Validation Exercise for a Non-Destructive Inspection Device for Blister Pack

Hazel N. Vargas Jiménez
Manufacturing Engineering
Rafael A. Nieves-Castro, PharmD
Industrial and System Engineering
Polytechnic University of Puerto Rico

Abstract *— This project focuses on the validation exercise of a non-destructive vision scan system for blister pack leak detection within a regulated environment. The methodology included a systematic approach, following the System Life Cycle for validation equipment. Collaboration with the team facilitated the delineation of project objectives and success criteria, ensuring alignment with regulatory requirements. A Risk-Based Approach guided validation strategy development, optimizing resource allocation and validation efficiency. The qualification phase involved testing and documentation, verifying system components and functionalities to ensure operational suitability. The project highlights the importance of thorough planning, risk management, and stakeholder collaboration in achieving validation success within regulated environments. The lessons learned from this project will inform future validation efforts, contributing to continuous improvement and adherence to best practices in validation methodology.*

Key Terms *— Decay test, Gross test, Leak Detection, Validation of Equipment.*

PROBLEM STATEMENT

The leak detector device is used to detect leaks and weak seals in individual pockets of blister packs in the primary packaging area. A defective seal on the blister is identified as a critical defect. As part of a continuous process improvement, the current leak detection technology device was identified to be obsolete. In addition, the current leak detection uses a destructive method to identify any faulty sample. Therefore, the site is on immediately needs to acquire an alternate solution for leak detection. The new non-destructive device for the blister pack used a vision scan system and is ideal for selective in-process inspection. This project wants to present the complete validation exercise for this new equipment.

Research Description

This project aims to validate a newly introduced non-destructive vision scan system for detecting leaks and weak seals in individual pockets of blister packs in the primary packaging area. The proposed vision scan system offers a non-destructive approach. This research presents a comprehensive validation exercise to assess the performance and suitability of the new equipment for industrial application.

Research Objectives

The purpose of the validation exercise is to:

- Evaluate the effectiveness of the non-destructive system in detecting leaks and weak seals in blister packs.
- Perform a full validation of the equipment ensuring proper documentation during the activities.

Research Contributions

This research contributes to the validation of a non-destructive vision scan system for blister pack leak detection, offering a viable alternative to traditional destructive testing methods. The findings will support informed decision-making regarding the adoption of this technology in the primary packaging area, leading to enhanced quality control and process efficiency.

LITERATURE REVIEW

The new leak detection equipment (Figure 1) [1] inspects blister packs without causing damage, making it ideal for selective in-process examination. Employing a combination of a 3D scanner and

structured light, the system detects alterations in blister pack sealing under vacuum conditions, allowing for the identification of potential leaks by analyzing volume changes in each pocket cavity. Upon initiation of the test cycle by the user, blister packs are loaded into the test area and subjected to predetermined pressure and vacuum conditions. Throughout the cycle, images capturing variations in the lidding material are captured and compared to detect any leaks present within the blister pockets. The user interface then promptly provides a pass or fail outcome for each blister tested after the cycle.

Figure 1
New Leak Detection Equipment

The new equipment has two types of tests, Decay Test and Gross Test. The Decay test identified pockets that as a microleak of exactly 50-micron. The Gross test identified any leak above 50-micron.

For the Decay test, the test chamber is placed under a predetermined vacuum level that correspond to the Decay method parameter and a structured light is projected in the test area. An image is acquired by the camara. This vacuum level is then maintained for a specified amount of time (Collapsing time method parameter) to allow adequate time for air to escape from any micron leaks if present. The test chamber is then subjected to a lower vacuum level (Reduced method parameter) and a second image is taken (with structured light projected into test chamber). The lidding foil of a good pocket will remain inflated (zero or very little volume change) between these 2 images (Decay and Reduced), however a pocket containing a micron leak will deflate slightly and thus result in a volume change [1].

For the Gross test, the test chamber is placed under a predetermined pressure level (Reference method parameter) and then a structured light is projected into the test area. An image is then acquired by the camera. The test chamber is then subjected to a predetermined vacuum level (Gross method parameter) and a second image is taken (with structured light projected into test chamber). The lidding foil of a good pocket will deflect (volume change) between these 2 images (Reference and Gross), however a pocket containing a gross leak will have no lidding foil deflection (zero or very little volume change) [1].

Validation of equipment is a crucial process in ensuring its reliability, accuracy, and suitability for intended use across diverse industries. It involves systematic evaluation and documentation of evidence to demonstrate that equipment consistently meets predefined performance criteria and complies with regulatory requirements or industry standards [2].

