementing this system? Where will further risk assessment be required?

This phase contains the following specific activities:

* Planning
* System Software Categorization
* Risk Assessment
* Supplier Assessment

#### 1.1 Planning

In this activity, you typically define the following:

* the overall requirements of the system
* the critical functions it will be controlling
* the available options for hardware and software platforms
* the overall regulatory impact of the proposed system
* the novelty of the system and its complexity
* the requirement for document control
* the testing that is required (what are the considerations for operating and maintaining the system?)
* what data and records will be generated that will subsequently need to be retained

#### 1.2 System Software Categorization

The range of activities required to validate a computerized system varies greatly depending on the type of software you are using.

The GAMP 5 guidelines now categorize software into 4 types. The category your software falls into will determine the validation approach, the amount of time the project takes and the deliverables.

The 4 categories are 1, 3, 4 and 5 (note: Category 2 was discontinued):

##### Software Category 1 – Infrastructure software

This is software that applications are built on and used to manage the operating environment.

Examples: Operating Systems (Windows, Mac OS, Android, Linux etc), Database engines, Middleware, Programming languages, Statistical packages, Network monitoring tools, Scheduling tools, Version control tools

##### Software Category-3 – Non-Configured Software

Software in this category allows parameters to be entered and stored in the system, but the software cannot be configured to suit the business process.

Examples: Setting the time (i.e. entering a parameter) on the alarm on your smartphone, Firmware-based applications, Configured Off-The-Shelf (COTS) software, Instruments (i.e. for measuring temperature, pressure, flow volume).

##### Software Category-4 – Configured Software

This software is often very complex. It can be configured by the user to meet the specific needs of their business process but the software code itself is not altered. Much of the software you come across in the Pharma/Medtech sector is category-4

Examples: Laboratory Information Management System (LIMS), Enterprise Resource Planning (ERP), Clinical Trial Monitoring, Distributed Control System (DCS), Chromatography Data System (CDS), Building Management Systems (BMS), Spreadsheets

##### Software Category-5 – Custom Software

This software is custom designed and coded to suit the specific business process.

Examples Internally and externally developed IT applications, Internally and externally developed process control applications, Custom firmware, Spreadsheets (macro)

#### 1.3 Risk Assessment

Think of a risk assessment as a way of visualising catastrophe before it happens (by trying to think up of as many failure modes as possible) and coming up with methods to mitigate those risks. A quality risk assessment is carried out to determine if the computer system has the potential to impact product quality, patient safety or data integrity in a way that could ultimately harm the patient.

#### 1.4 Supplier Assessment

Part of the concept phase will also be narrowing down the vendor options and getting an idea of the cost to include in the business case. This typically involves sending out a Request for Services document with some general details of system requirements to several vendors. The response from the vendors will detail how their system can meet those requirements, alongside an estimated cost. Where the response looks promising a request for a demonstration of the system will be made before an in-depth supplier assessment is carried out.

### 2. Project Phase

In this phase you finalise the planning; develop the user requirement specifications, functional specifications and design specifications; have the project built; and have it commissioned and qualified. Finally, you hand over the completed project to the end-user or client.

Specific activities in this phase include:

2.1 Planning

2.2 Using the CSV Process V model

2.3 Risk assessment

2.4 Writing Standard Operating Procedures

2.5 Training

2.6 Handover

#### 2.1 Planning

This stage defines what will be validated and what approach you will use. It also defines individual roles and responsibilities, and the acceptance criteria. It is typically completed by the end-user or client. The planning step of the project phase will contain activities that may overlap with the concept phase – there is not always a sharp delineation between the tasks of both phases.

Documentation completed within this stage includes:

##### 2.1.1 Validation Master Plan (VMP)

Every regulated pharma organisation should have a validation master plan in place to govern its approach to validation. A subsection of this is “computerized system quality and compliance”. Depending on the size of an organisation there may be several sub validation plans within the validation master plan (e.g. site, departmental or system-specific) or there may be multiple validation master plans, one for each business unit.

