# Particle Detection Tool for Liquid Product Inspection Machines

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## Abstract

Improvements opportunities were found during the inspection process of recent manufactured lots in new manufacturing single use technology, which was validated due to expected increase in product demand. An increase in fiber particulate matter which are more difficult to detect by the current inspection tools due to the particle dynamic, morphology and appearance in the liquid product. The implementation of a polarized camera is under management evaluation to increase the detection of translucent particles, similar to the ones observed during the inspection process.

## Introduction

Many pharmaceutical industries have adopted an innovative and transforming process known as Single Use Technology (SUT). The primary disadvantage found was observed during the downstream process, meaning the inspection of the products.

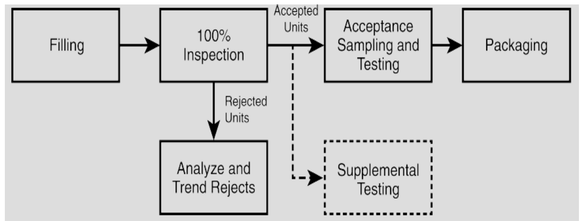


**Figure 1: Simplified Process Flow. Retrieved from USP 1790.**

Visual inspection processes used for the assurance of the product quality may be performed by qualified inspectors via manual or semi-automatic inspection or using an automatic inspection machine. Implementation of SUT introduced a higher quantity of particulate defects to the products.

## Background

Multiple inspection processes have been implemented preventively to ensure a lower rate of customer complaints by eliminating defective units while the product is still in the site. Inspection processes are designed to provide suitable conditions for the detection of both particulate and no particulate defects.
Semi-automatic inspection processes used what its called a polarization filtering effect to aid the operator with the detection of particulate matter in the product. Automatic inspection processes uses Static Division SD) sensors for the detection of particle defects. The SD technology uses variations of electrical signals or voltage levels sense in terms of light interference as particles are detected in the product. The following figure provides a detailed explanation on the SD technology.

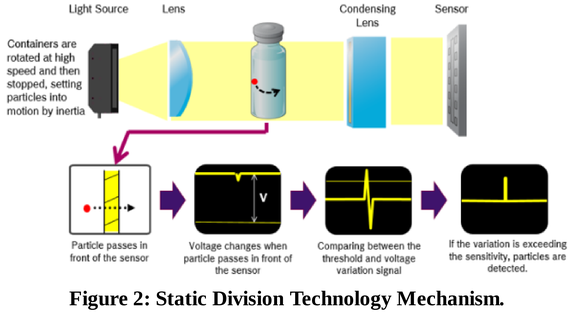


**Figure 2: Static Division Technology Mechanism.**

## Problem

After the introduction of single use technology to the manufacturing process of liquid vial product, the inspection process have been experiencing an increase in particulate matter in the final product.
Intrinsic particles of the process such as plastic fiber materials. Detectability of these type of particulate is more difficult due to the dynamic and morphology of such. Fiber and plastic particulate found during the inspection process may be describe as translucent and buoyant.

## Methodology

One very important point when an improvement wants to be made in a process is the understanding of what improvement program will properly attend the issue on hand. For the solution of a problem or situation and how to reduce the process variations the most suitable program is six-sigma tool. For years the six-sigma methodology has been described with five (5) phases: DMAIC (define, measure, analyze, improve and control). These five (5) phases represents all the necessary steps to properly solve a problem.

**Phase 1: Define**

In this phase we identify the situation in question. The situation or problem can be properly identified by understanding the problem or situation that needs to be attended. Voice of the customer, management requirement, can additionally influence the problem or situation defining phase.

**Phase 2: Measure**

This phase is about understanding the current states of the problem or situation. On this phase you MEASURE current process parameters, and/or any parameter that may be causing the situation or problem.

**Phase 3: Analyze**

Collected data will not means anything until its analyzed. This step is usually related to the MEASURE phase. This phase will help us determine the causes of the problem or the situation.

**Phase 4: Improve**

This phase defines the measurements to be taken to fix the situation or problem. This phase is where the solutions for the problem are put in place to solve the issue.

**Phase 5: Control**

After solving the issue, this phase provides sustainability of the resolution. This phase ensures the problem solution is in place to prevent further situations.