Validation involves various aspects, including calibration, qualification, and verification of equipment, as well as the validation of software, analytical methods, and processes. By conducting validation studies, organizations can identify and mitigate potential risks associated with equipment failure or malfunction, thereby enhancing product quality, safety, and regulatory compliance. Validation is a process that requires careful planning, execution, and documentation to establish confidence in the performance and reliability of equipment throughout its lifecycle. Effective validation protocols consider factors such as equipment design, operational parameters, environmental conditions, and user requirements to ensure robust validation outcomes. Through continuous improvement and adaptation to evolving technologies and regulatory frameworks, validation practices contribute to the advancement of quality management systems and the assurance of product integrity in critical industries [3].

The process of pharmaceutical equipment validation in the pharmaceutical industry involves several stages, each meticulously investigated and

documented to meet regulatory approval. It typically begins with the production of necessary documentation and user requirement specifications (URS), followed by the initiation of a validation project plan (VP) through a change request (CR) from existing facilities. Once management approves the project, a validation protocol is executed to verify compliance with URS and current Good Manufacturing Practice (cGMP) requirements.

The validation process may be divided into three phases: Pre-validation, Process validation, and Validation maintenance [2]. The Pre-validation phase includes Design Qualification (DQ), ensuring equipment and facility designs meet predefined specifications. Installation Qualification (IQ) confirms proper installation and calibration. In the Process validation phase, Operational Qualifications verify equipment functionality under specified conditions, while Performance Qualification ensures consistent performance aligned with URS and manufacturer specifications. Re-validation is conducted when equipment or systems undergo modifications to maintain validation status. Throughout these phases, documentation plays a critical role in ensuring compliance and facilitating continuous improvement [2].

The validation of the new equipment in the primary packaging area will be aligned with the basic requirement for the validation of the equipment. Figure 2 shows the System Life Cycle (SLC) that will be the base for this validation exercise.

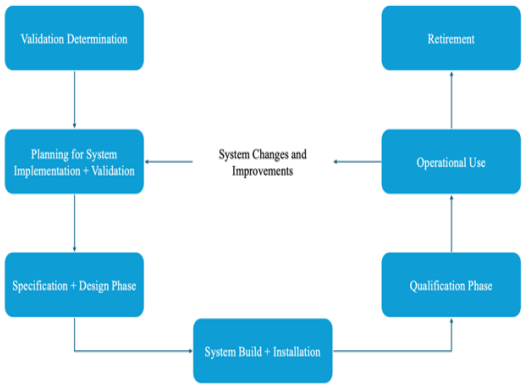

Figure 2
System Life Cycle for Validation of Equipment

METHODOLOGY

This project will focus on the development and execution of the validation of the new leak tester. First, an initial assessment and definition of project scope will be established. The project will continue with the qualification phase which includes Installation and Operational Qualification. To ensure the release for operational use, verification of several GxP programs including maintenance and calibration will take place. Validation SLC Phases and activities/ documents may be omitted, combined, or performed in parallel. Out of the scope of this project is the Specification, Design, system build, and installation. This phase included the following documents: Design Qualification, Factory Acceptance Test, and Site Acceptance Test.

Initial Assessment and Project Scope

The initial assessment and project scope phase included a comprehensive evaluation of the existing leak detection technology and the identification of potential alternatives. This assessment involves engaging subject matter experts (SMEs) to understand the shortcomings of the current method and to explore viable solutions. During this phase, the project team collaborates closely with SMEs to define the scope of the project, including specific objectives, deliverables, and success criteria. The scope of this project is the validation and implementation of a non-destructive vision scan system for blister pack leak detection. Key considerations include technical requirements, regulatory compliance, budget constraints, and timelines. The Change Control will be open to document the implementation of the new equipment in compliance with the site and regulatory agencies.

Validation Determination

A validation determination is not necessary in this case because is clear that the system will be used in a GxP manner. The supplier documentation is included and used for the definition of User Requirements. The level of detail of the User

Requirements will include the necessary description to justify the Operational Qualification testing.

Planning for System Implementation and Validation

Planning of the activities is performed through the Validation Plan. This document will describe the validation program's common elements such as roles, responsibilities, content, and requirements for validation elements, testing, and documentation requirements, and ongoing validation maintenance activities. The Risk Based Approach evaluation will be part of the Validation Plan and will form the basis and justification for the specific validation approach. This considers the intended use of the equipment, complexity of the equipment, criticality of data, critical process parameters, product quality, patient safety, and special requirements. The assessment also evaluates security, signatures, and data integrity. The results from the Risk Assessment will be used to determine the degree of testing required. The outcome of the Risk Assessment will be incorporated into the Validation Protocol.

