Redesign of the syringe inspection process

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Abstract *— In the syringe inspection room, the number of units inspected per shift had to be increased. A tool was proposed to increase from 4 to 5 syringes by inspection. Validation of the tool was performed, obtaining satisfactory results.*

Key Terms *—Syringe, Holder and inspection.*

INTRODUCTION

Drug product presentations manufactured at X-company in 1-mL glass syringes undergo 100% inspection process prior to the final assembly and secondary packaging. Currently, this inspection process is performed using the manual inspection system and the Syringe Automatic Inspection Line. During the manual inspection process inspectors hold four (4) syringes in their hands against white and black backgrounds in illuminated work stations/booths. The inspection is performed at a pre-established pace.

OBJECTIVE

In order to minimize inspector contact with the pre-filled syringe, X-Company is in the process of incorporating a syringe inspection holder that will hold up to five 1mL syringes simultaneously for manual inspection. Figure 1 provides an illustration of the proposed holder. Figure 1 shows the empty holder and Figure 2 show the holder loaded with five syringes for inspection.

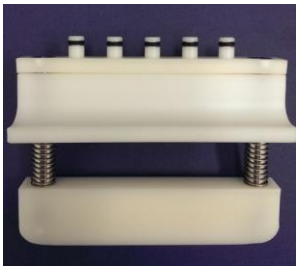

Figure 1
Proposed Holder

Figure 2
Proposed Holder with Syringes

SCOPE

The scope of this report is limited to the discussion of results obtained for the inspection area and Quality Assurance (QA) inspectors' certification in the manual inspection process for the detection of non- particle and visible particle defects on 1mL Syringe product, using the new syringe holder shown in Figure 1.

LITERATURE REVIEW

The purpose of the Installation Qualification (IQ)is to establish by objective evidence that the equipment as installed or modified according to specifications [1]. For equipment qualification, the requirements for installation qualification are presented in Table 1.

ANALYSIS

The methodology at the beginning and at the end of the manual inspection process light intensity was measured on each booth following procedure and documented on the corresponding form. The instrument used to measure the light intensity was documented and its calibration verified.

For non-particle defects, the inspection was performed at a pace of sixty (60) seconds per syringe set for one (1) hour, with ten (10) minutes break. For visible particle defects, the inspection

was performed at a pace of forty (40) seconds per syringe set for one (1) hour, with ten (10) minutes break. For this test the following tasks will be performed:

- Five (5) syringes were carefully removed from the Tub using the holder.
- The holder (loaded with syringes) was positioned against the white background and black background.
- The stopwatch was activated.
- The Inspection was performed by scanning the syringes from top to bottom.
- After the inspection, the defect detection rate and false reject rates were calculated and compared against the established acceptance criteria.

Table 1

Installation Qualification Sections and Requirements

Section	Requirement/Content
Purpose	State the equipment needs to be qualified
Scope	State whether the installation is for new equipment or modifying previous qualified equipment
Equipment/ System Description	Describe what the equipment does, how it is used, what process/products use it, and its basic design features
Supplier	Vendor certification and safety feature verification
Equipment Components	Identify and briefly describes each major component of the subject equipment Define the system/equipment boundaries with other systems or equipment Ancillary equipment used in conjunction with the equipment being qualified should be identified as appropriate
Utilities	Utilities required to operate the equipment should be identified
Construction, Installation, and Requirements	Specify the cleaning procedures that must be executed after the equipment is installed Document that the cleaning procedures have been successfully executed and completed
Supporting Documentation	List supporting documentation that may be used to identify or operate the equipment such as Engineering Turnover Packages, Purchase Orders, or Equipment Manuals
Maintenance Programs	Establish maintenance procedure. Include a listing of any preventive maintenance activities
Spare/Change Parts	Provide a list of spare parts and change parts, if applicable, required for system operation, including a description of the part and part number of reference
Drawings	List and include in the qualification protocol for the system drawings used to support the IQ
Testing and Acceptance Criteria	Acceptance criteria must be approved by the site designate review board or project team prior to executing any IQ Define the test procedure; IQ testing must be designed to confirm that the equipment is installed in accordance with manufacturers recommendation or document justification for exceptions Define the acceptance criteria; for an IQ this is usually a Pass/Fail result
Discrepancies	Discuss and justifies events per required deviation or exception procedure
Summary and Conclusion	Summarize IQ test results, which demonstrate that the equipment was installed correctly Provide a conclusion on whether the equipment installation is acceptable

NON-PARTICLE DEFECTS INSPECTION

The following steps for the non-particle defects test with the new tool in the inspection station:

- The syringes were turned by the flange as shown in figure 3. The holder was rotated on its vertical axis to facilitate the inspection.

