

ENGINEERING NEW SOLUTIONS FOR LIFECYCLE MANAGEMENT

As high-end biotech products continue to enter the market, for use by patients and caregivers outside the clinical setting, issues are arising surrounding compatability of prefilled syringes with safety devices and auto-injectors. Here, Graham Reynolds, Vice-President, Marketing and Innovation, Pharmaceutical Delivery Systems, at West, describes how choosing a new material, Daikyo Crystal Zenith, not only addresses these issues, but brings with it various additional benefits.

Growth in injectable therapies, driven by increased incidence of diseases such as diabetes and auto-immune and inflammatory diseases (including multiple sclerosis and rheumatoid arthritis), has resulted in the development and launch of an increasing number of new biologic drug products designed to treat these conditions. Most of these products require regular injectable delivery, often away from a clinical environment, by the patient or caregiver.

Evidence shows that there is continued growth in the number of biological products

market by revenue demonstrates that most if not all of these products are delivered through injection. These trends are driving the need for prefillable syringe systems and other drug delivery devices and systems that can be used in either a clinical or home care setting.

Such home-based administration has spawned an increased need for combination drug delivery systems that are safe and convenient, and that help improve the preparation and injection processes, while ensuring the efficacy and compliance of the drug product .

Among the earlier solutions for those with frequent injection needs were pen injectors and multi-dose cartridges. However, these products are limited to specific therapies such as diabetes and growth hormones, which often require weighed dosages or dose titration. While pen injectors are designed for frequent injections and for those who require variable dose capabilities, they are not ideal for chronic users of fixed-dose medications, including those suffering from dexterity issues.

Auto-injectors have been recognised as a convenient method for delivering drug products through an intuitive activation mechanism designed especially for patients who may have dexterity issues that impact their ability to inject a drug treatment effectively with a traditional syringe. As patients and caregivers

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becoming available, and that most of these require delivery by injection. Alternative delivery routes continue to be evaluated. However, technology limitations and drug characteristics have led to injectable delivery still being considered as the preferred, if not the only, delivery route. An analysis of the top 20 biologics on the



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Figure 1: Daikyo Crystal Zenith® Luer Lock Syringe (top) and insert needle syringe (bottom).

become increasingly involved in determining the best treatment option, biopharmaceutical and pharmaceutical companies, with the help of device companies, are adapting to meet the needs of the consumer.

Today’s auto-injectors represent a compelling, easy-to-use delivery solution rooted in simplicity, accuracy, durability, flexibility and quality.

Auto-injector systems traditionally utilise 1 ml, long, glass prefilled syringes. These systems have been successful, but they have notable limitations, including:

- **Breakage** – Any glass product runs the risk of breakage during manufacture, storage and shipping. Additionally, glass syringes which were traditionally designed for manual injection create challenges for auto-injector manufacturers when these systems need to be designed to cope with the wide dimensional tolerances and inherent weaknesses of glass syringes. Incidents of glass breakage during activation of an auto-injector have led to US FDA concerns and recalls in specific cases.
- **Performance Issues** – Studies have shown that silicone oil, necessary to ensure lubricity and effective operation in glass syringe systems, can be distributed unevenly, leaving surface

areas with insufficient lubrication. This will greatly increase the force required to operate the auto-injector and could lead to delivery of a partial dose to the patient if the piston should “stall” before it reaches the end of the syringe.

“THE CRYSTAL ZENITH 1 ML, LONG INSERT NEEDLE SYSTEM IS THE FIRST SYSTEM OF ITS KIND TO USE NO SILICONE OIL FOR SYRINGE FUNCTIONALITY AND REQUIRES NO ADHESIVE TO HOLD THE NEEDLE IN PLACE.”

Increasing the force necessary to eliminate this stall factor can create additional challenges due to extra force on weaker parts of the glass syringe, such as the flange area. In developing the ConfiDose® disposable auto-injector system, West can provide a system that overcomes many of the inherent challenges related to glass syringes by distributing the forces onto less fragile areas of the syringe, and safely providing a higher force that can allow for the delivery of high-viscosity products.

- **Interaction between the biologic and the syringe system** – Silicone oil and tungsten residues have been reported to induce protein

aggregation in prefilled syringes, causing particle generation.

The solution to these issues can be found in creating a syringe system from novel materi-

als, including cyclic olefin polymers. One such solution is the Daikyo Crystal Zenith® insert needle syringe system (see figure 1, bottom).

THE NEED FOR PLASTIC SYRINGE SYSTEMS

In 2006, commercial lots of a drug product delivered by an auto-injector that contained a glass prefilled syringe were recalled in several European countries because of problems with slow or incomplete delivery of the drug. There was a similar occurrence in 2009 in the US, when an auto-injector batch was recalled due to high force-to-fire values.

Such issues with performance and quality have the potential to affect a company's bottom line significantly, not to mention patient safety and the effective application of the drug product. Failures of finished drug product (defects during manufacturing process and distribution), as well as internal failures in product development and production, can greatly increase manufacturing costs. Recalls based on breakage, aggregation or performance may require costly preventive actions and process improvement, and the overall response from the market to such problems can shake consumer confidence in the company and its product.

The Daikyo Crystal Zenith® 1 ml, long insert needle syringe system is a first-in-class solution to the issues faced by many manufacturers.

"WEST AND DAIKYO WORKED CLOSELY WITH FILLERS AND MACHINE VENDORS TO DEVELOP THE INSERT NEEDLE AS A READY-TO-FILL SOLUTION THAT IS COMPATIBLE WITH EXISTING FILL LINES."

