Validation Exercise for a Vial Secondary Serialization Packaging Line Upgraded

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Abstract

Serialization has been the focus during the past years due to the new worldwide regulation related to the track and trace of pharmaceutical products. Companies dedicated all their efforts incorporating new technology to their actual packaging lines. Some has to update their serialization systems versions to improve their process. For this update a complete validation strategy and exercise was developed: from Commissioning and Qualification to Packaging Line Integration. Ten (10) protocols were executed, documents were updated and reports were generated to assure the system was satisfactorily upgraded. From 202 steps executed, 73.80 % passed right and 53 steps failed generating discrepancies and re-test exercises related to protocol errors, error in reference documents and equipment failures. It was concluded that main offenders were Lack of Information, Human Error, Wrong Information found on Vendor's documents and Configuration errors. A closing meeting was held to identify lessons learned and improvement's opportunities for upcoming packaging line upgrades.

Introduction

For many years, the manufacture of products has faced serious problems of counterfeit, adulteration and misbranded that results in damages to both consumers and manufacturers.

- "The World Health Organization (WHO) estimates that as much as 30% of the medicines sold in parts of Asia, Africa, and Latin America are counterfeit. In 2011, 64% of antimalarial drugs in Nigeria were found to be counterfeit. Worldwide, an estimated 10% of all medicines are counterfeit."
- "The problem of counterfeit drugs and drug adulteration has been a worldwide issue for decades. An estimated 80 percent of counterfeit drugs come from overseas with most of them manufactured in India and China."

One of the areas that has boomed in these days is the interest of "track and trace" those products that are directly used at health level like controlled drugs, over-the-counter (OTC) medicines and medical device products. The goal of develop regulations focus on the most vulnerable points at the supply chain. Countries like China, Brazil, Turkey and United States have developed its own laws and regulations.

Serialization: the solution

Serialization has been adopted with the purpose of controlling and reducing the vulnerability of counterfeiting by assigning a unique number to each product and monitoring its passage through the supply chain until it reaches the end user. Identification of the product begins with the most single unit that can be marked (e.g. each unit in a blister, a bottle with tablets, a syringe, a vial) and ends with the identification of the highest packaging level: the pallet as shown in Figure 1. Some of the information required for serialized products includes date, batch number, human readable markings, number of containers per transaction, among other details.

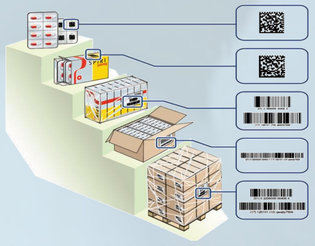

Figure 1 - Relationship between packaging stages and it unique identification

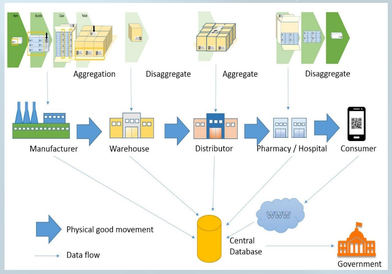

Figure 2 – Example of a serialized product movement through the Supply Chain units

Finally, individual units are separated back and its distribution is monitored until it arrives to the consumer. Figure 2 shows how units moves in the supply chain. All information regarding the creation and movement is collected in a central database. This exercise requires a complete commitment from all the units.

Serialization in the United States

In the United States of America, the Drug Quality Security Act (DQSA) was established to meet the worldwide track and trace requirement. Title II known as the Drug Supply Chain Security Act (DSCSA) contains in its Part 582 the requirements for the identification and tracking of the products. The law requires pharmaceutical industries to establish electronic tracking systems for their products. The regulation came effective on January 2015 and by November 2023 the system must be fully operative. The database created will allow the Food and Drug Administration (FDA) to determine the legitimacy of a product in the market.

Methodology

This project will focus in the development and execution of the validation upgrade for upgrade for an existing packaging line that will be converted in a serialized packaging line at a biopharmaceutical industry in Puerto Rico. This exercise was defined by management as a full Computer System Validation (CSV). Each of the elements that compose the Systech Vision Systems, Advisor, Sentri and others packaging equipment will be validated independently. After their validation, an integration exercise will take place at packaging line to assure there is no impact in their production activities. Figure 3 shows the traditional model used during software validation.

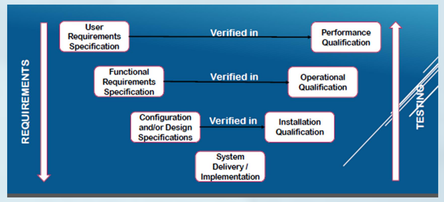

Figure 3 - Validation V-model for software.

