

## Case Study – Foreign Particulate Matter Testing

### Making the Pieces Fit for Contaminant Sourcing

#### Overview

The manufacture of pharmaceuticals can be a complex process, involving various raw materials, numerous steps of production, and many stages where failure can occur. One type of failure encountered in the production of a drug product is unintentional introduction of foreign particulate into a drug product. Having an understanding of process, raw materials, and various steps of production can help to identify potential sources for contaminants. An example of how thorough analysis of a material, followed by systematic comparison to potential source materials, is outlined here.

Gateway Analytical, a leader in providing analytical services for particulate identification, strives to help customers resolve issues during their drug development and manufacturing processes. With over 20 years of expertise, we can provide guidance in the remediation of many common and uncommon issues. Our unique forensic-based testing methods allow us to address pharmaceutical issues quicker than the competition, including results as fast as 24 hours from receiving of the sample. Gateway Analytical is FDA registered, cGMP compliant, DEA licensed, and ISO 17025 certified. We ensure that all testing is performed to provide results efficiently and effectively, while maintaining the highest quality standards.



*Figure 1: Stereomicroscopic image of unknown particle*



*Figure 2: Stereomicroscopic image of flooring sample*

#### The Challenge

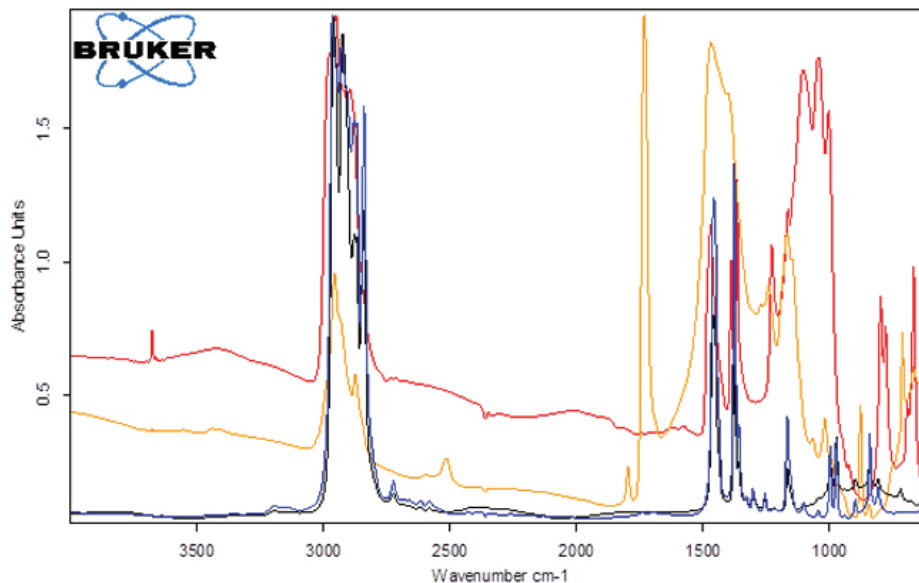
A pharmaceutical manufacturer, through visual inspection, identified a dark particle within a parenteral drug product. The company isolated the material (Figure 1), and sent it to Gateway Analytical for not only identification, but also, comparison to probable sources from the filling room. These materials include a liner from a cart, a sample of the flooring, and plastic cap. Initially, microscopy (optical and fluorescence) of the materials in question was performed.

## Initial Investigation

The unknown material was found to be most similar to the floor material (Figure 2) using both types of microscopy, however FTIR (Fourier Transform Infrared Spectroscopy) and SEM/EDS (Scanning Electron Microscopy – Energy Dispersive Spectroscopy) were utilized on all materials, not only to gain a full identification of all of the materials, but also to help the customer build a process database, to reference for future contamination issues.

## Detailed Analysis

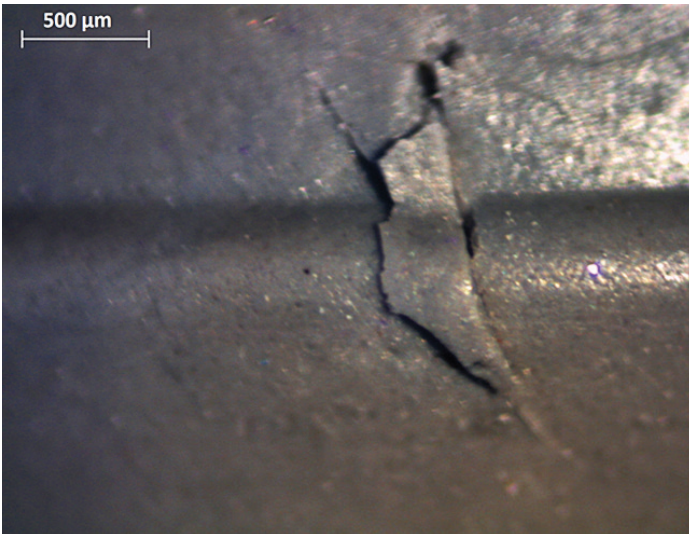
FTIR (spectral overlay in Figure 3) and SEM/EDS analysis (Table 1) showed that, unfortunately, none of the source materials matched the unknown particle's data. After analysts spoke with the customer regarding their observations, Gateway recommended that the vial from which the contaminant was extracted be submitted for analysis. Initial observations showed that a portion of the stopper in the vial was missing, and that the unknown material filled the void in the stopper almost perfectly (Figure 4). Microscopic, FTIR (Figure 5) and SEM/EDS (Figure 6) analyses confirmed that the unknown material and the stopper material were alike chemically; the physical match further supported the opinion that the stopper in the vial was the source for this unknown material.