##### 2.1.2 System Overview

In order to satisfy the regulatory inspectors, you need to give a brief description of the system

It’s best to take a top-down approach and start with its operating environment. This would include other networked or standalone computerised systems, other systems, media (how you store your electronic records), people, equipment and procedures.

In addition, you need to describe:

* Hardware /Firmware
* Software
* Computer System (Controlling System)
* Operating procedures and people
* Data managed by the system
* Equipment controlling function or process

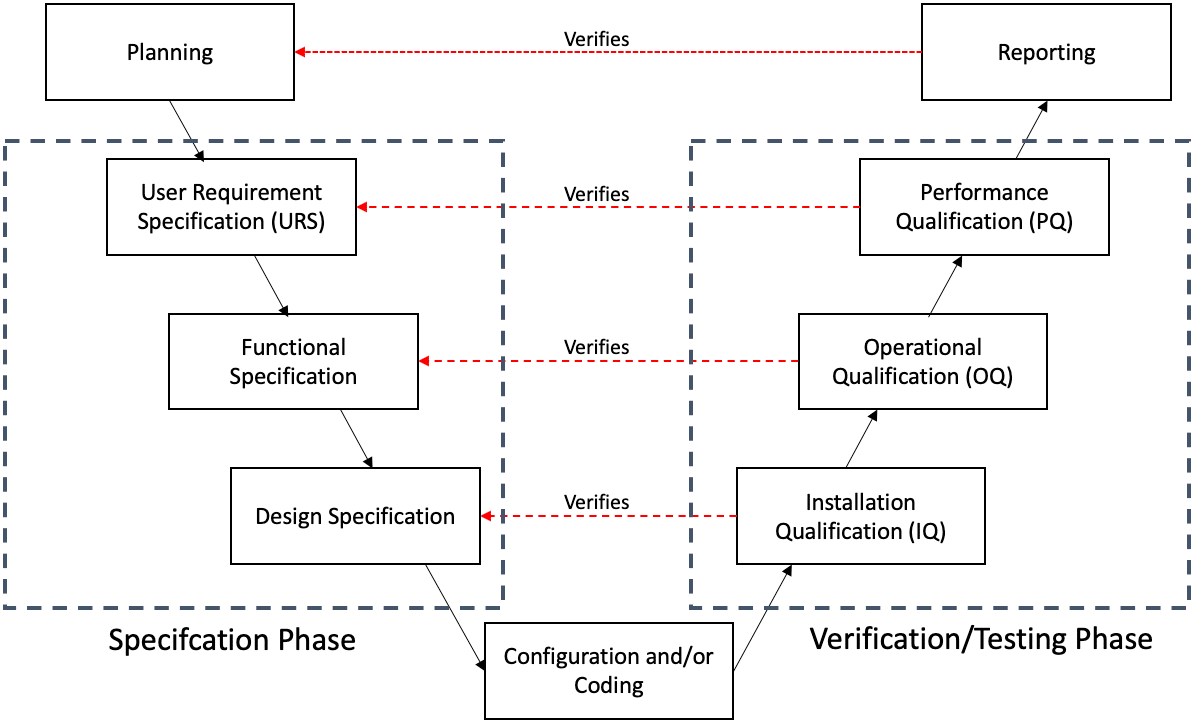
During this phase, you take the V-model approach (see diagram below) to determine the specifications and the verification and testing deliverables.

#### 2.2 Computer System Validation Process V-Model

In pharmaceutical manufacturing, most companies and organisations follow the Good Automated Manufacturing Practice (GAMP®5) V-Model to validate their systems as it meets the requirements of the industry regulators. The model is used to visualize the relationship between user requirements and specifications, and the verification and testing performed on them (see diagram below).

You start at the top left (planning), proceed down (through to configure and/or coding), and then back up to the right, ending at (reporting). The left-hand side of the V represents what the computer system does (i.e. what you use the software for), along with how the computer system works. The right-hand side of the V represents how you test the system to confirm that the system is fit-for-purpose (i.e. will make safe medicines for patients).

