RISING TO THE REGULATORY EVIDENCE CHALLENGE FOR HIGH-QUALITY COMBINATION PRODUCTS

In this article, Victoria Morgan, Director Strategic Marketing, Biologics, and Stacy Gates-Rector, PhD, Principal Scientist, Scientific Communications, both at West Pharma Services, explore how West is supporting pharma companies with packaging challenges through the supply of high-quality prefillable syringe plungers and provision of a highly co-ordinated technical documentation package.

When it comes to the regulation of medical devices, standards are only going in one direction. The recent revision to the medical devices requirements, which resulted in the publication of the EU Medical Device Regulation (MDR),[1] shows how the activities of pharmaceutical companies must continually adapt and adhere to ever higher regulatory thresholds, driven by an impetus to enhance quality, safety and effectiveness.

However, while all stakeholders applaud this direction of travel, there is no escaping the fact that it has made the product development journey more challenging. As well as ensuring that combination products are designed, specified and developed to meet updated regulations, pharma companies must also deliver a comprehensive dossier of data to evidence compliance. Answering the full breadth of these requirements relies on having access to the right data at the right time and presenting it in the correct form, or the process can quickly become mired in complexity, delays and unnecessary cost.

West is able to support pharma companies faced with these packaging challenges, not just through the supply of high-quality prefillable syringe plungers, but also through the provision of a highly co-ordinated technical documentation package (TDP). This service offers significant value for streamlining the gathering, assimilation and delivery of supporting data across multiple criteria, having already allowed several customers to demonstrate regulatory compliance with greater speed, efficiency and ease.

A DEVELOPMENT BORN OUT OF TRAGEDY

In 2010, it was revealed that almost 400,000 women had received breast implants from PIP (Poly Implant Prothése) that featured unapproved industrial-grade silicone instead of approved medical-grade silicone. Many of those with industrial-grade silicone ruptured, causing serious illness and, in some cases, death (Figure 1).[2]

In September 2012, this incident, set against a backdrop of a no longer fit for purpose framework, prompted the European Commission to propose a switch to the new medical device regulations from its existing medical devices directive to ensure the safety, effectiveness and quality of medical devices in the EU. The EU's MDR (2017/745/EU) was officially published on May 5, 2017, and came into force on May 25, 2017. The MDR replaced the EU's previous Medical Device Directive (93/42/EEC) (MDD) and the EU's Directive on active implantable medical

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Figure 1: As a result of the PIP breast implant scandal in 2010, the European Commission introduced new rules for the regulation of medical devices to ensure safety, effectiveness and quality of medical devices in the EU.

devices (90/385/EEC). Compared with the EU directive it replaced (93/42/EEC), the MDR places far greater emphasis on patient safety linked to the use of a device and sets out a far more comprehensive set of enforced requirements for pharmaceutical manufacturers to follow.

The MDD had a legacy of nearly 30 years and was focused primarily on getting a product to market. The MDR, however, expands its sphere of influence to consider the full product lifecycle – development, testing, manufacturing, commercialisation, efficacy, safety and long-term use. This is not to say that the MDD ignored those elements, merely that the MDR specifies their application in greater detail.

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The implications of this update are wide ranging for both manufacturers and notified bodies as the level of rigour around required quality increases. The new regulations impose stricter rules on product design and development, clinical evidence and post-market surveillance, among other considerations.

Alongside stricter rules comes increased scrutiny by the regulatory authorities. This includes greater oversight of clinical studies and more stringent requirements for post-market surveillance, reporting of adverse events and increased transparency and traceability of products throughout the supply chain.

ALLEVIATING THE BURDEN OF PROOF

One aspect where pharma partners are really feeling the weight of that burden and subsequent scrutiny is the creation of the relevant documentation. This includes a detailed review of technical documents to evidence a device's general safety and performance requirements (GSPRs). It also requires the interrogation of the clinical evaluation report, which contains testing data on the clinical use of a device.

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As part of a wider information-gathering process, these documents are reviewed in accordance with Annex I of the new MDR, which informs the risk-based assessment conducted by the notified body.

