Gateway® ANALYTICAL

Quality laboratory services making our world healthier and safer...one particle at a time!

Case Study – Manufacturing & Packaging
Evaluation of Pharmaceutical Vials for Glass Delamination

Overview

Glass delamination if not discovered early can be big problem for pharmaceutical manufacturers. It has the potential to cause costly product recalls and investigations. Because of this, the FDA highly recommends that manufacturers perform stability studies to evaluate the interaction of the drug formulation with the glass vial in addition to pre-testing analysis on smaller batches of the product before going into full production.

The Challenge

Glass delamination, which is a reaction from a form of glass corrosion, are small, thin, glass fragments, termed “glass lamellae”, which are shed from the interior portion of glass containers and vials. The glass lamellae cause quality control issues as they are shed into, and suspended in the liquid drug contained in the glass vial. Due to the microscopic size of most glass lamellae detection during visual product inspection can be very difficult.

The cause of glass delamination can often be attributed to several combined factors. Some of the most commonly found factors include: glass container chemistry, manufacturing and sterilization processes, chemistry and pH level of the liquid drug preparation, and the storage duration and temperature of the liquid drug while inside the glass container. Due to the complexity of potential causes, different analytical techniques and technologies are often required to decisively determine if glass delamination has occurred. Often however, manufacturers do not have the technical expertise or the technology necessary available in-house to perform a full analysis.

The Problem

A leading pharmaceutical manufacturer suspected that their drug formulation was crystallizing in the liquid after observing a twinkling effect in the filled vials. Though they did some initial analysis in-house, they lacked the technology necessary to fully assess the drug formulation and determine the cause.

The Solution

The manufacturer decided to select two filled vial samples, one for analysis and one for reference from the lot and send them to Gateway Analytical for detailed analysis. Initial review of the drug formulation yielded that no crystallization was present. However, after further visual inspection, Gateway Analytical deducted that glass delamination could be the cause of the twinkling that was observed. Samples were then prepared for further evaluation in order to determine the presence or absence of glass delamination in the vial.

Sample Preparation

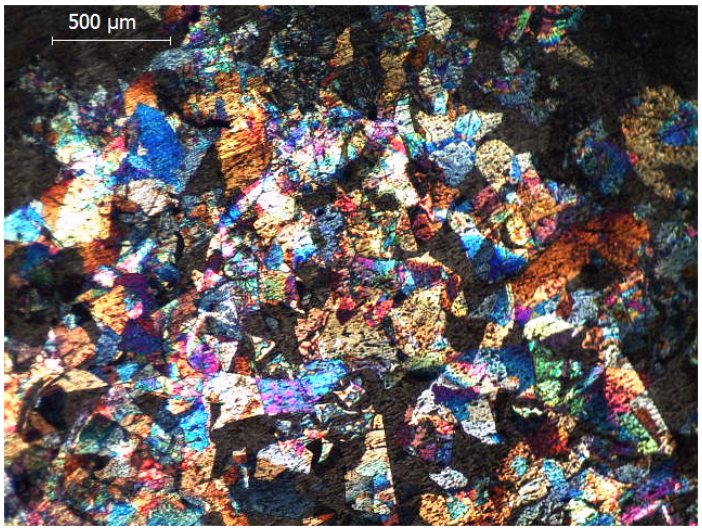
Vacuum filtration was first performed in the Gateway Analytical ISO Class 5 Certified sample preparation area in order to filter the vial liquids onto filter membranes and isolate the observed flakes. The empty vials were then carefully broken into smaller pieces to examine their interior surfaces for signs of delamination.

Stereomicroscopy

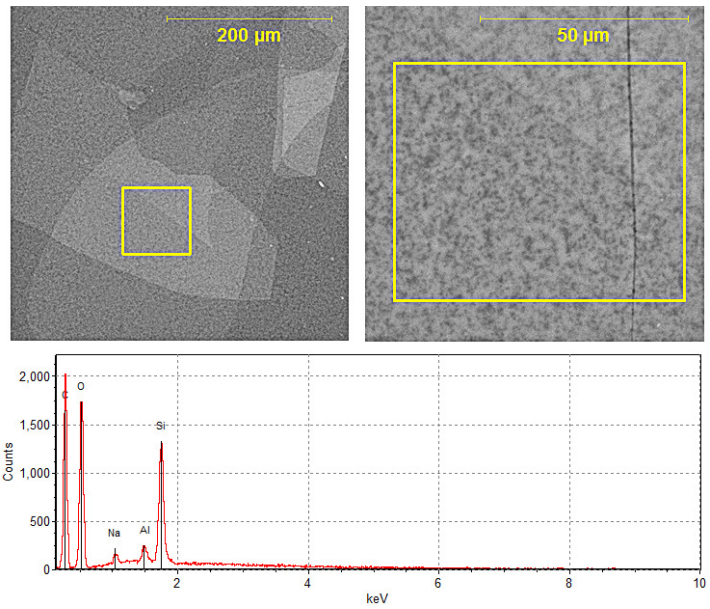
First the filter membranes were examined using a stereomicroscope. Gateway Analytical observed the presence of thin reflective flakes, but were unable to make definitive assessments of delamination. Representative flakes were then isolated from the membrane using meticulous micro-preparation techniques and prepared for further micro-analytical analysis.

