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# FOUR WAYS POLYMERS TRUMP GLASS FOR CONTAINING CUTTING-EDGE INJECTABLE BIOLOGICS

In this article, using applications in West's product portfolio as examples, Nicolas Brandes, PhD, Business Development Manager, Daikyo Crystal Zenith, West Pharmaceutical Services, Inc, makes the case that polymers offer superior benefits compared with glass as a material for primary containers and delivery systems for parenteral drugs, including in particular biologics.

Glass came before plastic. Still widely used, glass became a standard for containment of injectable drugs decades ago. But that was before the rise of present-day cutting-edge biologics, such as monoclonal antibody drug products used for the treatment of cancer, and autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, Crohn's disease and psoriasis. These emerging drugs comprise nearly half of the top-20 sellers, and they continue to gain market share.

Biologics comprise genetically engineered proteins derived from living cells, and they work by targeting specific components of a disease. For example, biologics designed to treat rheumatoid arthritis may target components of the immune system that play a role in inflammation.

But biologics and glass don't always mix. This problem calls for new, custom-designed polymer containment and delivery systems. In fact, this issue has become so acute that pharmaceutical manufacturers are now making packaging systems an integral component of drug development and research, as opposed to an afterthought to be dealt with right before bringing it to market. Increasingly, they're choosing polymers, not glass, for containment. How much of a stake do these new materials claim in the industry? As demand for biologics continues to grow, the use of prefillable systems has increased with total market units of prefilled syringes estimated to reach 3.9 billion units by 2018.

There are four main reasons why biologics pair better with plastics.

## PROVIDING MORE STABLE CONTAINMENT

Some biologic drug products do not react well with glass; sometimes interactions between a drug and its glass package arise, requiring new approaches to containment and delivery. For example, modern biologic formulations sensitive to silicone oil or tungsten may require alternative packaging. Other undesirable effects include breakage, delamination, particulates in the suspension, and design flexibility that do not allow for higher doses.

These problems are giving rise to new injection systems evolving to meet the needs of biologic formulations as well as alternate forms of delivery. Some new biologics in development have shown to be highly viscous. They can also require subcutaneous administration, with delivery devices designed to accommodate higher injection volumes.

Enter cyclic olefin polymers (COP), which can be moulded into a variety of shapes and designs. These unique systems with larger fill volumes and tighter dimensional control can be used, while still remaining compatible with established manufacturer filling technologies. These high-quality polymers add value to sensitive biologics through enhanced cleanliness and decreased interaction with the drug product.

Primary containers made from materials such as the Daikyo Crystal Zenith® polymer (Figure 1) can be moulded to contain higher dose volumes or provide delivery options for viscous drug products. These mouldable

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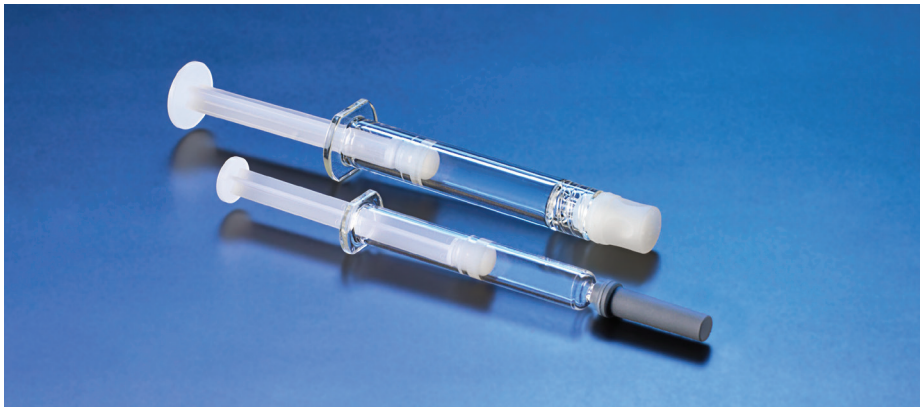

Figure 1: Daikyo Crystal Zenith® polymer syringe systems.

materials offer drug manufacturers the flexibility to create new delivery systems around customised primary containers. When combined with high-quality rubber components with barrier films, such options enable pharmaceutical companies to offer their product in combinations that clinicians and even patients may notice. The containment system could become a differentiator that helps them choose which medication among several competing choices they prefer to use.

