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Featured Application

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Glass Delamination Analysis

Overview

Glass delamination is a phenomenon which occurs when the top layers of glass flake off due to breakdown of the glass surface, often occurring in pharmaceutical vial products. This process can occur during the manufacturing process or as a direct result of reactions with drug product and the vial surface. The most common issues caused by glass delamination are recalls of parenteral drug products, investigation into glass container manufacturing, patient/end-user safety, non-conformance investigations and regulatory concerns. USP <1660> details the testing requirements for assessing the durability of glass container surfaces.

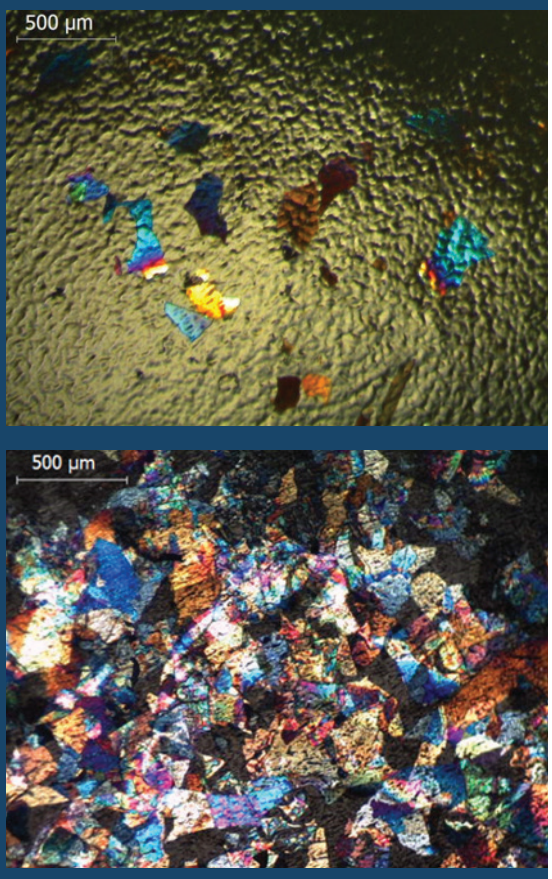

Figure 1: *Stereomicroscopic images of glass lamellae*

What is Glass Delamination?

Glass delamination results in small, thin, glass flakes, termed "glass lamellae," which are shed from the interior portion of glass containers and vials. Glass lamellae are shed into and suspended in the liquid drug contained in the glass vial. Detection of glass lamellae can be very difficult during visual product inspections.

Why Does Glass Delamination Occur?

There is no single variable – occurrence is due to many variables, including:

- Chemistry of the glass container
- Manufacturing process of the glass container
- Sterilization of the glass container
- Chemistry and pH of the liquid drug preparation
- Storage time and temperature of the liquid drug in the glass container

USP <1660> Guidelines

All testing and analysis Gateway Analytical performs for glass delamination fall under the USP <1660> guidelines. As the recommended approach for the evaluation of the inner surface durability of glass containers, these guidelines provide predictive testing solutions for glass delamination. By finding the issues and resolving those before production is complete, pharmaceutical customers can save both crucial time and expenses as their process moves forward.

Method Evaluation & Descriptions

Gateway Analytical employs specialized sample preparation protocols, optical microscopy and SEM/EDS methods to characterize glass delamination products. The typical analytical protocol for routine glass delamination includes:

- Stereomicroscopy of a Received Sample: This process allows the examiner to make observations related to the drug product while in the vial. Observations are made for the presence of "Twinkling" effect caused by light reflecting off glass particles when delamination is present.
- Identifying Fill Line and Susceptible Areas: Often delamination occurs at the drug fill line and other susceptible areas such as the neck and heel.
- Filtration: The drug product is filtered and rinsed to allow observation of glass lamellae.
- Vial Prep: The vial is broken to expose the interior surface for evaluation of corrosion, pitting, mechanical defects and delamination.
- Stereomicroscopy of Filters for Lamellae: Coaxial lighting is used to examine the filters for lamellae. Distinctive, thin, colorful or reflective flakes indicate glass lamellae. The glass lamellae are typically thin, flat, smooth and usually at least one straight/angular edge. (Figure 1)

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- Manual SEM Analysis of Filters for Lamellae: The filter surface is evaluated using SEM/EDS to detect elements consistent with glass in the lamellae. The stereomicroscopy and SEM/EDS of the filters are combined to confirm that particles are both morphologically and elementally consistent with glass lamellae. (Figure 2)
- Automated SEM Analysis of Filters for Lamellae: This analysis has shown limitations in the ability to provide information related to particle count and sizing information of lamellae. Current research is underway to implement automated LIBS and/or automated microscopic analysis for this function.
- SED Imaging of Vial Interiors: Vial interiors are imaged in SED mode using scanning electron microscopy. The surfaces are evaluated for delamination (Figure 3) and abnormalities, such as pitting (Figure 4). The most common areas of interest are the fill line, bottom, heel and vial neck areas.