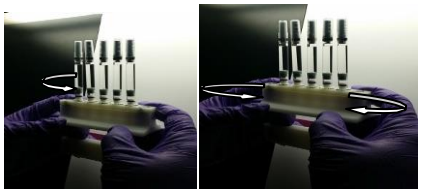

Figure 3
Turned by the flange

- The holder was tilted backward and then forward as shown in Figure 4 to inspect the following points:
    - Needle Cone
    - Needle Shield
    - Syringe Body
    - Stopper
    - Product in or over the stopper
    - Flange

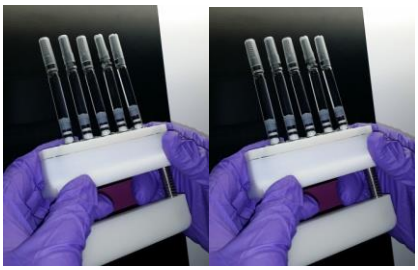

Figure 4
Tilted backward

- The inspection procedure was repeated against the black background, until completing the established inspection time.

VISIBLE PARTICLE DEFECTS INSPECTION

The following steps for the visible particle defects test with the new tool in the inspection station**:**

- The syringes were turned by the flange as shown in Figure 5.

Figure 5
Turned by the flange

- The holder was tilted sideways as shown in Figure 6 to displace the product inside the syringe and then returned to the upright position.

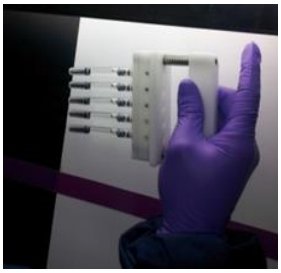

Figure 6
Tilted sideways

- The side of the holder was gently tapped to release any particle and/or bubble that may have become adhered to the stopper.
- The visible particle inspection process was repeated against the black background as in Figure 7.

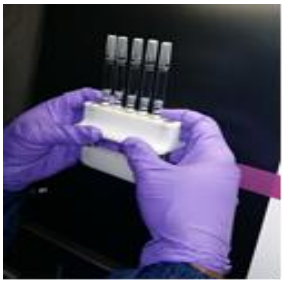

Figure 7
Inspection in the black background

ACCEPTANCE CRITERIA

Tables 2 and 3 present the acceptance criteria used to validate the tool for the non-paricle and particle cases, respectively.

Table 2
Non-particle defects

Non-particle defects:	
Critical defects:	100% defect detection
Major Defects:	NLT 90% defect detection
Minor Defects:	NLT 85% defect detection
False Rejects:	NMT 5%

Table 3
Visible particle-related defects

Visible Particle-related defects:	
Defect Detection:	NLT 85%
False Rejects:	NMT 5%

DEVIATION REPORTS

No deviations were occurred during the protocol execution.

CONCLUSIONS

The technical protocol was executed without deviations. A total of 36 inspectors (29 packaging and 7 QA inspectors) were evaluated for certification following the methodology established on the Technical Protocol.

Syringes with non-particle defects (152 defects) were evaluated 5,472 times; (2,520 times the critical defects, 2,088 the major defects, and 864 the minor defects). Syringes with visible particle defects were evaluated 540 times (36 times per visual particle defects).

The non-particle defect detection rate met the certification requirements for critical, major and minor defects. The average defect detection rate for Critical non-particle defects was 100%, meaning that inspectors were capable of identifying every critical defect in the test set every single time.

The average defect detection rate on Major defects was 97%, exceeding the protocol's requirement of NLT 90%. The average defect detection rate on Minor defects was 97%, exceeding the protocol's requirement of NLT 85%. The overall detection rate by all the inspectors was 98% for all the Non-Particle defects. This defect detection rate was achieved while maintaining a

false rejection rate of 0%, which is significantly below the protocol's recommended false reject rate of NMT 5%.

Syringes with visible particle defects were evaluated 540 times (36 times per visible particle defects). Particle defects were detected 518 times out of the 540 for a 96% overall detection. The overall false reject rate was 1%. The false reject rate by inspector met the protocol's requirement of NMT 5%.

Based on the results obtained during the execution of the Technical Protocol, it is concluded that all the inspectors that were evaluated for certification met the defined acceptance criteria and can be considered certified on the manual inspection using the manual holder.

REFERENCES

[1] Duser, N. (2014, Jan 14). ivT Network Available: http://www.ivtnetwork.com/article/6-steps-compliant-equipment-qualification