More than a packaging solution:

Using high quality glass vials to improve efficiency and reduce costs in pharmaceutical manufacturing

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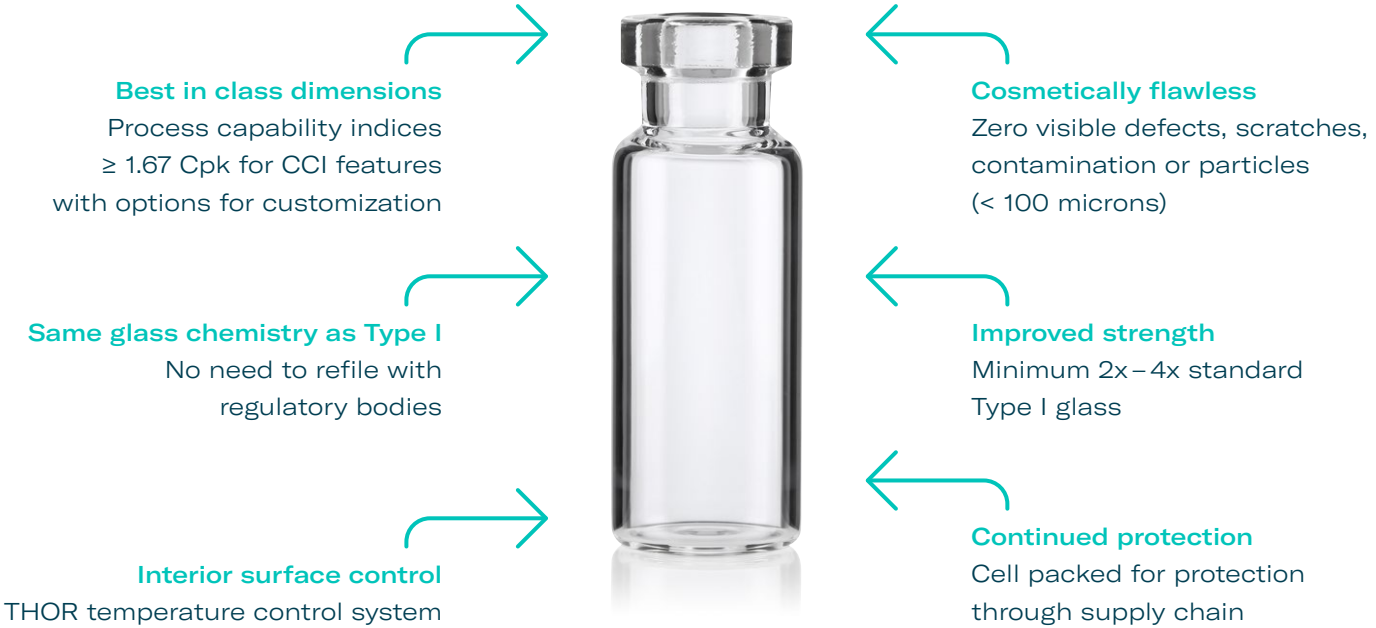
Introduction

Carefully worked out packaging solutions are essential for ensuring the integrity of pharmaceutical products. Since packaging is also an integral part of the production process, it offers a powerful route to improving pharmaceutical manufacturing productivity and reducing the total cost of ownership (TCO) of the product. Glass containers, and glass vials in particular, have always played a fundamental role in the packaging of medicines. In recent years, the demands placed upon them have become increasingly stringent, especially in improving manufacturing efficiencies and accommodating the needs of modern vaccines and sensitive biologics for parenteral administration.

This white paper briefly reviews some of the challenges for the pharmaceutical industry when working with glass vials and examines recent advances in glass vial production. It makes the case for partnership and working with industry experts in glass manufacturing technology who also understand the processes involved in manufacturing pharmaceuticals. Case studies illustrate how new approaches to glass vial production support pharma companies in meeting regulatory requirements while maintaining the flexibility to meet fluctuating demand, drive efficiency gains and reduce TCO.



Glass vials today

Parenteral drugs require high-quality temperature-resistant glass vial packaging to maintain product integrity and ensure patient safety. Type 1 borosilicate glass is the industry standard, providing a chemically inert container for injectable preparations across a wide pH range. Vials that are used for packaging injectable drugs must exceed certain ISO quality standards and the manufacturing processes involved in delivering to these regulatory standards are complex.

