Analytical & Testing Services

A forensic approach for combination devices

Tips for ensuring you have the right primary container – and forensic techniques in case you don't.

Stevanato Group

MANAGING COMPLEXITY, DELIVERING VALUE

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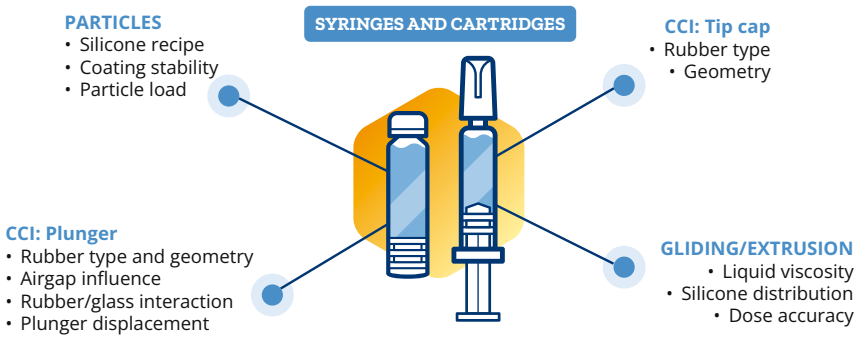
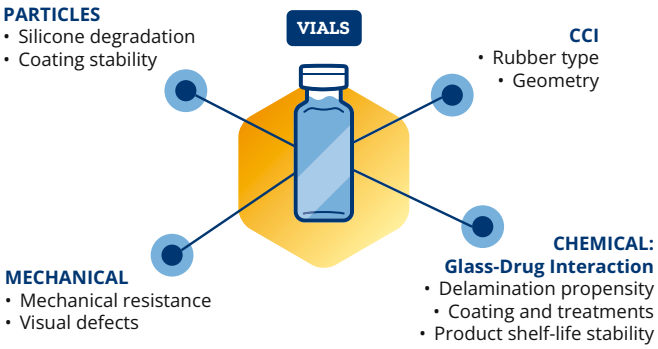
Abstract

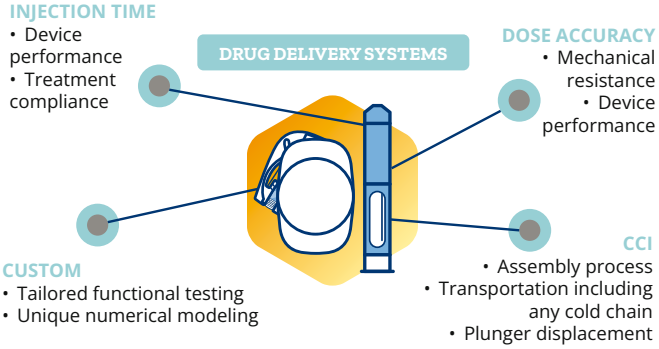
A key but underestimated challenge for pharma companies is ensuring the primary container safeguards the integrity, safety, and efficacy of a new drug. Relevant compatibility tests between a drug substance and its primary container exist at each stage of the product development cycle – smoothing the way to eventual regulatory approval.

Underestimating how a new drug can interact with its primary container, or testing it too late, can cause serious delays or expensive corrections – and it may even lead to the drug having to be reformulated. While companies use multiple robust tests on a new drug product, similar scrutiny should be applied to the combination of drug and container to avoid potential degradation or failure of either component.

Stevanato Group harnesses decades of experience to help pharma companies identify relevant testing to de-risk the product development lifecycle and quickly uncover root causes of product failures. The figures below show several considerations for vials, cartridges, syringes, and drug delivery devices that may need to be evaluated in conjunction with your drug substance.







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Stevanato Group's **Technology Excellence Centers (TEC)**, has worked with companies of all sizes, including CDMOs and CMOs, to proactively test drug containers and combination devices to mitigate more expensive problems later in the product development cycle. Stevanato Group TEC also has a number of methods to forensically investigate when the customer discovers non-conforming product to identify a root cause. Here are a few examples of problems that the company has encountered – and corresponding forensic instrumentation the TEC has to tackle them:

Problem:

Unidentified particles, fibers, and even components in a combination product.