Table 1 – Example of Some Validation Test Cases

Test	Justification
Test Equipment Calibration / Certification Review	Record calibration/certification information.
Alarms and Interlocks Verification	Verify that alarms/interlocks are triggered by the corresponding conditions
Source Code Review	Verify that the equipment Source Code of the PLC is clear, correctly and no dead codes are present
Control Panel Verification	Verify that the control panel devices operate as per manufacturer specifications
System Security Verification	Assure that the software security is adequate to avoid unauthorized access
Screen Navigation Verification	Assure each of the screens available from the equipment are configured, operates and displays the functions as required
Boundary Conditions Verification	Verify that the parameter values within the specified boundary conditions are accepted and those outside are denied
Backup and Restore Verification	Document that a procedure or steps for the back-up and restore of the program used in the equipment and PLC's is available, complete and secure
Input/Output (I/O) Verification	Verify that equipment input and output devices (e.g. sensors, switches) are properly hardwired to the PLC I/O Cards and addresses were configured as per requirements
Setup Parameters Verification	Verify that the setup parameters for each presentation are documented and classified as critical or guide.
Efficiency Test Run	Verify that the equipment is capable of continuously and repeatable processing products, counts and bottles at the specified production rates and efficiencies
Communication Test Failure Verification	Verify if the different components of the control system can register a communication loss with peripherals
Power Failure Verification	Verify that the equipment does not lose any relevant operational data during a power failure

Scenario

At the selected biopharmaceutical, there is an existing packaging line for vial. This vial packaging line was selected to perform the serialization packaging line upgrade validation. Because available time at lines is limited, the Front-End Loading (FEL) strategy will be used to perform the validation exercise. For the FEL strategy, the vial serialized packaging line installed at a biopharmaceutical industry in Puerto Rico will be used to perform all testing related to Site Acceptance Tests (SATs) Systech Vision Systems, Advisor, Sentri and others packaging equipment. Leverage to common test will also be performed if required.

Results and Discussion

- A total of ten (10) protocols were executed.
- The 73.80% of the steps were satisfactory executed and a 26.20% required any kind of evaluation and/or re-evaluation.
- A total of 53 discrepancies were generated.
- From a total of 53 discrepancies generated:
  - ➢ Fifteen (15) discrepancies were classified as protocol generation error, meaning a 28.30% of them.
    - ✓ Errors in the protocol are due to the lack of information available for some of the tests.
  - ➢ Thirty-one (31) discrepancies were classified as wrong information found in protocol reference documents , meaning a 58.50% of them.
    - ✓ Wrong information found in protocol reference documents (SOPs, Manuals, Design Specification, Navigation Guides, Systech manuals error), incorrect images on Vendor's documents. As a corrective action, it was requested to each equipment vendor to update and correct their manuals. All manuals were corrected and approved prior to finish the validation exercise.
  - ➢ Seven (7) discrepancies were classified as wrong information found in protocol reference documents , meaning a 58.50% of them.
    - ✓ Errors in the system like equipment and configuration errors were a result of system gaps that included screens that freeze and required to reinitiate the equipment (making the test fail), system malfunction, sequence operation errors, logical security errors, network connection errors, among others.

Results and Discussion

Also, some of the tests that were performed could not be completed in the serialized packaging line, generating deviations because some systems were not yet ready or correctly installed.

For the biopharmaceutical industry, this upgrade validation exercise was considered a complete learning curve and will be used for future serialization packaging line upgrades Lessons learned will help to improve planning for the others packaging lines to be serialized in the future. Other opportunities of improvement identified include themes like:

- Project design distribution - Project management techniques will be refined (e.g. better time distribution based on current experience since the first time they were estimated)
- In depth analysis of Serialization packaging equipment manuals - These documents are the key at the moment of beginning the generation of documentation. This information allows the Serialization SME to develop more accurately the tests that will be included in the validation protocol.
- Request close support from each Serialization packaging equipment expert - When upgrading from an existing packaging line to a new serialized packaging line, more support from Equipment representative is required to understand changes in the system. Constant communication with them is necessary during the equipment integration a validation.

Conclusion

Since the regulation came effective on January 2015, most of the companies are focused on complying with the Law and incorporate serialization to their processes. Due to this, a few companies have focused in make upgrades of their packaging lines.

It can be concluded that the main objectives were satisfactorily attained. During the research part of this validation, it was found that although there was no enough public data available related to this theme, the information obtained helped in the development of the initial validation strategy. A general mapping of the main activities was initially developed and details were added during the validation exercise. A final project structure was developed and will be used for the next packaging lines upgrades. The complete validation exercise was successfully completed.

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