Scanning Electron Microscopy/Energy Dispersive X-ray Spectroscopy

Gateway Analytical then performed SEM/EDS analysis and was able to determine the presence of silicon-rich flakes which were elementally and morphologically consistent with delamination. This also suggested that the flakes were in fact property of the glass vial and not a foreign contaminate.



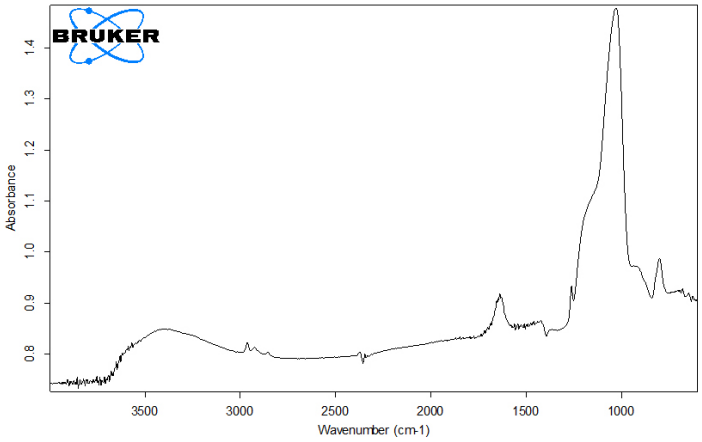
Stereomicroscope image of thin reflective flakes identified following vacuum filtration onto a filter membrane.



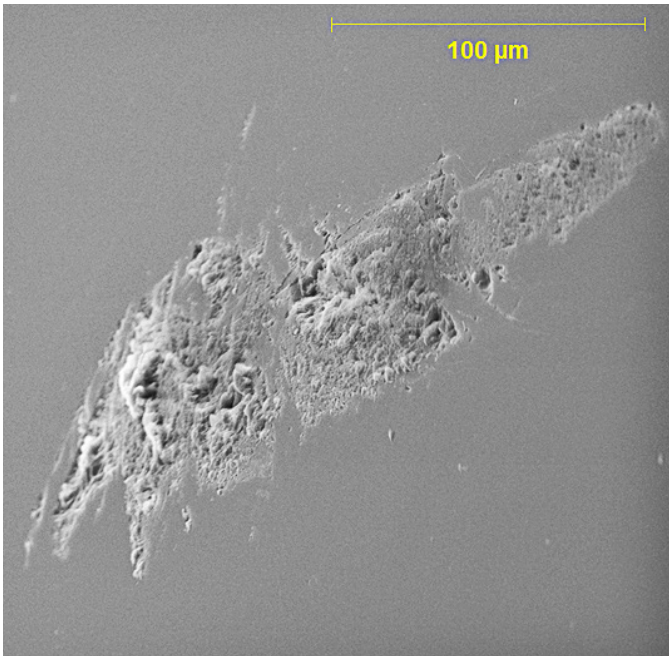
SEM-EDS image and associated spectra of Si-rich flakes.

Fourier Transform Infrared Spectroscopy

Flakes were then isolated for FTIR analysis which simultaneously collects data in a wide spectral range in order to provide the confirmation of the presence of silica.



FTIR spectra indicating the presence of amorphous silica.



High resolution SEM image of interior vial surface

High Resolution SEM Imaging

After the spectral analysis confirmed that the flakes were in fact silica; high resolution SEM imaging was taken of the interior surface of the vial. This provided information about the topography and composition of the vial in addition to a visual confirmation of the glass delamination.

Results

Using a combination of specialized and micro sample preparation techniques, SEM/EDS, FTIR and high resolution SEM imaging, Gateway Analytical scientists where able to determine that what the manufacturer originally thought was a drug crystallization issue was in fact glass flakes that were caused by glass delamination. The manufacturer discontinued the development of additional lots until further analysis of the drug and it's interaction with the vials could be reviewed after receiving the analytical report.

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