

Computer system validation

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Computer System Validation (CSV) establishes documented evidence which provides a high degree of assurance that systems are operating properly and can maintain data integrity. Although organizations may know that CSV is a regulatory requirement and that it makes good business sense to perform CSV, it can be a process that is neglected or started later than appropriate. As with any project, the hardest part is getting started. This article will provide some helpful hints in overcoming the inertia of CSV projects after describing the deliverables of the CSV process.

The Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-Operation Scheme (jointly referred to as PIC/S) are two international instruments between countries and pharmaceutical inspection authorities that lead the international development, implementation, and maintenance of harmonized Good Manufacturing Practices (GMPs). Currently, this is performed by 27 Participating Authorities by developing and promoting harmonized GMP standards and guidance documents. PIC/S released *Good Practices for Computerised Systems in Regulated "GXP" Environments* on 1 July 2004. This document provides a logical explanation of the basic requirements for the implementation, validation, and operation of computerized systems.

The Food and Drug Administration's (FDA) *Current Good Manufacturing Practices for Finished Pharmaceuticals* (21 CFR 211), *Good Laboratory Practice for Nonclinical Laboratory Studies* (21 CFR 58), and *Quality System Regulation* (21 CFR 820) require validation of computerized systems.

The existence of a well-defined CSV process is critical to the success of any CSV effort.

CSV Process

The process performed may be tailored based upon the size, the scope, the complexity, and the use of the system. The following is a list of activities that may be included in that process.

Risk Management

The first step in the CSV process is to perform and document a risk assessment. The objective of the

- ★ Regulatory authorities require computer system validation (CSV)
- ★ This article describes the deliverables of a well-defined CSV process and provides insight into making CSV a manageable set of activities

assessment is to evaluate potential hazards in the software and to identify potential risks to the success of the project. The August 2003 *Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application* stresses the importance of having a "justified and documented risk assessment and a determination of potential harm of the system on product quality and safety and record integrity." The PIC/S guidance document also stresses the importance of a documented risk assessment. When conducting a risk assessment, consider the following: the criticality of the software being validated, and the type of software (for example, off-the-shelf, configurable, or custom). In order to manage the risks identified during the initial assessment, the risk assessment document is a living document that will be revisited and revised throughout the CSV process.

Validation Plan

The Validation Plan is a document that describes all of the activities that will be performed during the CSV effort. It is the roadmap for the project. It identifies the activities, the output for each activity, and the organization or department responsible for performing the activity. The complexity of the software and the risks identified during the risk assessment should be considered when determining the CSV activities, tasks, and deliverables.

Requirements Specification

An important deliverable of the CSV effort is documented software requirements. These define "what" the system is supposed to do. Typical software requirements specify the software system inputs and outputs, a description of the system's functions, the performance requirements, and the application interfaces. The *General Principles of Software Validation; Final Guidance for Industry and FDA Staff* dated 11 January 2002 reinforces the importance of the Requirements Specification by stating that "It is not possible to validate software without predetermined and documented software requirements."

Design Specification

The Design Specification documents "how" a system is built. It typically includes development procedures and coding guidelines (or other programming procedures), system or component structure, algorithms, control logic, data structures, data flow diagrams, input/output formats, interface descriptions, communication links, and security measures.

Development Documentation

A defined lifecycle or methodology should exist to guide development efforts. A properly executed methodology will provide documented evidence that the system was built right, i.e., according to good engineering and design practices. This evidence should be part of the CSV documentation. The development documentation may include evidence of reviews and testing.

- ★ Design reviews are independent examinations of existing or proposed design elements for the purpose of detection and correction of deficiencies in the design. Code reviews are verification that the coding guidelines have been followed and that the design has been appropriately implemented. These static analyses provide an effective means to detect errors before execution of the code.
- ★ Developer testing includes unit, integration, and system level testing. Unit testing, often referred to as "white box" or structural testing, is based on a detailed knowledge of the source code and the design specifications. It challenges the control decisions within the program and the program's data structures including configuration tables. Integration testing evaluates the interfaces between two or more units. System testing is a more formal and rigorous testing performed under normal and stress conditions to verify that all components of the system work independently and as a whole. System testing documentation usually consists of a System Test Plan, system test cases (typically in the form of test scripts), test results, anomaly tracking, and a System Test Summary Report.

