Blockbuster Drugs Need Blockbuster Components

Many of the world's blockbuster drugs are now delivered via a prefilled syringe system or auto-injector. To ensure patient safety, pharmaceutical manufacturers need high-quality components that feature reduced particulates and ensure consistency of delivery while fitting the changing needs of higher-volume delivery systems.

West's 1ml long NovaPure® plunger is made from best-in-class elastomeric formulations and developed to optimize injection performance and consistency.

These blockbusters – many of them biologics – differ from traditional injectables: larger molecules and long-acting formulations often are distinguished with increased viscosity (5-30cP) and increased dose volume (1.0mL - 3.5mL). Such new characteristics require more customized containers, larger volume delivery systems and plungers that can accommodate higher doses.

Enter NovaPure® components from West Pharmaceutical Services. West provides drug delivery systems and components to the top drug manufacturers around the world. NovaPure components, which include the 1-3mL and 1mL long NovaPure plungers and 13mm and 20mm NovaPure lyo and serum stoppers, utilize Quality by Design (QbD) principles[i] to help ensure superior quality and function for patients who need these injectable biologics in higher doses. With a QbD approach, components are manufactured in a manner that ensures reliability and, most importantly, patient safety.

New Drugs – New Containment

Manny patients who are diagnosed with chronic diseases now have new hope for a better quality of life with biologic drugs. This trend is likely to continue in the future, with the IMS Institute for Healthcare Informatics predicting that the market for biologics will grow to $221 billion by 2017.[ii]

Along with the rise in biologic drugs comes a corresponding increase in self-administration systems. Patients receiving these medications can gain new freedom from a physician's office or clinic visits for each treatment. As the availability of these drugs continues to grow, drug manufacturers increasingly require safe and effective packaging that addresses both the specialized characteristics of injectable biologic drugs and the high-performance requirements of self-injectors.

Market trends toward patient self-administration have made prefillable syringe systems – and self-injection systems that utilize them – ideal choices for many single-dose drugs. For drug manufacturers,

prefilled syringe systems for biologics and other injectable drugs offer convenient, fixed-dose options that are easily adaptable to automated injection devices.

Moreover, prefillable syringe and self-injection systems can reduce therapy and injection costs, as well as significantly reduce overfill when compared to single-dose vials. Prefillable syringe systems may also optimize the number of doses from the existing drug supply, while offering delivery options that can help to differentiate drug products in an increasingly crowded market.

Effective treatment requires that a drug's delivery system is easy to use, reliable and consistent. As part of an integrated delivery system, packaging components play an important role in drug quality, patient safety and device performance. They, therefore, must be given careful consideration as part of the drug development process. Many pharmaceutical customers employ NovaPure stoppers for pharmaceutical containment and NovaPure plungers for their integrated delivery systems.

Regulatory agencies around the world are driving drug and packaging manufacturers to build quality into their products from the start to ensure consistent quality throughout a drug product's lifecycle. The increase in biologic drugs coming on the market, especially as combination products, has increased regulatory scrutiny of compatibility between drugs and their packaging components and delivery.

In the United States, the Food and Drug Administration (FDA) defines a combination product as, "A product comprised of any combination of a drug and device; a device and biological product; a biological product and a drug, or a drug, a device and biological product."[iii] Manufacturers of combination products in the U.S. must abide by two FDA regulations for good manufacturing practice:

- cGMP Finished Pharmaceuticals part 21 CFR 210-211
- QSR Regulation for Devices 21 CFR 820

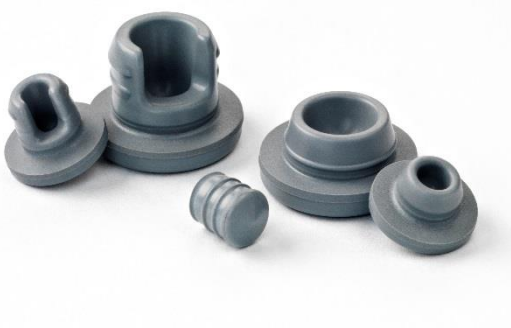
Some of the primary areas covered by CFR 820, and that differ from CFR 210-211, include management responsibility, purchasing controls, corrective and preventive action and design controls. As part of the industrialization of syringe plungers using the QbD approach, aspects of 21 CFR 820 must be incorporated into the manufacturing process. These regulatory requirements are challenging drug makers to look for consistent, reliable, high-quality packaging components that meet the standards of good manufacturing process as well as the high expectations of end users.

The adoption of QbD concepts in the design and manufacturing of packaging components is gathering momentum within the industry. QbD delivers an improved, data-driven output, providing manufacturers with superior product and process understanding that minimizes risk, emphasizes patient-critical quality requirements and enhances drug product effectiveness.

The scientific, risk-mitigation based QbD approach is fast becoming an essential strategy for bringing high-quality therapeutics to market quickly and efficiently. By building QbD principles into design and development from the very beginning, manufacturers can decrease variability in the manufacturing process and the end product. High-quality components designed using QbD processes can enhance the

performance of drug delivery systems and protect sensitive drug products with exceptional cleanliness and barrier properties, while helping to ensure patient safety and drug product efficacy.

Quality is the Differentiator



West NovaPure® stoppers are consistent, reliable, high-quality components that are developed under Quality by Design principles to mitigate risk and meet patient needs.

According to the recent "Drug Delivery Products" report from industry market research firm The Freedonia Group[iv], demand for parenteral drug delivery devices is projected to rise more than 10 percent annually to $86.5 billion in 2019, with prefillable syringes accounting for the largest and fastest growth. These findings show that combination products using prefilled syringes, auto-injectors and other self-injection systems are rapidly gaining momentum among drug manufacturers.