Computer System Validation Process V-Model



##### 2.2.1 User Requirements Specification (URS)

The user requirements specification maps out what the user needs from the software and how they will use it. It also contains any constraints such as regulations, safety requirements or operational requirements. The specifications must be agreed between the end-user/customer and supplier. The URS will have input from the process owners, system owners, technical subject matter experts (SMEs), quality and the supplier where required.

##### 2.2.2 Functional Specification (FS)

The functional specification contains a detailed description of how the system will meet each of the requirements outlined in the URS such as:

* how the software works
* what data needs to be captured
* user interfaces

##### 2.2.3 Design Specification (DS)

The design specification describes in detail how each function is to be designed or configured. It is a more technical follow-on document from the functional specification and may contain configuration specifications or code – its intended audience is the system developer.

##### 2.2.4 Configuration and/or Coding

In this step you build, develop or purchase the software (depending on the software category) and then configure it to meet the criteria laid out in the previous specification documents. This is typically completed by the vendor.

##### 2.2.5 Installation Qualification (IQ)

Installation qualification (also referred to as “configuration or integration testing”) confirms that the software or system is installed and set up according to the design specification.

##### 2.2.6 Operational Qualification (OQ)

Operational qualification (also referred to as “functional testing”) confirms that all functionality defined in the functional specification is present and working correctly. In the case of bespoke software, it confirms that there are no software bugs.

##### 2.2.7 Performance Qualification (PQ)

Performance qualification (also referred to as “user requirement testing”) confirms that the software will meet the user’s needs and is suitable for their intended use, as defined in the user requirements specification.

##### 2.2.8 Final Report

The last step in this validation method is to write the summary report declaring that the system is fit for its intended use and that every deliverable that was planned has been delivered.

In the V-model, you’ll notice a link between the two sides of the V. For example, the reporting stage verifies the planning stage, the performance qualification stage verifies the user requirement specification stage and ensures that the specifications have been achieved.

#### 2.3 Risk Assessment

Risk assessment may be utilised at various stages of the validation lifecycle. Within the project phase, the risk assessment will review the same document at each stage of the V model to ensure the risk classification and controls are accounted for in the validation actions that are carried out.

#### 2.4 Standard Operating Procedures

Standard Operating Procedures (SOPs) are a key part of CSV documentation. They outline how the computer system should be used. Any staff using a particular system will be thoroughly trained on the relevant SOPs to ensure they are using the system correctly; in the way it was intended.

#### 2.5 Training

You need to train key users of the system on how to use the system software, applications, and procedures.

#### 2.6 Handover

You need to write a handover plan to define when the application will move into the operation phase and how any disruption will be managed, making sure that the system can be used and supported in a controlled manner.

The handover process must verify the following:

1. The system is fit for purpose.
2. Roles and responsibilities are defined e.g. process owner/s, system owner.
3. All personnel are appropriately trained e.g. standard user, system admin.
4. Operational and support procedures/personnel are in place.
5. Supporting quality controls and personnel are in place to maintain compliance.
6. Any residual risks have been accepted.

### 3. Operation Phase

The following processes must be in place before the system goes live, and be observed throughout operation:

3.01 Change Management

3.02 Configuration Management

3.03 Patch and Update Management

3.04 Security Management

3.05 Business Continuity Management

3.06 Disaster Recovery Planning

3.07 Service Level Agreement

3.08 Backup and Restore

3.09 Incident Management

3.10 Periodic Review

3.11 On-Going Projects

3.12 Electronic Data Archiving

3.13 Documented Control

#### 3.01 Change Management

You must implement procedures and processes to document, evaluate and approve any changes to the system once it’s live.

#### 3.02 Configuration Management

You must identify and document the functional and physical attributes of the system and controls on their status e.g. live, retired, under amendment.