## Results and Discussion

The six-sigma business strategy will introduce the before explained six sigma methodology, while ensuring all the levels in the company from the administration to the operators are working towards the same goal, reduction of the process variability.

**Phase 1: Definition**

Particulate observed after the implementation of the single use technology, was analyzed and concluded to be compatible with the polymer components found inside the plastic bags used for the formulation and filling process.
These polymer particulate attributes includes, but are not limited to, light weighted with a tendency to float in liquid product and clear/translucent flexible films or fibers which would have a lower detection in the SD technology.

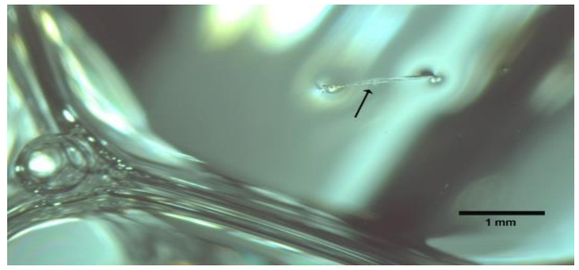


**Figure 3: Fiber Particulate Example in an Injectable Vial.**

**Phase 2: Measure**

The implementation of the new manufacturing suite with single use technology, the particulate load was evaluated for both suites. The particulate load increased up to a 167% if traditional technology is compared with single use technology.

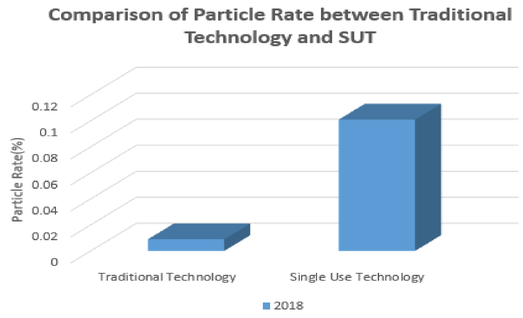


**Figure 4: Traditional Technology and SUT Particulate Load Rate.**

**Phase 3: Analyze**

Instead of relying the particulate detection to the static division tools installed in the automatic inspection machine, a polarized camera aiming for the detection of fiber particles will support the operation. The polarized camera will capture an image of the container after it [the container] is force in a fast spin motion. This spin to the container will set particulate into motion inside the vial, allowing properly detection by the camera.

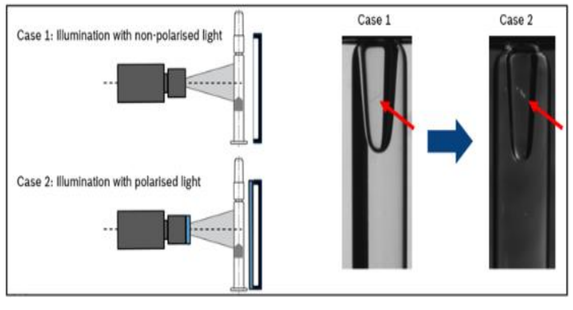


**Figure 5: Non-polarized and Polarized Camera Captions for Inspection Processes.**

**Phase 4: Improve**

Upon implementation of the polarization camera tool a series of protocols and procedures must be revised to ensure the process remains in a validated status, meeting the process requirements.

Documentation such as Validation Plan and User Requirements Specifications must be generated at the beginning stage of the implementation phase.

Consequent to the approval and successful testing of the tools, qualification protocols will be required to qualify the tool installation, operation and performance.

**Phase 5: Control**

Standard operational procedures will have to be revised to include any cleaning, handling and operation of the tool. Every operator, group leader, supervisor, mechanic and engineers that support the operations in the inspection area will be provided with an on the job training, given by both in site and external personnel. Inspection team technical services will be in charge of the documentation regarding on the job trainings and assurance that no personnel operates the equipment without proper training.

## Conclusions

Quality assurance of the product manufactured in the industry is a work for every department. The effectiveness of a polarization camera that will increase the particle detection, thus assuring the customer gets the best quality of product the objective of customer driven improvement tool six-sigma.
Even though 100% removal of defects can not be assure by any of the inspection processes, improvements driven to the further reduction of defect in the manufactured lots is what makes an company reliable.

## Future Work

Polarized tool for automatic inspection process its believe to increase the detection of particle defects. Project will be presented to the administrative and managerial personnel on the company for approval of implementation in the site process.

## Acknowledgements

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