Clearly, the organization that performed the software development must complete the Design Specification and the Development Documentation. When using vendor-supplied software, it will not always be possible to obtain the Design Specification or the Development Documentation. In this instance, consider an audit of the software vendor as one of the CSV activities. The vendor

audit is completed to determine the adequacy of the vendor's processes and documentation.

Part 11 Assessment

In FDA-regulated industries, a Part 11 Assessment is a documented evaluation of the system's compliance with 21 CFR Part 11. In the event that gaps are identified, a Remediation Plan should be written to address controls that will be implemented to bring the system into compliance.

Installation Qualification

The Installation Qualification confirms that each component of the system has been installed according to the manufacturer's instructions. A document should exist that describes the step-by-step process for performing the installation as well as a mechanism to verify that it was done correctly.

User Documentation

User manuals and training materials for the system should be developed and/or evaluated for appropriateness. It is also necessary to document the training of the user community.

User Acceptance Testing

User Acceptance Testing (UAT) confirms that the system meets the user's business needs. UAT documentation usually consists of a UAT Plan, test cases (typically in the form of test scripts), test results, anomaly tracking, and a UAT Summary Report.

Procedures

The procedures describing the use and ongoing support of the system should be prepared. Typical procedures are those that define User and Administrator Training, Use of the System, Physical and Logical Security, User Account Creation and Maintenance, System Maintenance, Version Numbering, Configuration Management, Error and Incident Reporting, Change Control, Equipment Maintenance, Backup and Restore, Disaster Recovery, Data Archiving and Record Retention, Periodic System Evaluation and Revalidation, and System Retirement.

Traceability Analysis

The Traceability Matrix traces each requirement through design, implementation in the code, and evaluation during testing.

Validation Summary Report

The Validation Summary Report provides a recap of all of the CSV activities and results, any deviations

from the original Validation Plan (such as eliminated activities or activities that were identified and added during the CSV process), conclusions regarding the validation effort, recommendations for use, and approval for release of the system for production use.

Overcoming the inertia

CSV projects often seem overwhelming. In order to appropriately scale the effort, some organizations define a procedure that specifies what validation activities are required based upon the size of the system, the type of software, and the intended use of it.

Document templates for each CSV deliverable can also be a tremendous help in getting a particular validation document started since it is much easier to add information to an existing template than to start with a blank page.

Completing these efforts, in many cases, is not someone's full-time job. By dividing up the activities into manageable units of work and assigning the responsibilities to different members of the team, the CSV effort seems easier to accomplish.

The information obtained from the initial risk assessment helps to identify where the CSV activities and resources should be focused. It will also provide input into the selection of the CSV team. The CSV team typically consists of individuals from the following areas:

- ★ Information Systems (IS) who are often responsible for the infrastructure activities,
- ★ Regulatory/Quality Assurance who are often responsible for verifying the CSV effort and the system is in compliance with both internal company requirements as well as applicable regulations,

- ★ Users who are responsible for verifying the system meets the business needs, and
- ★ Management who are responsible for providing the necessary resources to complete the CSV project.

An organization may decide that some of the activities can be outsourced. External resources may accomplish many of the CSV activities, but the organization should participate in a review of the deliverables to verify compliance to the organization's standards. The organization is ultimately responsible for the validation effort and therefore must be intimately familiar with it.

It is useful to assign a team leader to manage the CSV activities. The team leader documents all decisions regarding CSV activities and resources in the validation plan. As stated previously, this document is the roadmap for the project which identifies the activities, the output for each activity, and the organization or department responsible for performing the activity.

Conclusion

In conclusion, CSV is an international regulatory requirement. The CSV effort may be a daunting task, but by performing a risk assessment to target the CSV effort at the areas of the system providing the greatest risk and by following a well-defined CSV process, the effort can be broken into small, manageable activities. The team leader can effectively manage the completion of all required activities to ensure that the system consistently performs as it is intended to perform.

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