#### 3.03 Patch and Update Management

Similar to Microsoft Windows or Apple OS, you may need to install updates on the system on both a regular and ad-hoc basis. This will be done on the advice of the supplier but the customer will be included in the planning.

#### 3.04 Security Management

You need to define the controls required for securing a computerized system in its operational environment. This typically involves authentication controls and access levels controls so the system data can’t be tampered with . In addition, you must provide technical security (such as antivirus software) and a company firewall to protect against spyware and malware.

#### 3.05 Business Continuity Management

You need to develop a detailed plan to regain access to the system and its data following a disaster such as a power outage, fire damage, water damage or a virus attack. The plan must outline how you will restore critical business processes following a disruption while continuing to provide products or services.

#### 3.06 Disaster Recovery Planning

This is a subset of Business Continuity Management (BCM). It contains the steps to follow to regain access to the hardware, software and data following a disastrous event

#### 3.07 Service Level Agreement

This is an agreement with both the system supplier and a data centre provider for escalation of issues that includes agreed response and resolution times depending on the issues categorisation.

#### 3.08 Backup and Restore

Backup and restore is a mechanism to protect electronic information and records against loss of original data. Copies of the system configuration and data are made on a regular basis (e.g. daily) so that it is retrievable in the event of a disaster. To do this, you must copy the software, data and electronic records to a separate, safe and secure area where it is available and protected so you will be able to restore it in its original format if required.

#### 3.09 Incident Management

This will involve recording issues encountered by the system. End users will be able to raise these issues using an electronic IT helpdesk system.

#### 3.10 Periodic Review

You need to conduct periodic reviews to ensure a computerized system remains compliant with regulatory requirements throughout its operational life, remains fit for intended use, and continually satisfies company policies and procedures. For example, the validation team (in conjunction with relevant stakeholders) might conduct a periodic review every 2 years.

#### 3.11 On-Going Projects

In the operation phase of the life cycle, you might discover that certain aspects of the system need to be updated or changed. For example, the user interface might be causing problems with users not being able to input data accurately. Or you might want to expand the reach of the system or update and improve its processes. You would manage these changes like mini-projects using the V-model approach (as outlined above).

#### 3.12 Electronic Data Archiving

You need to develop a suitable data archiving strategy that moves data that is no longer actively used in the environment it was created, to a separate data storage area for long-term retention. You would also complete data archiving in the retirement phase of the validation life cycle.

#### 3.13 Documented Control

The computer system is now in operation. You must keep all aspects of the system and the operating environment in a state of documented control to maintain its validated status.

### 4. Retirement Phase

In the retirement phase, the system might be shut down completely or upgraded to a new system. Either way, you need to assess what data needs to be migrated from the existing computerised system, what data needs to be retained and what data needs to be destroyed.

Specific activities in this phase include:

4.1 Data Migration

4.2 Electronic Data Archiving

4.3 Data Destruction

#### 4.1 Data Migration

Data migration involves moving data from one platform to another. To do this you need to create a data migration plan. The following considerations should be taken into account:

1. That all required data has been moved.
2. The context of the data, its attributes and metadata have been preserved.
3. Any requested transformation has yielded the expected result.
4. No unexpected transformation has been introduced.

Similarly to implementation, you need to take a risk-based approach to migration. You need to perform a data flow analysis exercise to identify points of weakness in the transition from the old to the new system. And you’ll need to provide documented evidence of these actions.

#### 4.2 Electronic Data Archiving

Data archiving is the process of moving data that is no longer actively used to a separate data storage device for long-term retention. You need to develop a suitable data archiving strategy for moving data in this way The considerations for data archiving are essentially the same as for data migration, as you are moving data from one platform to another. The archiving platform may be the same as the live system but with slower and less costly storage for data that is still required to be readily available for trending or updating.

#### 4.3 Data Destruction

Where data is no longer required you may completely remove it from the live system, the archiving solution and any back-ups. You must ensure that the method of destruction completely removes all the data, particularly where it pertains to personal data governed by data integrity regulations (e.g. overwriting or destroying hard disks, shredding or burning rendered off paper records).