For many applications, glass vials are treated simply as commodity packaging items that are subject to standard pharmaceutical procurement procedures. Nonetheless, this can mean missed opportunities to ensure that the vials are optimally matched to the characteristics and demands of individual manufacturing processes. High-quality glass vials that are tailored to specific processes can contribute significantly to improved efficiency and to driving down the TCO.

Today, advances in glass technology and the adoption of Quality by Design (QbD) approaches to manufacturing glass vials are delivering pharmaceutical containers with unprecedented levels of quality. This means high-quality “off-the-shelf” products, but perhaps more importantly, pharmaceutical manufacturers and expert glass makers are increasingly working in partnership to deliver the most effective and efficient solution for each individual pharmaceutical process.

Challenges with glass vials

The technology used and the approach taken to manufacturing glass vials can have a major impact on the pharmaceutical manufacturing process, downstream processing or the use of the packaged pharmaceutical product. Glass vials can affect patient safety as well as manufacturing efficiency and the TCO of a pharmaceutical product.

Patient safety tops the list of all priorities with major efforts underway to drive down recalls, eliminate drug shortages and reduce market notices. Since glass is the preferred packaging material for many drugs, high-quality glass vials that perform consistently and to expectations play a crucial role in ensuring drug safety and performance for the end user. While glass is inherently strong, microflaws and defects introduced during vial manufacturing can result in breakages on filling lines and in the field. Consistent defect-free glass vials are therefore critically important components that are integral to the entire drug life cycle.

In terms of the pharmaceutical manufacturing process itself, each has its individual challenges. Consider, for example, vaccine production, which may involve steps such as freezing-flash freezing during production and subsequent frozen storage and lyophilization. Many different pressures and stresses are applied to the glass vial throughout the manufacturing cycle. If microflaws are present, the application of a range of stress factors to both the material and the form of the vial may result in breakage, with associated wastage, rework and increased manufacturing costs.

In addition to the intrinsic quality of the glass material, vial-to-vial and lot-to-lot variability are at the root of many of the production challenges faced by pharmaceutical manufacturers. Since production technologies tend to operate on the form dimensions of the vials, having the ability to reduce this variability offers scope to run filling lines more efficiently with fewer stoppages and to increase speed and capacity without the installation of new equipment. The importance of this has been apparent during the COVID-19 pandemic where being able to quickly scale-up production of existing pharmaceutical treatments or to rapidly produce new vaccine products in existing plants have proved critical in achieving the necessary volumes.

With respect to the TCO of any given pharmaceutical product, packaging, the waste stream, and costs related to downtime, breakage and machine throughput are all part of an often complex calculation that encompasses multiple internal and external costs and risks. Glass vials can play a significant role in driving down TCO. Having the right vial for the process does not just ensure efficient operation. Vials based on a proven high-quality glass technology platform and tailored to individual pharmaceutical manufacturing processes take account of each one's inherent challenges and sensitivities, helping to mitigate many of the risks.

Advanced glass making technology combined with QbD approaches to manufacturing glass vials are now delivering glass containers that offer better product reliability without additional regulatory burden as well as improved customer line performance (e.g., better filling line efficiencies, less downtime for glass-related events, and reduced TCO). However, no two pharmaceutical manufacturing processes are the same and the most effective solutions involve partnership working around this technology platform. It is incumbent upon the glass manufacturer to work with each customer to examine and understand the entire product life cycle to design a glass vial solution that delivers the best possible operational performance.

Advanced approaches deliver new solutions

Taking a QbD approach to glass vial manufacture ensures that quality is built into every stage of the process, avoiding many of the issues with conventional manufacturing methods that rely only on inspecting for defects rather than also designing them out of the process. Moreover, this approach includes using the highest quality raw materials as well while still allowing an easy transition from typical Type I glass. Coupling this with advanced glass making techniques delivers a final product free of the flaws that can cause in-use issues.

Gx® Elite Glass (Gerresheimer) technology, a high-end solution built on industry standard Type 1 borosilicate glass chemistry, is a prime example of this approach, as the following comparisons and case studies illustrate. It provides a platform for the production of standard ISO glass vials and is the starting point for tailored pharmaceutical manufacturing solutions. Advances achieved through combining a QbD approach for the product and optimization of the glass converting process enable the production of cosmetically flawless vials with consistent dimensions, increased break resistance and chemical durability.

The vials are made using a production process in which glass tubes are inserted vertically into a rotary forming machine. The free end of each tube is heated and forming tools are used to create the shoulder, neck, and flange or finish of the vial. The tube is then pulled apart under heat and a vial is completed from the short, separated section by heating the other end to form a base. Once formed, the vials pass through a stress-relieving furnace to remove any tension that could lead to later cracking. Geometric and cosmetic inspections are conducted throughout the process on all individual vials (so-called 100% inline inspection).