For particles and fibers, multiple sources of contaminant in a drug product or its container exist, including the manufacturing and handling process, protein aggregation in the presence of silicone oil, or glass lamella that delaminate from the glass surface due to the presence of the drug. Contaminants of any kind can be hazardous and therefore lead to recalls, failed release testing, or loss of expensive drug products.
In general, understanding the chemical composition of these particles, fibers, and unidentified components can help identify their source or manufacturer.

Solution:

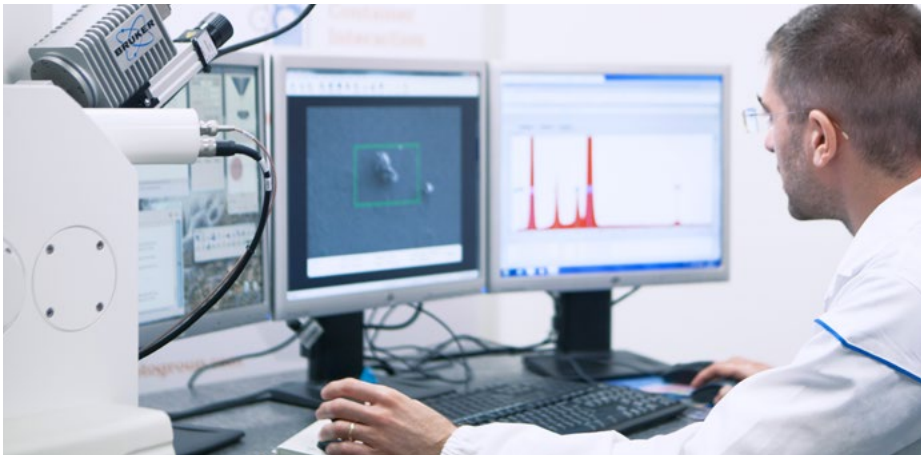
MFI, SEM EDS, and FTIR for identification

For subvisible particles in solution, microflow imaging (MFI) uses a camera to capture images of particles passing through its flow cell. Attributes such as particle size, transparency, and shape can then help identify the particle based on its morphology, such as for silicone oil or aggregated protein.

Stevanato Group also uses techniques ranging from scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDS) to Fourier transform infrared (FTIR) spectroscopy to chemically characterize visible and subvisible contamination.

SEM EDS and FTIR can help identify elemental and molecular structures respectively, to be compared to libraries of known materials.

TEC has a library of identified materials – including materials from the product manufacturing process – to help with distinguishing polyester fibres from an employee's personal protective equipment or different manufacturers of glass. TEC also has an extensive library of elastomer manufacturers that can help with reverse engineering products when component documentation is not available.



Problem:
Glass breakage

Glass breakage is an obvious safety issue that could even disrupt the administration of a patient's life-saving dose of medication. But identifying the source of a breakage can be a complex process. The cause could be an overaccumulation of flaws and stress during the forming and handling process – or during use inside a drug delivery device, such as an autoinjector or pen injector. The material strength of the glass can be reduced when flaws are introduced – for example, when glass touches other glass in bulk handling equipment. These flaws are then weak spots that can become the failure point when the glass is pressurized in a drug delivery device or stressed by high-temperature washing or depyrogenation cycles.

Solution:
Glass fractography and Failure Analysis

Stevanato Group has extensive experience in the handling of glass products for the pharma industry. Tools such as stereomicroscope and SEM can help to identify origins and describe flaws and fracture attributes such as Wallner lines or hackles in fractured or broken glass containers to determine where the fracture may have originated.

Chemical analysis (including SEM EDS) of the impact zone may also illuminate what material came into contact with the glass, such as metal from machinery. Custom testing fixtures can also be created to better mimic how the glass syringe is held and loaded, allowing for repeatable stress testing of a large batch of glass containers.

Conclusion

Stevanato Group TEC offers a wealth of experience and a variety of forensic methods to investigate your product both proactively and if it is failing. In addition to the techniques described above, Stevanato Group offers additional functional, compatibility, and investigational methods like extrusion force and glass delamination.

Regardless of phase, company size, or drug product, there is always a relevant test to de-risk or troubleshoot your product. Reach out to Stevanato Group today so we can help you develop and execute a phase-appropriate test plan for a more successful world-class product tomorrow.