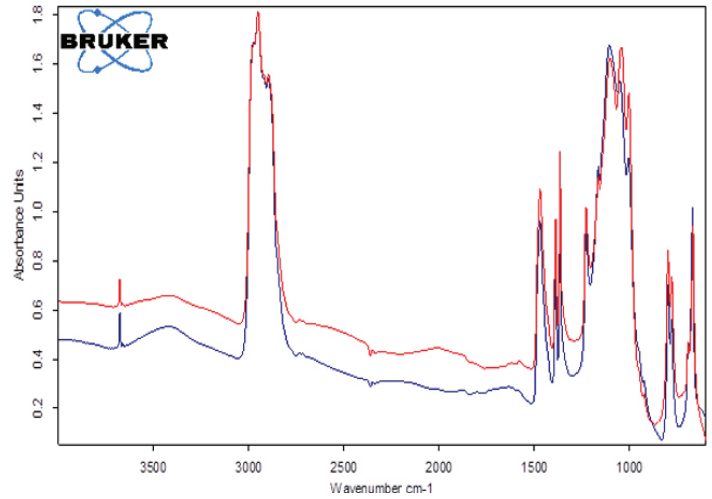
**Figure 3:** Unknown material FTIR spectrum (red) overlaid with potential source materials

MATERIAL	MAJOR	MINOR	TRACE
Unknown material	C, Si	O, Mg	Al, S, Ti
Plastic cap	C	–	O, Mg, Al, Si, S, K, Ti
Flooring sample	C, Ca	O, Si, Ti	Na, Mg, Al, S, Cl, K
Cart liner	C	–	O, Mg, Al, Si, S, K, Ti

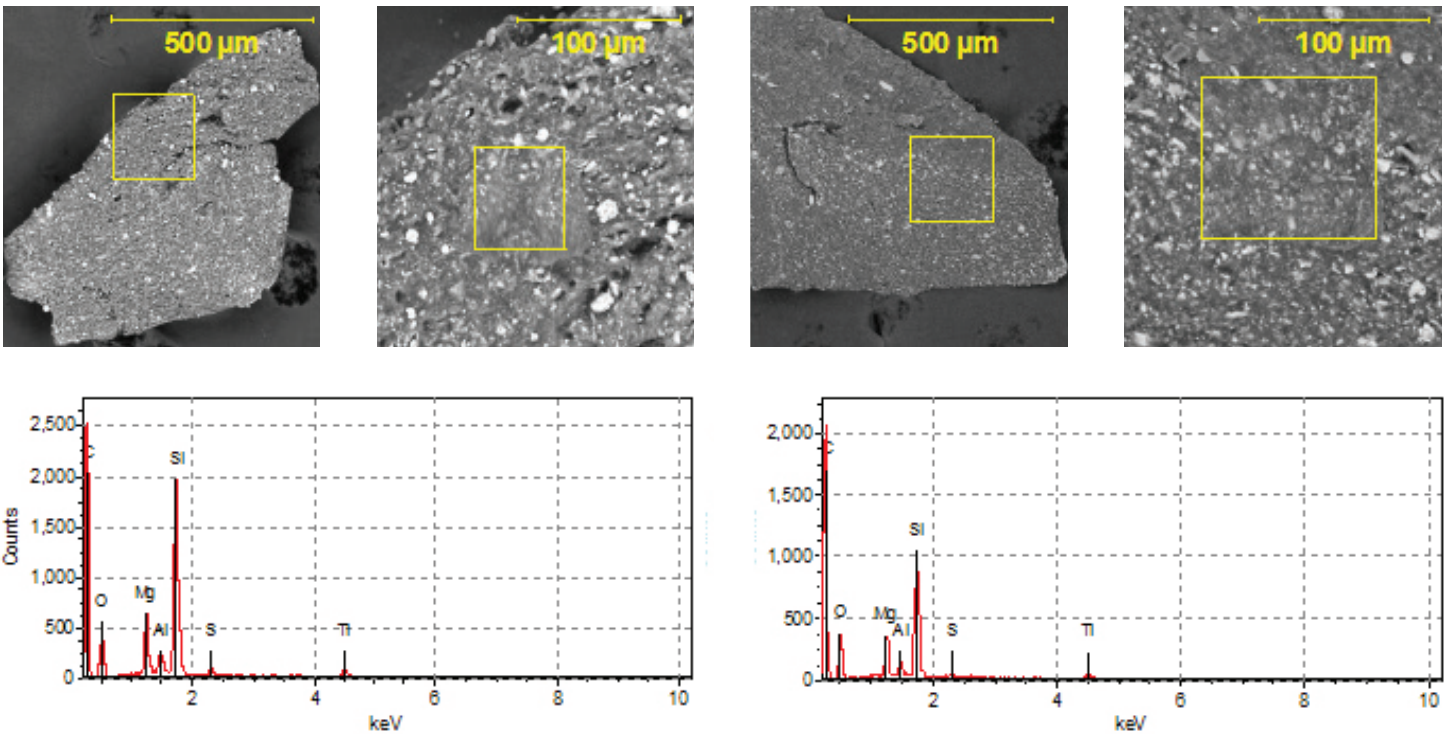
**Table 1:** SEM/EDS, Elemental data from unknown and source materials



**Figure 4:** Physical match of unknown material in vial stopper



**Figure 5:** Unknown material FTIR spectrum (red) overlaid with stopper spectrum (blue)



**Figure 6:** SEM/EDS images of the unknown material (left) and stopper material (right)

## Final Result

Gateway Analytical has the ability to not only aid in the identification of foreign particulate, but also to help identify likely sources for those contaminants. Our scientific team does this by making comparisons, building reference material databases, and working closely with our customers to understand their problems to ultimately identify solutions.



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