## MAKING IT EASIER ON PATIENTS

Treatments for some chronic conditions require multiple and repeated dosing at frequent intervals. Combine that with the new healthcare trend of enabling self-administration in the homecare setting, giving patients an even greater role in deciding which delivery system works best for them. As healthcare systems shift frequent treatment into the home care setting, self-injection systems must not only be designed with a patient-centric focus to improve adherence and outcomes, but also give the pharmaceutical manufacturer an edge in product differentiation.

Biologics are gaining traction in this market sector thanks to attributes that allow for self-administration. But their next-generation formulation and delivery options present multiple challenges when determining containment requirements that can accommodate dose volume, frequency of dosing, a large number of treatments and multiple delivery mechanisms.

Because patient preferences for drug administration will differ, it becomes increasingly clear that there is no "one size fits all" delivery system solution. Some people feel more confident using a prefilled syringe with a needle-safety device, while others prefer a system where the needle cannot be seen, such as a patch-injection system. All can potentially yield freedom from clinical visits and greater patient control of treatment regimens.

While patient preferences will be as varied as much as patients differ from one another, they will likely share some preferences in common. For instance, most will likely rank convenience and portability high on their list of attributes that may help them follow treatment plans more closely.

To address these issues, manufacturers of polymer primary containment and delivery systems have made strides to reduce particulates and improve the quality of materials that are in contact with the drug. They also can customize for larger doses. A typical prefilled syringe dose for a combination product is 1 mL, considered standard for subcutaneous injections by a syringe or auto-injector. Many biologics, however, require doses greater than 1.5 mL, which polymer syringes can accommodate.

## ENHANCING SAFETY

The pitfalls of glass as well as a sharpened focus on safety – now that chronic disease patients are treating themselves more frequently at home – drives pharmaceutical companies' demand for increased quality from drug containment and delivery system manufacturers. While glass remains the standard for injectable drug containment for the prefilled syringe market, the material's higher dimensional variability in manufacturing could be a concern when evaluating the functionality of the syringe or cartridge in conjunction with the delivery system.

Injector systems can aid patients with self-administration while overcoming the challenges associated with biologics. New patch-injector systems can include polymer cartridges that can be designed specifically to hold high-volume doses of sensitive biologics and offer syringe-like filling on standard filling lines. Many of these systems offer subcutaneous, pre-programmable electronic injection that can deliver the drug over extended periods. They can be made more usable with human factors studies, and their electronic indicators can aid in patient medication adherence and improve caregiver monitoring. The SmartDose® system (shown in Figure 2, discussed in more detail in ONdrugDelivery, Issue 51 (July 2014), pp 26-28) strikes a balance between high-quality drug containment and user-friendly delivery.

In spite of the internal system's complexity, SmartDose has been designed for simplicity and patient comfort, while facilitating the delivery of innovative drug products. West has completed the development and validation of the SmartDose electronic wearable injector to support our customers' human clinical trials. We have also

Figure 2: SmartDose® electronic wearable injector for large-volume subcutaneous delivery.

completed our own first-in-human study successfully, which has demonstrated the performance of the system. We are working with our customers at various stages within their drug development process, including clinical studies.

Other options include designs that center on more traditional containers, such as vials, cartridges or prefillable syringes. Customised cyclic olefin polymer syringes have the potential to contain a higher volume of drug than a conventional glass syringe. Polymer options include the Daikyo Crystal Zenith® 1.5 mL insert needle and 1mL long insert needle syringe systems (Figure 3), which may help prevent breakage. The insert needle syringe may help keep medications pure by reducing exposure to extractables and significantly reducing the risk of protein aggregation caused by silicone oil or tungsten, which are not used within the syringe.

