Identifying particulate matter with Hound for rejected small volume parenterals

Introduction

Parenterals are subject to stringent requirements when it comes to purity. These solutions are regulated by the national pharmacopoeias and must be free of any visible particles >50 µm. Serious efforts in production and quality assurance are required to ensure product quality and regulatory compliance.

When particles are found it is possible to quickly determine their identity with Hound (Figure 1). Hound counts, sizes and identifies particles by automated, imaged directed Raman or Laser-Induced Breakdown spectroscopy paired with spectral reference libraries to quickly identify contaminants. In this application note, Hound was used to determine the particle identity of contaminants found in small volume parenterals.

Figure 1: Hound images then identifies sub-visible and visible particles.

Methods

A 50 mL, small volume parenteral (SVP) reject contaminated with white particles and fibers was opened and filtered through a gold coated filter round using a 4 mm diameter funnel to the desired particle loaded area. The filter round was loaded into Hound for automated image data collection and analysis using a 40 s exposure time for the analysis of 100 fields (500 µm x 500 µm) with a minimum particle cutoff of 50 µm (Figure 2). Each particle larger than 50 µm was identified by automated image analysis.

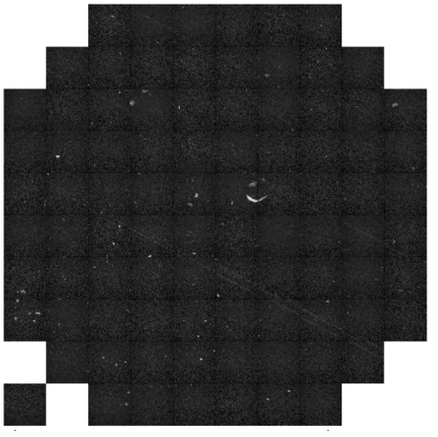

Figure 2: Automated field scan for the 4 mm particle loaded area of a filter round.

Results

All particles >50 µm were automatically identified by Hound (Figure 3). Each of the identified particles provided a recognizable spectra that was identified. The main contaminant was identified as a polyethylene fiber (Table 1). This large fiber was observed during visual inspection and was the source of contamination that caused rejection. Four additional polyethylene particles and four

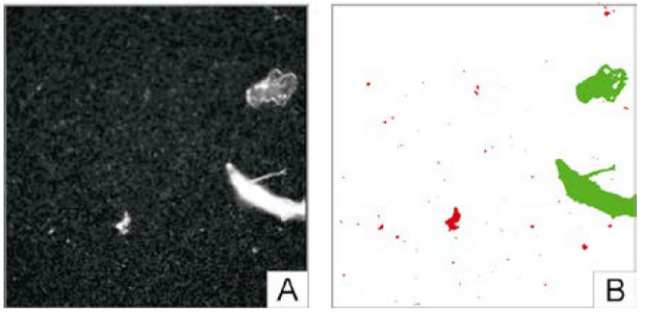

Figure 3: **(A)** Dark field image of one 500 µm x 500 µm field. **(B)** Image analysis highlighting measured particles (green) and all other particles (red).

cellulose particles were also identified but were not flagged during visual inspection.

Substance	Number	≥ 50 µm	≥ 100 µm
Cellulose	4	4	0
Polyethylene	4	2	2

Table 1: >50 µm particles from the 50 mL SVP solution.

Summary

Hound automates the identification of sub-visible and visible particles, like SVP contaminants. After automated image analysis Hound provides statistically relevant particle identification that allows for rapid determination of contaminant composition.

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