## Supporting Processes

Finally, let’s take a look at the supporting processes or activities that take place across different phases of the life cycle such as risk management, document management, repair activity and traceability matrix.

Specific activities in this phase include:

1. Risk Management

2. Traceability Matrix

3. Repair Activity

4. Document Management

### 1. Risk Management

You need to apply risk management throughout the lifecycle of a computerized system and decide how to manage the process for various categories of systems. You should also look at an approach to conducting risk assessments on computerized systems based on their impact on product quality, patient safety and data integrity.

### 2. Traceability Matrix

You need to develop a traceability matrix – this is an important project document for tracing all user requirements to design specifications and appropriate verification tests.

### 3. Repair Activity

You need to develop a process by which non-functional systems (i.e. systems which have stopped working) are returned to a functional state under the control of a repair activity procedure.

### 4. Document Management

The documentation associated with CSV is extremely detailed. Someone reading through it should be able to repeat the process simply by following the steps outlined in the document. As a result, the language used must be clear and concise.

Before any computer system is used, documents will outline specifics such as:

* Defining the purpose of the computer system in question
* The features it needs
* The hardware it needs
* When it will be used
* The requirements that it is expected to meet

The specifications defined here will then be used throughout the CSV process – continuing throughout the life of the computer system.

In addition to this, the system will continue to be tested throughout its lifecycle. Rigorous routine testing will be used to show that the system continues to meet the predefined requirements that were laid out in the design phase.

All CSV documentation can be called for review and audit at any point of the system life cycle. It would be expected that the documentation meets appropriate standards at all points.

Even after a company has stopped using a particular computer system, you will need to keep the documentation showing that it was correctly validated while in use in the event that the regulatory authorities need to retrospectively check the data integrity of a past event.

Final Summary

As you can see, the computer system validation process is time-consuming and expensive but necessary in order to keep data quality safe, accurate and secure.

## The Growth of Computer System Validation Opportunities

As manufacturing processes become increasingly automated, the need for CSV professionals is growing. This trend is only expected to continue.

There is also an acute shortage of trained CSV professionals in certain geographic areas, including Ireland. For this reason, salaries for these roles are extremely competitive.

One of the single biggest misconceptions of the CSV role is that you need to be able to code. This is usually not the case. However, we do sometimes see a requirement for the ability to code in some roles where the job description overlaps with automation engineering. And you will always need a solid understanding of the computer process you will be validating.

If you have the relevant skills, as well as the experience of pharmaceutical or medical device manufacturing, you might be closer than you think to be a great candidate for CSV rolls within pharmaceutical companies.

# ALCOA++ principles



A number of attributes are considered of universal importance to data. These include that the data are:

## Attributable

Data should be attributable to the person and/or system generating the data.

Based on the criticality of the data, it should also be traceable to the system/device, in which the data were generated/captured. The information about originator (e.g. system operator, data originator) and system (e.g. device, process) should be kept as part of the metadata.

The system should assign a unique identifier to the user, allowing actions to be unambiguously linked to the user and the action date. This implies:

* The system should implement timestamping for data
* Each user should have a unique login consisting of a user id and a password
* Password management policies should be in place, including the creation of complex password and regular password updates
* The system should have an automatic logout function to disconnect user after a period of inactivity. (time-out)
* An effective audit trail should be maintained by the system.

## Legible

Data should be maintained in a readable form to allow review in its original context.

Therefore, changes to data, such as compression, encryption and coding should be completely reversible.

To ensure that data always remains readable, even years later, it is necessary to:

* Ensure that data backups include both the data itself and its metadata.
* Preserve the combination of software version, operating system, and hardware tobe able to restore the data in its original context.
* Conduct regular Backup and Restore tests.
* Perform data migration, if necessary, during software or operating system updates and/or changes

## Contemporaneous

Data should be generated by a system or captured by a person at the time of the observation.