Applying QbD to this manufacturing process means taking risk and knowledge-based decisions, having systematic approaches to process development and pursuing continuous improvement. Improvement in terms of glass vial quality might include greater dimensional stability, minimal flaws and defects, higher strength, interior surface control and more secure packaging. Within this overall system for Gx® Elite Glass, a complete evaluation of the glass-converting process encompassed raw materials, temperature control, detection and inspection, and handling. It resulted in a range of different process solutions being engineered to remove defect creation during forming and transfer operations.

Benefits for pharmaceutical company

Building in the necessary quality reduces the need for inspection of incoming goods by the customer. The improved strength and dimensional stability of the vials reduces pharmaceutical filling line breakage and finished product rejects, supporting overall cost savings. With the ability to meet the demands of high-speed filling lines, they also open up faster line performance and the cost-efficiencies that it brings. Improved container integrity also lowers the risk of recalls or market rejections. With no move away from Type I borosilicate chemistry, a transition to these high-performance vials requires no regulatory re-filing.

Evaluations in practice

Several customers have evaluated Gx® Elite glass products. What follows is an overview of their projects and the performance results.

Case Study 1:
Low Risk Regulatory Re-filing

As a result of US Food and Drug Administration (FDA) observations, Customer A's manufacturing site was committed to high levels of vial inspection. They evaluated Gx® Elite 2 mL vials with the goal of reducing vial inspection and improving processing. Three pharmaceutical lots of Gx® Elite 2 mL vials were processed under normal operating conditions and vials were sampled and evaluated for the presence of critical, major and minor defects. These were compared with the previous 10 lots processed using Gerresheimer standard converted vials. By applying the two-proportions hypothesis test, it was concluded with 90% certainty that there was a substantial difference in performance between the two types of glass vial with a reduction in the reject rate of as much as 90%.

The customer has since commercialized the new vials as an annual reportable change and the second day inspection required by the FDA has been eliminated. Forward calculations forecast that defect reduction will allow the production output of significantly more units per year, alongside which are cost savings with the reduced need for inspection and resource allocation for glass-related investigation and corrective action.

Case Study 2:
Defect Reduction

Customer B evaluated the Gx® Elite vial to determine if this would have an impact on defect reduction during normal filling operations. Again, the Gx® Elite vials were processed under current manufacturing conditions and evaluated against the previous 10 lots processed using Gerresheimer standard converted vials. Three lots were processed and evaluated for: glass particulates, cracks/checks, cap seal integrity, vial dimensions, and cosmetic defects. No defects were observed with the new vials. This result is significant because defects were found in the previous 10 lots using the typical vials.

This customer has approved the glass for use and expects further opportunities for improvement where vials of other sizes are used.

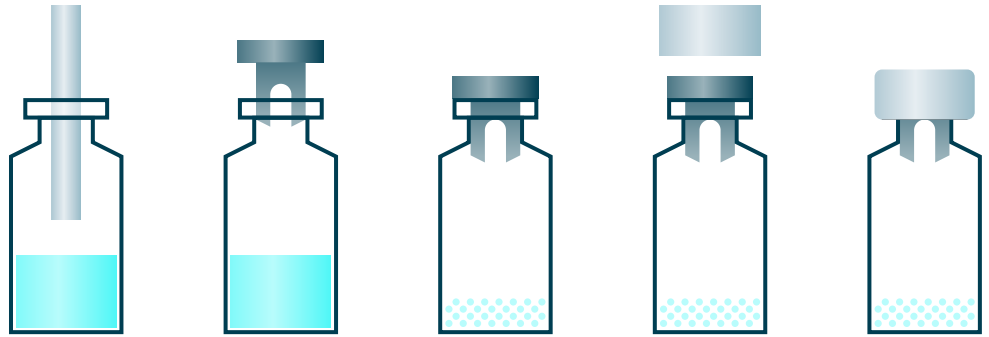
Case Study 3:
Lyophilization Challenges

Customer C experienced breakage and downed vials following processing changes. Speeding up the lyophilization process had exposed the vials to extreme stress, resulting in breakage caused by microflaws in the glass. Robust, cost-efficient lyophilization processes are essential for many drugs to ensure their stability and an adequate shelf-life.