Qualification

The requirements for performing the qualification activities will be documented in a Validation Protocol/Report. The document is based on the User Requirements and Risk Assessment. The validation protocol will be a combined document. The Method for each presentation of blister pack was developed by the vendor and will be tested in the Operational Verification test. The following Table 1, summarizes the test cases that will be part of the protocol:

Table 1
Installation and Operational Qualification

Test	Justification
Test equipment / calibration	Record calibration and certification information.
Hardware and Software Verification	Verify the proper installation of the system hardware and software. In addition, this test includes the verification of the hardware components at system level.
Application Configuration Verification	Verify that the system application is configured properly.

(Continue)

Table 1
Installation and Operational Qualification

Screen Navigation by Access Level Verification	Verify that the system application allows the users to navigate through each screen and verify that each user level have the corresponding access.
Access Level Security Verification	Verify that the system functionalities are restricted according to the privileges configured per access level.
Local Users and Groups Management Verification	Verify that the local users and groups management functionalities are working properly.
Access Control Verification	Verify that the system functionalities access control functionalities are working properly according to its design and configuration.
Time Synchronization Verification	Verify that the equipment can synchronizes with the company time server.
Configurable Boundary Limits Verification	Verify that the configurable boundary limits for the numeric entry fields are working properly.
Warnings and Alarms Verification	Verify that the system triggers the warnings and alarms when the corresponding thresholds or conditions are activated.
Sequence of Operation and Batch Report Verification	Verify that Test Application operates according to the system specifications. In addition, this test verifies the Batch Report generated by the system.
Alarm Report, Audit Report, Calibration Report, Method Report and User Report	Confirm that system is capable to provide an Alarm, Audit, Calibration, Method, and User report in a printable format with the corresponding data.
Non-Destructive Test Verification	Verify that the Leak Test analysis is non-destructive.
Power Failure Verification	Verify that the equipment can recover from a power failure event.
System Application and Database Backups	Perform and document the system application and database backups.
Interlock Verification Test	Verify the safety interlocks
Operational Verification	Verify and document that system can successfully detect 50-micron leak Blister Product.

RESULTS AND DISCUSSION

The implementation and validation of the non-destructive vision scan system for blister pack leak detection proceeded according to the outlined methodology. The project commenced with an initial assessment and project scope definition, which involved a thorough evaluation of existing leak

detection technologies and the identification of suitable alternatives. Collaboration with subject matter experts (SMEs) facilitated the delineation of project objectives, deliverables, and success criteria. The project scope was narrowly focused on the validation and integration of the new system. Table 2 presents a summary of the individual activities performed in the protocol. The execution of them generates nominal attribute data: pass or fail. The entire timeframe of the validation was 10 months. For the complete validation exercise, a total of 908 steps were executed of which 905 were satisfactory. Only 3 steps failed, and deviations were generated.

Table 2
Test Results (IOQ)

Protocol	Steps passed	Steps failed
Test equipment / calibration	11	0
Hardware and Software Verification	24	0
Application Configuration Verification	114	0
Screen Navigation by Access Level Verification	130	0
Access Level Security Verification	40	0
Local Users and Groups Management Verification	52	0
Access Control Verification	56	0
Time Synchronization Verification	1	0
Configurable Boundary Limits Verification	156	0
Warnings and Alarms Verification	34	2
Sequence of Operation and Batch Report Verification	89	0
Alarm Report, Audit Report, Calibration Report, Method Report and User Report	65	1
Non-Destructive Test Verification	7	0
Power Failure Verification	7	0
System Application and Database Backups	2	0
Interlock Verification Test	8	0
Operational Verification	112	0
Total	905	3

The deviation included a detailed description, the identified root cause, and corrective action. After an evaluation of the root cause, there was no need for re-execution. The discrepancies were identified as not critical, and the data was retrievable. The root causes were identified as protocol generation errors. Errors in the protocol are due to the lack of information available for some of the tests.

During the evaluation of the operational verification, the system was able to successfully detect 50-micron leak in the blister product. The total of blister pack evaluated was 200 blisters with a total of 1,200 pockets evaluated. Figure 3 shown the test results of the entire batch. The points represent individual pockets with a value of gross and decay in volume units. The decay limit is 255 mm^3 and the gross limit is 442 mm.