The time point of the observation and the time point of the storage should be kept as part of the metadata, including the audit trail. Accurate date and time information should be automatically captured and should be linked and set by an external standard.

* The data should be saved immediately in the computerized system
* Temporary, unsaved storage should be minimized
* Timestamp management should be strict and immutable (users should not be able to modify the timestamp, it should be synchronized with an official time server)
* Backups should be frequent

## Original

Data should be the original first generation/capture of the observation.

Certified copies can replace original data. Information that is originally captured in a dynamic state should remain available in that state.

* The computerised system used should be validated
* Data generation, data capture and data management processes must be described in a Standard Operating Procedure
* Access control and permissions must be defined (appropriate access permissions should be assigned to users to limit unauthorized editing or deletion of electronic data. Only authorized personnel should be able to create or modify data).
* Data backups should be performed securely (Regular and secure backup mechanisms should be implemented to prevent data loss. Backups should be verified and stored in secure locations)

## Accurate

The use of computerised systems should ensure that the data are at least as accurate as those recorded on paper.

The coding process, which consists in matching text or data collected on the data acquisition tools to terms in a standard dictionary, thesaurus, or tables (e.g. units, scales), should be controlled. The process of data transfer between systems should be validated to ensure the data remain accurate.

Data should be an accurate representation of the observations made. Metadata should contain information to describe the observations and, where appropriate, it could also contain information to confirm its accuracy.

* During the equipment qualification phase, the accuracy must be verified for:
  + The data mentioned in reports/tickets
  + The calculations performed by the system
  + The graphs
  + The data recorded in the audit trail
* Data transfer between two computer systems should be validated
* The measuring instruments should have undergone proper metrological verification
* The audit trail should be regularly verified

## Complete

To reconstruct and fully understand an event, data should be a complete representation of the observation made.

This includes the associated metadata and audit trail and may require preserving the original context.

* Ensure that data includes the numeric value, the unit of measure, the experimental conditions, the sample ID, the user ID, the device ID, and any other necessary details.

## Consistent

Processes should be in place to ensure consistency of the definition, generation/capturing and management (including migration) of data throughout the data life cycle. Processes should be implemented to detect and/or avoid contradictions, e.g. by the use of standardisation, data validation and appropriate training.

* During the computerised system validation:
  + Verify the detection of out-of-range values
  + Verify that the system calculations are consistent and conform to the specified rules and formulas
  + Verify the consistency of the reports and data exports generated by the system. This should include tests to check if the data is correctly extracted, sorted, filtered, and aggregated according to the specifications
* Data should be representative of the actions performed. The timestamp provided by electronic systems should correspond to a common internal reference (e.g. PC times synchronized with the time server)
* Ensure data migration during the installation of a new software version.

## Enduring

Data should be maintained appropriately such that they remain intact and durable through the entire data life cycle, as appropriate, according to regulatory retention requirements.

* Define the electronic data to be archived and specify the retention period.
* Data protection: Electronic data should be protected against loss, corruption, or unauthorised access. This implies implementing regular backups, robust security system and access management policies.
* Manage the backup and archiving of electronic data (data and metadata, versions of the software, hardware, and/or operating system).
* Accessibility and Recovery: Electronic data must be organised and archived to allow efficient search and retrieval. This can include indexing, using appropriate metadata, implementing electronic archive management systems, conducting data restore and migrating tests.

## Available when needed

Data should be stored throughout the data life cycle and should be readily available for review when needed.

* Data backup and restore testing

## Traceable

Data should be traceable throughout the data life cycle. Any changes to the data, to the context/metadata should be traceable, should not obscure the original information and should be explained, if necessary. Changes should be documented as part of the metadata (e.g. audit trail).

* Identify and record all the important steps of the data lifecycle: creation, saving, updates, archiving and destruction. This should include all the specific tools of a digital environment: metadata, audit trails, electronic signatures, timestamps, and access controls.
* Tracking changes: Each change must be logged in the audit trail, including the user ID, the data value before and after the change, and a comment about the cause of the change