Figure 1 summarizes the process. Comparison of the new and standard vials in the customer's process showed increased machine speeds of up to 25% (**figure 2**), a reduction in defects of up to 80% for breakage and cracking (**figure 3**), and up to 90% for cosmetic defects (see **figure 3**). This has led to a longer term study to determine TCO.

Figure 1

A robust and cost efficient lyophilization process accelerates time-to-market cycles and increases shelf-life stability of biopharmaceuticals



STEP 1
Product is aseptically filled into vial

STEP 2
Stopper is partially inserted and the vial is placed in a lyophilizer

STEP 3
When lyophilization is complete the stopper is seated

STEP 4
Aluminium cap is placed on the vial

STEP 5
The aluminium cap is crimped onto the vial neck

Figure 2

Machine speed: Gx® Elite versus standard

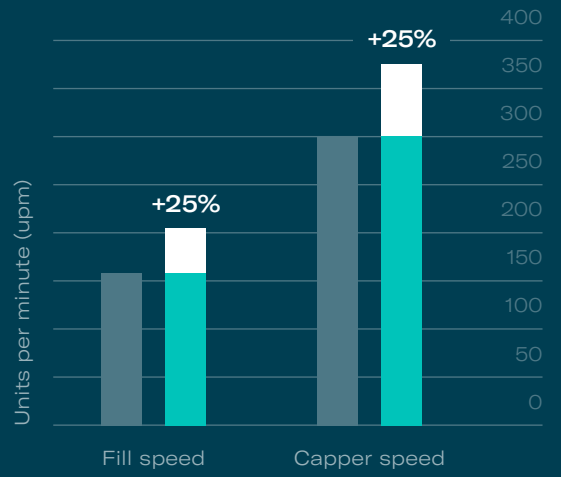
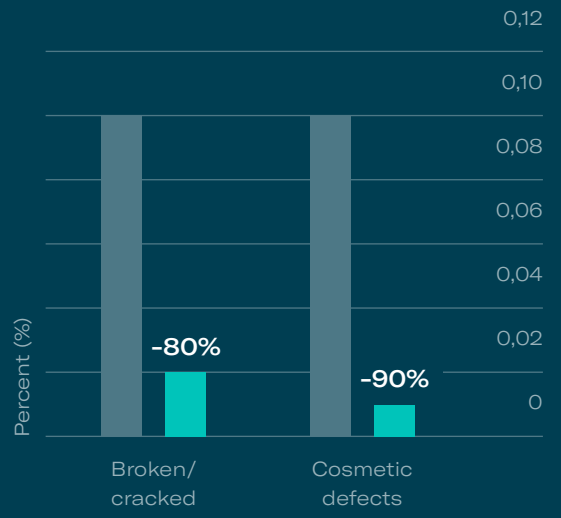


Figure 3

Breakage/defects: Gx® Elite versus standard



Tailoring the solution to drive process efficiency

With a secure technology platform for the production of advantageous glass vials, there remains the issue of who is best placed to determine the impact of vial properties on production processes and on the product's subsequent journey and use. Since the deep knowledge about a specific pharmaceutical process lies with the drug manufacturer and the glass technology expertise resides with the glass manufacturer, there is a strong case for working in partnership to develop solutions that accommodate the often-nuanced workings of specific pharmaceutical manufacturing processes.

Moving from thinking of glass vials as a simple commodity toward them being a powerful tool for driving process efficiency and reducing TCO can be a demanding transition. Vial manufacturers must demonstrate that their teams can quickly and thoroughly understand their customers' needs and that they can support them with effective, tailored solutions.

solution provider

Summary

In today's environment, the high-quality glass vials used to package many sensitive pharmaceutical drugs are much more than simply a commodity item. Vials that are not only made from materials of the highest quality, but that are also tailored to the specific pharmaceutical manufacturing process, support better throughput, less wastage, greater process efficiency and a safer, more user-friendly packaged product. All these factors contribute substantially to driving down the total cost of ownership.

Innovative glass making technology combined with a QbD approach to manufacturing is producing vials with superior characteristics designed to meet the increasingly stringent demands of modern drug packaging. Vial selection is a critical decision and for some processes, standard off-the-shelf versions of these high-quality vials will adequately meet product and process needs. For others, however, it presents an opportunity for process improvement. Glass vial manufacturers that have a secure and proven technology platform for their products and expert teams focused on working with and understanding their customers' pharmaceutical processes, are a critical part of the pharmaceutical manufacturing mix. The tailored solutions that result from this type of partnership hold out the potential of significant gains in safety, efficiency, and cost effectiveness.

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