Problems with primary containment materials can result in delayed regulatory approvals, packaging variability and in the worst-case scenarios, shortages of needed drug product on the market. All three problems can significantly damage a pharma company's bottom line as well as its reputation. But quality sometimes comes with high costs, so the challenge for drug containment manufacturers becomes achieving the balance between managing the costs of providing higher quality products while staying mindful of the customer's profitability. Polymers can meet at the intersection of reasonable costs and higher quality.

## MANUFACTURING WITH PRECISION

Pharmaceutical and biotech companies can design and develop an integrated system together when they partner early in the drug development process, creating appropriate delivery systems together, sooner. It's particularly effective when these partners implement Quality by Design (QbD) concepts, which are gaining acceptance within the pharmaceutical industry.

In a QbD approach, patient needs drive product specification. The process starts with examining a number of factors: intended clinical setting, dosage strength and delivery mode, sterility, particulate specifications and the container closure system itself. This data-driven component of container development helps ensure the biologic reaches the market in a delivery system that not only helps to protect the drug product's efficacy, but will also help a patient adhere to treatment during any part of the therapeutic lifecycle.

It is the convergence of the drug product itself, the drug manufacturing process and its container closure and delivery systems that establishes the quality attributes necessary for control of specifications such as subvisible particulate, extractables and other quality issues. An example of QbD-designed components includes the West NovaPure® brand of elastomeric components. These products, including vial stoppers and plungers for 1 mL long glass syringe systems were developed with a science-based approach to deliver patient-focused quality over a three-year period. The process paid off by reducing end-of-line rejections and providing high-quality and delivery performance in a variety of systems.

Figure 3: Daikyo Crystal Zenith® 1 mL Long Insert needle polymer syringe system.

Components created through QbD processes that were used in a prefillable syringe system have been shown to optimise break-loose and extrusion performance, provide low part-to-part variability and particulate specification while ensuring high cosmetic quality. When combined with a barrier film, such as West FluroTec® lamination, the components have helped to improve auto-injector performance through dimensional consistency.

## SAFETY, EFFICACY BY DESIGN

From manufacturing to delivery, modern biologics require solutions for lifecycle containment. All components that come into contact with a biologic should be designed with patient safety and ease-of-use in mind, but must also suit the sensitivity of the drug product itself. In addition, regulatory agencies and pharmaceutical companies have increased quality expectations in an effort to enhance patient safety.

Glass containment, while suitable for many drug products, may present compatibility issues with biologics, resulting in safety concerns with regard to protein aggregation and glass particulate. High-quality, polymer containment components can be the foundation for effective, easy-to-use delivery systems. They provide quality containment for sensitive products while, at the same time, offering tighter dimension control, low variability and design flexibility to help create administration systems that may help with patient adherence to treatment regimens.

These options present a total lifecycle solution for injectable drug products that will continue to revolutionise packaging and delivery for biologic drug products. As these drugs gain market share, greater scrutiny is paid to the interaction between the drug product and its container closure system. Stability during shelf life, particulate burden and the ease of delivery to patients are important factors to consider.

Biologic drug products often have unique formulations that require high quality, break-resistant systems that will not react with the antibodies. Packaging systems will require flexibility in design, novel primary containment and innovative delivery systems, such as the West SmartDose electronic wearable injector, as well as a thorough understanding of how the needs of the patient, the drug product, the primary container and the delivery system must come together to drive product differentiation, patient compliance and safety.

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*Daikyo Crystal Zenith® and FluroTec technologies are licensed from Daikyo Seiko, Ltd. SmartDose® is a registered trademark of Medimop Medical Projects Ltd, a subsidiary of West Pharmaceutical Services, Inc.*

*West seeks partners for its SmartDose® injector technology platform. This platform is intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical / biotechnology company.*

## ABOUT THE AUTHOR

Dr Nicolas Brandes is responsible for business development and all project and product management activities related to Daikyo Crystal Zenith products in Europe, working hand in hand with West's strategic partner Daikyo Seiko in Japan. Dr Brandes received his PhD in Biology from the University of Wuerzburg, Germany in 2010, after performing his research studies at the University of Michigan, US.

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