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POLYMERS, GLASS AND PARTICULATES: CHOOSING THE BEST CONTAINMENT FOR CUTTING-EDGE BIOLOGICS

In this piece, Kevin Cancelliere, Marketing Director, West Pharmaceutical Services, Inc, provides a run-down of the benefits that cyclic-olefin polymers syringes can bring compared with glass, including better dimensional tolerances and the ability to be moulded into more complex shapes for innovative delivery systems, as well as reduction of particulate contamination, in particular for biomolecular therapeutics that are not compatible with glass.

As more biologics and biosimilars come onto the market, they present unique packaging and containment challenges. Many biotech drugs are sensitive injectable drug products that can interact with containers and packaging components made from glass, potentially leading to delamination, particulates or protein aggregation. Additionally, some biopharmaceuticals have a high pH; others require storage at extremely cold temperatures. These nuances and sensitivities are putting demand on drug manufacturers and their packaging and delivery system providers to provide innovative, sophisticated solutions for securely containing and delivering advanced therapies while ensuring both drug efficacy and patient safety.

For materials that are sensitive to glass or that may require larger dose volumes or custom configurations, cyclic-olefin polymers (COPs) may offer a solution. These materials for drug container closure systems can provide a smart alternative to traditional glass containment systems for advanced therapeutics. They can also help drug manufacturers differentiate their product through container closure systems that offer more flexibility in the types of shapes and configurations used to package and deliver the next generation of injectable therapeutics.

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CHALLENGES OF GLASS

The pharmaceutical industry has traditionally used glass as a primary material for containment systems due to a variety of characteristics that enable generally safe and efficient drug storage. Glass is readily available and in many cases works very well. Yet glass is not an inert material. Its chemistry can and does interact with certain medica-

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Figure 1: Daikyo Crystal Zenith® 1 mL Insert needle syringes.

Figure 2: A selection of vials made from Daikyo Crystal Zenith®.

tions in ways that can alter a drug's safety, stability, purity or effectiveness. Certain additives used in glass container closure systems, such as silicone oil applied to the inner walls of glass syringes, may also interact with sensitive injectables.

In its guidance, "Immunogenicity Assessment for Therapeutic Protein Products," the US FDA called attention to risks commonly associated with container closure systems, including denaturation and aggregation of proteins at glass-air interfaces; delamination and particulate formation in certain drug formulations; protein aggregation associated with silicone-lubricated containers; and leachables from container components. These issues may affect product quality and immunogenicity.

The recommendations come at a time when such issues have led to an increase in the number of FDA recalls. For instance, in 2011, ten drug product recalls were caused by glass particulates in injectable drug products. The pace continued in 2012 with recalls of 19 lots of four different injectable oncology products caused by the discovery of glass particles.[1,2]. The direct and indirect costs of a drug product recall may result in the loss of millions, and may also affect a company's reputation, market share and consumer trust. Although recalls caused by glass breakage and particulate peaked in 2011, the issues persist and patient safety may be affected. In fact, in the past ten years the FDA has recalled 25 drugs for breakage, and more than 20 more for particulates. It adds up to more than 100 million drug units recalled in total.[2]

GLASS ALTERNATIVES TAKE CENTRE STAGE

To help solve fundamental incompatibilities that may exist between a drug formulation and its container closure system, manufacturers are exploring and adopting alternative materials for drug packaging and containment systems – including COPs such as West's Daikyo Crystal Zenith® – that can help assure the stability of an injectable drug product.

Because COPs are more stable than glass, these polymer-based containment systems can help mitigate the risk of particulate contamination. Additionally, they can be moulded to a variety of shapes to provide customised containment solutions throughout a drug product's lifecycle. Such choices early in development may also aid decisions later in the manufacturing cycle. COPs also offer improved dimensional tolerance and design flexibility, so innovative container/device combinations can be considered to help optimise the overall system design based on the needs of the patient. In addition, COPs can be moulded to suit innovative delivery systems, offering differentiation in the market. For example, an insert needle prefillable syringe, such as the Daikyo Crystal Zenith 1 mL Insert needle syringe (Figure 1), could be utilised for a drug product with metal and silicone oil sensitivities.

ASSESSING MATERIAL COMPATIBILITY

No matter which container closure system is considered for an injectable drug, it is essential to assess the compatibility of the system's materials with the drug product in order to understand the impact on quality.

Selection of suitable container closure systems can be best judged through the performance of risk assessments based on an understanding of the physical, functional and chemical characteristics of the container closure system along with drug product. During drug development, materials that will be in contact with the drug product should be evaluated for protection, function, compatibility and safety. The drug-container interaction, adsorption, chemical resistance and the stability of packaging over time and in extreme environments are critical to the manufacturing, storage, distribution and integrity of the marketed product. By carefully assessing how the materials in a drug's container closure system interact with the drug product over time, manufacturers can best understand the potential risks to drug quality and patient safety.

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PARTNERING FOR QUALITY

To ensure the safety and efficacy of a drug product, pharmaceutical manufacturers should partner with drug packaging and delivery experts to properly evaluate material compatibility and select the highest-quality container closure system for a particular drug product.

Collaborating with a single partner with diverse expertise in primary packaging, delivery systems and custom design can help ensure the optimal packaging and containment solution throughout a drug product's lifecycle. Packaging manufacturers who also provide analytical laboratory services can offer product recommendations on the latest alternative technologies and provide prescreen stability work early in the process to ensure that the containment materials do not react with the drug product.

One of the most important services a packaging company can provide is material and stability testing. While it may not be possible to tell which drug product and delivery system interactions may result in delamination, several tests can help predict the possibility. Delamination can occur at any point in the drug manufacturing process, including vial manufacture and heat treatment or sterilisation processes. Container closure systems can be examined microscopically for visible indications of defects, particles, pitting or delamination before filling. For example the neck and base of a vial (see Figure 2) represent areas of high stress in the glass; microscopic evaluation of these areas after exposure to a stressed environment can detect the potential for delamination. Validating packaging and containment choices through materials testing processes can help eliminate problems that could potentially lead to costly recalls and safety issues with patients.

As the next generation of drugs become available, the limitations of glass container closure systems are becoming more pronounced. As a full product lifecycle solution, COP-based systems are quickly becoming an ideal solution for their ability to provide a high-performance, low-risk alternative. Working together, pharmaceutical and packaging and delivery systems companies can develop innovative COP containment solutions that can safely contain today's advanced biopharmaceuticals.

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REFERENCES

1. *"Breakage and Particle Problems in Glass Vials and Syringes Spurring Industry Interest in Plastics". IPQ In the News, IPQ Publications LLC, August 7, 2011.*
2. *"Enforcement Reports," FDA. (Retrieved from (www.fda.gov/Safety/Recalls/EnforcementReports/default.htm)*

ABOUT THE AUTHOR

Kevin Cancelliere joined West Pharmaceutical Services in January 2013 as Director of Marketing, Pharmaceutical Delivery Systems. Kevin brings almost thirty years of broad operational and strategic marketing and sales experience to this position. He comes to us from Vicept Therapeutics where he was Senior Director, Project Management for an investigational drug for the treatment of Rosacea. Prior to Vicept, Kevin was the Senior Director, US Marketing at Wyeth Laboratories. Kevin holds a BS in Biology from De Sales University and a Masters in Biochemistry from Thomas Jefferson University.