Polymers like Crystal Zenith resin possess many advantageous properties, including glass-like transparency, which permits visual inspection of the manufactured components and of the parenteral products that are delivered to the end user. In addition, Crystal Zenith polymer is highly break resistant and forms an excellent moisture barrier.

Plastic prefilled syringes can eliminate the need for silicone oil and adhesive, depending on the quality attributes of the entire prefilled system, and do not use tungsten pins that are commonly used in forming glass syringe barrels. The Crystal Zenith 1 ml, long insert needle system is the first system of its kind to use no silicone oil for syringe functionality and requires no adhesive to hold the needle in place.

Instead, the system relies on lamination of the syringe piston with Flurotec® barrier film, which helps to lower protein adsorption and serves as a barrier to leachable substances. The fluorocarbon film provides an effective barrier against organic and inorganic leachables and extractables, and helps to maintain the strength and shelf-life of most drugs. When used in combination with B2-Coating, Flurotec coating provides lubricity without the need for silicone oil.

When used within an auto-injector, such as West's ConfiDose® auto-injector system, Crystal Zenith polymer's tight dimensional tolerance and consistency of syringe functionality can help to make an auto-injector's operation

predictable – which makes it an easy-to-use, safe option for the patient, while mitigating risk associated with performance issues or breakage for manufacturers.

A BREAKTHROUGH IN ENGINEERING EXCELLENCE

The Crystal Zenith insert needle syringe system is manufactured by West in conjunction with its partner, Daikyo Seiko Ltd, at a state-of-the-art delivery systems facility in Scottsdale, AZ, US. Because it is unique to the market, new processes were created to manufacture the system.

Since the insert needle is molded directly into the syringe, robotic handling is used to

optimise quality and minimise biologic contamination. Once manufactured, the syringes are sent through a rigorous vision inspection that mitigates contamination and defect risk. This process helps to lower rejections on the pharmaceutical company's production line.

In addition, the needle is X-ray inspected to ensure proper positioning, which benefits the end-user by minimising pain upon injection, as well as ensuring sterility. Proper positioning also helps to assure effective drug delivery. The insert needle syringe system is produced in a ISO Class 7 clean room, and is then packaged in trays and sealed, prior to sterilisation.

West and Daikyo worked closely with fillers and machine vendors to develop the insert needle as a ready-to-fill solution that is compatible with existing fill lines. As such, manufacturers do not need to pre-treat the needle in any way – it is a fully-validated, sterilised system, designed to be compatible with their existing filling lines, or those that exist at leading contract fillers.

The combination of the unique Crystal Zenith material, engineering excellence, high quality manufacture and West's extensive knowledge of the needs of the pharmaceutical and biotech industries, driven by over 80 years' leadership in packaging and delivery systems for injectables, has led to an exciting new development, which may become the packaging solution of choice for all high-value biotech products.

A TESTED SOLUTION TO LIFECYCLE MANAGEMENT

The insert needle syringe system builds on West and Daikyo's portfolio of products made with Crystal Zenith resin. The material has been in production and in commercial use with marketed drugs in the US, Europe and Japan for many years. Customers can select Crystal Zenith materials with confidence that the material is market-approved.

In addition to the insert needle syringe system, customers can select from a variety of lifecycle containment solutions – thus keeping their product in the same material from discovery through commercialisation. Solutions include:

- Screw-top containers to store and transport drug products or drug substances
- Vials for serum and lyophilised drugs
- Luer lock syringes (shown in Figure 1, top)
- Cartridges for biopharmaceutical drug delivery applications
- Customised containers can be developed, specifically designed to interface with a delivery device

By using a Crystal Zenith resin product through the drug's lifecycle, a company can: offer superior protection in a silicone, tungsten and adhesive-free system; simplify regulatory filings; and avoid manufacturing delays caused by the need to continually test container closure systems.

As a one-source solution to production, West offers the technical expertise pharmaceutical companies need to develop a unique system for their drug product.

Materials like Crystal Zenith resin are the new standard for high-end biopharmaceuticals. Thanks to flexibility in design, such materials can be created to suit almost every need at any time during the lifecycle of a drug.

By choosing a single source for manufacturing, drug companies will not only mitigate risk and help to ensure patient safety, they will also receive the benefits of a partnership that will aid in the traditional areas of regulatory and compliance support, but also in the design and manufacture of unique systems that can differentiate products in a crowded market.

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Advance Your Delivery System with Daikyo Crystal Zenith[®] Insert Needle Syringe Technology

Breakage. Functional Performance. Aggregation.

These issues and more can affect your product, and thus your top and bottom line. And glass syringes may be at the heart of the problems.

Made of cyclic olefin polymer, the Daikyo Crystal Zenith Insert Needle Syringe System provides an innovative solution to the limitations of glass syringes, especially with sensitive biologic drug formulations.

System advantages include:

- High break-resistance
- 100% vision inspection assures the highest quality
- Flurotec[®] film on the piston for barrier protection and superior functional performance
- No silicone oil on the syringe barrel or piston
- No tungsten or adhesive
- Tight dimensional tolerance and consistent functionality when used in auto-injector systems

Evolve to a superior prefillable syringe technology.

Contact a West representative to learn more about the Daikyo Crystal Zenith Insert Needle Syringe system. Call 800-231-3000 or visit westpharma.com today.



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