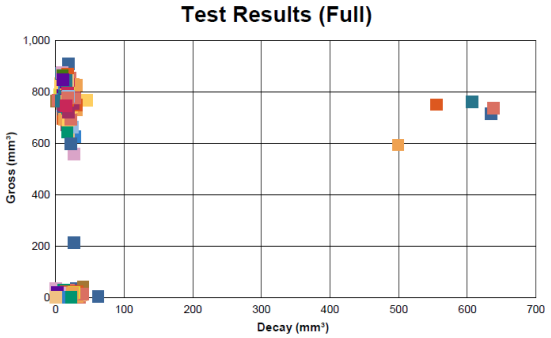

Figure 3
Operational Verification Test Results

Table 3 shown the difference in Gross values between good and bad pockets. It also shown the difference in Decay values for good and pockets with micron holes. The difference values give a level of confidence in terms of the results for individuals pockets and the Methods limits for the blister pack.

Table 3
Gross and Decay Summarize Values

Gross		Decay	
Min Good	557	Max Good	45
Max Bad	213	Min Bad	499
Diff	344	Diff	454

The impact of controlled documents is detailed below. These documents were created.

- Change Control
- Validation Plan
- Risk Assessment and Traceability Matrix
- User Requirements
- Installation and Operational Qualification (IOQ)
- Standard Operating Procedure (SOP)
- Electronic Data Compliance Assessment
- Application Administrative Procedure

The execution of the validation process employed in implementing the non-destructive vision scan system for blister pack leak detection

was satisfactory. By adhering to established GxP principles and leveraging supplier documentation for user requirement definition, the project maintained a clear trajectory toward validation success. The Risk-Based Approach adopted in planning and executing validation activities ensured that resources were allocated judiciously, focusing efforts on areas of highest risk. This approach not only streamlined the validation process but also gave confidence in the system's compliance and performance.

The qualification phase, characterized by the creation of a detailed Validation Protocol/Report, provided a structured framework for conducting IQ and OQ tests. By systematically verifying system components and functionalities, the validation team could ascertain the system's suitability for operational use.

One key lesson learned from this project is the importance of thorough planning and documentation in the validation process. By conducting an initial assessment, defining clear project scope, and developing a detailed Validation Plan, the project team established a solid foundation for validation activities. This meticulous planning enabled the team to identify potential risks, allocate resources effectively, and ensure compliance with regulatory requirements throughout the validation process.

Additionally, by assessing risks associated with equipment use, data integrity, and patient safety, the team could focus validation efforts on areas of greatest concern, optimizing resource utilization and enhancing overall validation efficiency. The key lesson learned from this project is that thorough planning, risk management, and stakeholder collaboration are essential elements for the successful validation of critical systems in regulated environments. By adhering to these principles, organizations can mitigate risks, ensure compliance, and achieve validation success.

CONCLUSION

The validation of the non-destructive vision scan system for blister pack leak detection used a rigorous and systematic approach to implementing critical systems within regulated environments. Through planning, risk management, and stakeholder collaboration, the project achieved its objectives while ensuring compliance with regulatory requirements.

An important aspect of the validation process was the adoption of a Risk-Based Approach, which guided validation strategy development and resource allocation. By assessing risks associated with equipment use, data integrity, and patient safety, the project team could prioritize validation activities effectively, optimizing validation efficiency and mitigating potential risks.

The qualification phase was characterized by the creation of a detailed Validation Protocol/Report, which includes Installation Qualification (IQ) and Operational Qualification (OQ) tests. Through meticulous testing and documentation, the team verified system components and functionalities, ensuring the system's suitability for operational use. The validation exercise provides documented evidence that the new Leak Tester is working for its intended use. Moving forward, the lessons learned from this project will inform future validation efforts, continuous improvement and adherence to best practices in validation methodology.

REFERENCE

[1] Todd, J. (2021) *User Manual VISIONSCAN 3D*. Sepha LTD.

[2] Jindal, D., Kaur, H., *et. al*., “Validation – In pharmaceutical industry: Equipment validation: A brief review”, Adesh University Journal of Medical Sciences & Research, (2020, Dec 19) II (2), 94-98.

[3] Tangri, P., & Rawat, P. S. (2012). “Validation: A critical parameter for quality control of pharmaceuticals”. Journal of Drug Delivery and Therapeutics, 2(3). [Online] https://doi.org/10.22270/jddt.v2i3.151