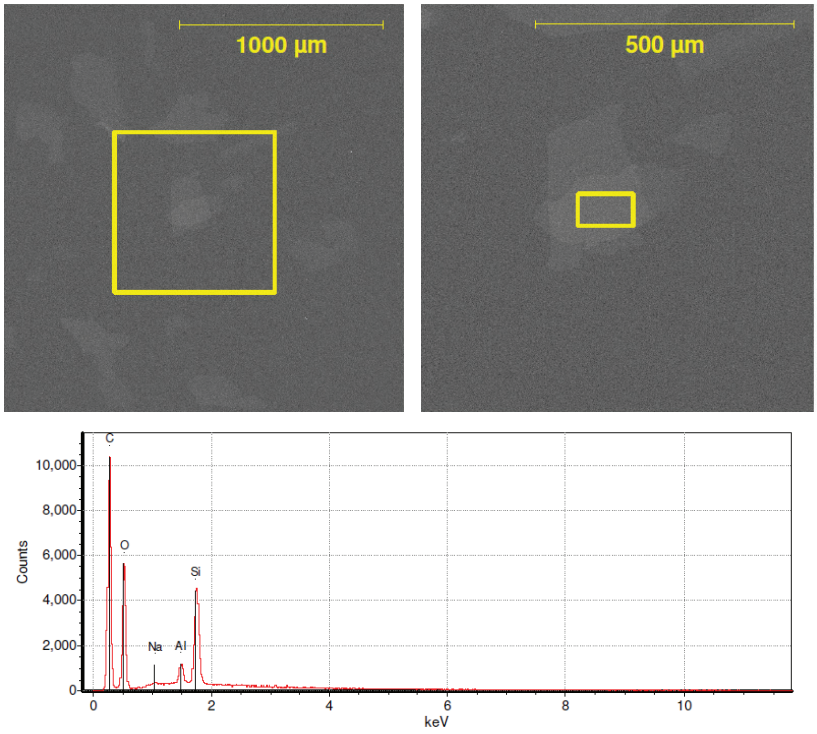

Figure 2: *SEM/EDS images of typical glass lamellae*

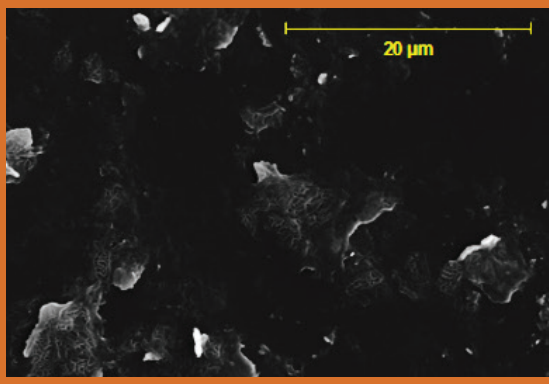

Figure 3: *SED image of glass delamination in interior surface of glass vial*

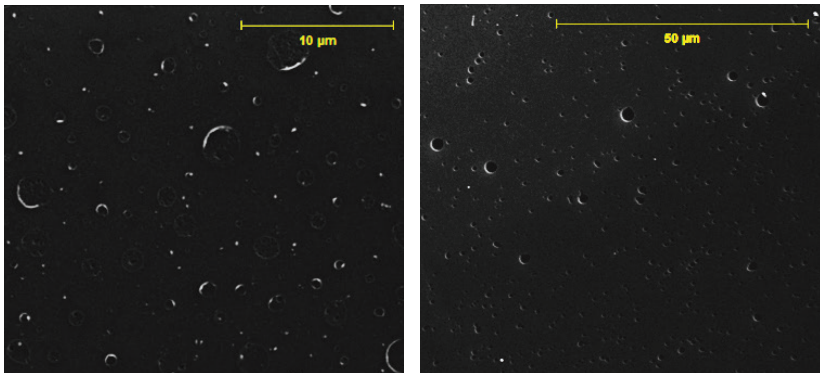

Figure 4: *SED images of "pitting" on interior surface of glass vial*

Quality Control Testing

Quality Control is a critical aspect of glass delamination analysis. The pursuit of quality in all aspects of service and all service offerings is critical to the results, interpretation and defense of analytical data:

- Testing should be conducted under cGMP conditions
- Validation of Method and Instrumentation
- Training, Proficiency Testing

Glass Delamination Services:

- Glass Delamination Analysis
- Validation and Testing of Unused Vials
- Glass Delamination Training Modules
- USP <1660> Support