For patients requiring frequent dosing, prefillable syringe systems offer ease of use and enhanced convenience and, when combined with an auto-injector system, can provide a more portable drug delivery system. Prefilled syringe systems can also potentially minimize microbial contamination and reduce medication dosing errors.

With many biologic drugs in development requiring injectable dosage forms, drug manufacturers are increasingly exploring prefillable syringe and self-injection systems for their administration. However, these advanced therapies often have very specialized needs. Many are highly viscous and use larger dosing volumes, requiring larger containment systems and slower dosing regimens. Additionally, because of their complexity, biologics pose greater risk of adverse interaction and incompatibility with the materials of their container/closure system. The demands on packaging components are changing in this new era. It is essential to package these drugs with high-quality components that can help protect safety, efficacy and purity.

By considering the impact of prefillable syringe systems and their components on a particular drug product early in the drug development process – and employing QbD strategies to overcome development challenges – drug manufacturers can minimize the quality risks and position the product to meet their product lifecycle needs.

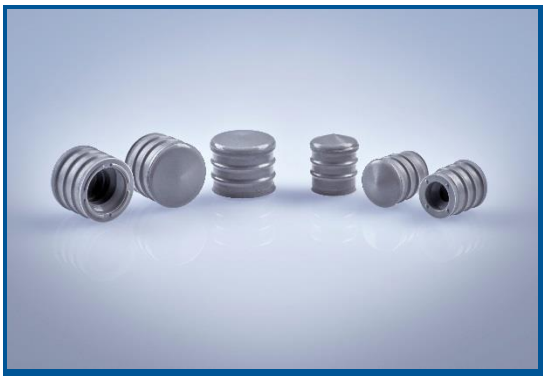
The QbD approach promotes a holistic understanding of the drug product, its integrated delivery system and the manufacturing process. An effective QbD strategy starts with defining desired product performance goals and identifying the product's Critical Quality Attributes (CQAs). The product and process are then designed to meet those attributes, by building a mechanistic understanding of how the process parameters impact the CQAs, enabling manufacturers to control and reduce variability.

The design and manufacturing of high-quality components should follow a development lifecycle program that uses a Quality Target Product Profile (QTPP) to establish CQAs for control of any number of performance variables. The QTPP can serve as a guideline throughout the development process –

which should include risk-based design inputs, Finite Element Analysis (FEA) modeling, data generation on multiple concepts and final product performance verification with barrels from multiple suppliers – to ensure that targeted specification values for breakloose and glide force are met.

As a result of this knowledge, a company can continually monitor and improve its manufacturing process to ensure consistent product quality.

Plungers a Key Component for Injectable Drug Delivery



West's 1-3mL NovaPure® plunger—an innovative, high-quality component for pre-filled delivery systems.

Prefillable syringe plungers are a particular class of products that are essential to understand and assess during the QbD process. Plungers (also called pistons) are critical elements because they serve as the primary seal for container/closure integrity, maintaining drug purity during shelf life, and function to deliver the drug to the patient. Plungers are typically made from butyl rubber and can be coated with a fluoropolymer film that can increase lubricity and serve as a barrier between the drug and the elastomer, reducing the potential for extractactables and leachables. Evolving industry demands for higher-quality components have increased the need for plungers developed using QbD processes.

By applying a holistic, QbD approach to the design and development of plungers and other prefillable syringe components, packaging manufacturers can gain a thorough understanding of both the product and the process. This, in turn, enables multiple benefits for manufacturers and end users, including:

- Improved functionality by optimizing breakloose and glide forces
- Improved patient confidence by encouraging device use and more accurate dosing
- Mitigated risk of extractables and leachables
- Enhanced efficiency in manufacture and support of a reliable drug supply

Use of QbD principles ensures that components are developed using science-based and data-driven decisions. The knowledge gained throughout the QbD process can be used on an ongoing basis to maintain continuous improvement by the manufacturer.

New Component Offerings for High-Quality Packaging Solutions

Patient safety needs and increasing regulatory concerns are spurring drug manufacturers to look more closely at component quality attributes for packaging their injectable drugs. The increased trend toward biologic drugs and self-administration requires manufacturers to select components having a high level of reliability, consistency and compatibility with complex drug products and delivery systems throughout their lifecycle.

Drug packaging components play a vital, but often overlooked, role in drug safety and efficacy. They are a critical part of integrated combination products and are essential to ensuring delivery systems are safe, intuitive and easy to use, but it can be difficult to know which component is the best quality fit for a particular drug product.

Fortunately, there are new component offerings on the market designed to address the need for high-quality packaging solutions. These include prefillable syringe plungers designed using QbD principles to provide high reliability for breakloose and glide force, dimensional accuracy and consistency, extractable and sub-visible and visible particulate control and low parts per million (ppm) defect attributes.

To maximize a drug product's safety and efficacy, pharmaceutical companies and their packaging and delivery partners are building quality principles into the entire manufacturing process, from design and development to commercialization and administration. Selecting a packaging partner with expertise in QbD early in the development process can help pharmaceutical manufacturers lower their total cost of ownership through reduced compliance risk, filling rejection rate and process costs. Full return on investment can be realized once a drug product is commercialized and has gained patient loyalty through ease of use, therapeutic benefit and high confidence in the delivery device.

Most importantly, components created through a QbD approach offer features designed to ensure the highest levels of reliability and performance, ultimately helping the pharmaceutical industry to achieve its most critical goal: providing the safest and most effective drug products for their patients.

[i] The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Pharmaceutical Development: ICH Q8/Q(8)R. December 2008.
[ii] IMS Institute for Healthcare Informatics. The Global Use of Medicines: Outlook through 2017. November 2013.
[iii] U.S. Food and Drug Administration. Combination Products. Accessed February 2016.
[iv] The Freedonia Group. Drug Delivery Products. December 2015.