Because of its rigorous nature, the process for assessing conformity is not necessarily a straightforward one, as the process is new and notified body assessments can diverge, with room for interpretation on both the pharmaceutical company and notified body sides. These open areas of interpretation can potentially result in delays to the marketing authorisation applicant receiving a notified body opinion if submissions are not satisfactory. Issues such as incomplete submissions are commonplace. In such cases, there is often insufficient information provided to demonstrate compliance with the MDR, or even that the supplied technical documentation is poorly structured. All of which can complicate the notified body's already arduous task of appraising all the supplied materials.

Historically, the process of gathering such technical information has been somewhat reactive and iterative, perhaps even haphazard, as each question is addressed individually rather than approached from first principles as a whole. As a result, the gathering of data and documentary evidence has become arduous, expensive and time consuming – aspects of any process that can lead to project creep and enhanced risks. West recognises that such a fragmented approach potentially adds unnecessary time, cost and complications to an already stressful process, and the company has identified the opportunity for a smarter, more streamlined, approach.

Simply put, West embraces its Quality by Design (QbD) principles and ensures that

they are now a feature of its documentation offer. With the company's knowledge of the process, clarity around the kind of information and data required, and a deep understanding of its pharma partners, West is able to compile and co-ordinate all necessary technical information relating to the components for filing with timeliness and efficiency – all from a single point of contact. This approach further reduces the burden of accessing the right information at the right time, as opposed to navigating through several gatekeepers of data, which is often the case within the supply chain.

Following the completion of a successful pilot programme with a global top 10 pharma company, West termed this offer the "TDP". The pilot supported a pharmaceutical customer with an MDR filing for a new drug product delivered via a prefilled syringe system by addressing the recognised challenges associated with the filing process, including the need for cross-organisational stakeholder management and the co-ordination of consistent responses.

In what became a close and mutually beneficial collaboration between two assigned stakeholders within each organisation, West adopted a strategic, proactive approach to gathering, assimilating and presenting the required data at a level of detail and in a format that would satisfy scrutiny by the notified body. By focusing efforts on the "right first time" delivery of high-quality and highly relevant information connected to the specific GSPRs, the company was able to minimise requests for supplemental information, avoid complex multi-document iterations and truncate the entire certification process.

Historically, such an undertaking would have been incredibly resource heavy, with multiple stakeholders making up to 50 information requests in a three-month period. With hundreds of hours required, this would have been an expensive exercise. Under the new protocol, the TDP was presented without observations, enabling the customer to move quickly, efficiently and cost-effectively to marketing authorisation application.

"Together with the TDP, NovaPure® plungers adhere to QbD principles featuring the tightest specifications within the West portfolio, readily applicable within today's formulation and manufacturing process."

QbD FROM PACKAGE TO PLUNGER

Not only was the pilot programme a success for the customer, it also provided West with the TDP platform that supports applications for 1 mL long and 1–3 mL NovaPure® plungers. This comprehensive package features over 30 documents, including compliance bulletins, biocompatibility reports, quality statements, comprehensive performance data, extractables evaluations, packaging configurations and component drawings. This package is then enhanced with data specifically related to the customer and its drug product.

Together with the TDP, NovaPure® plungers adhere to QbD principles featuring the tightest specifications within the West portfolio, readily applicable within today's formulation and manufacturing process. The TDP platform is designed with functionality that makes navigating and/or extracting information from the package a clear and concise process, which helps to prevent unnecessary delays to the assessment process.

CONCLUSION

The global prefilled syringes market size was US$7.22 billion (£5.8 billion) in 2022 and is projected to grow from $7.91 billion in 2023 to $16.32 billion by 2030 at a Compound Annual Growth Rate of 10.9%.[3] As such, increasing numbers of pharma partners will be subject to the MDR as they look to access the opportunities within the EU. With a deadline for a quality management system being set in place for May 26, 2024, pharma partners need to look towards organisations that can support them with a comprehensive TDP that not only delivers the requisite data requirements, but also saves time, money and resources.

NOVAPURE®

NovaPure® is a registered trademark of West Pharmaceutical Services, Inc. in the United States and other jurisdictions.

ABOUT THE COMPANY

West Pharmaceutical Services is a leading provider of innovative, high-quality injectable solutions and services. As a trusted partner to established and emerging drug developers, West helps to ensure the safe, effective containment and delivery of life-saving and life-enhancing medicines for patients. With 10,000 team members across 50 sites worldwide, West helps to support customers by delivering approximately 47 billion components and devices each year.

REFERENCES

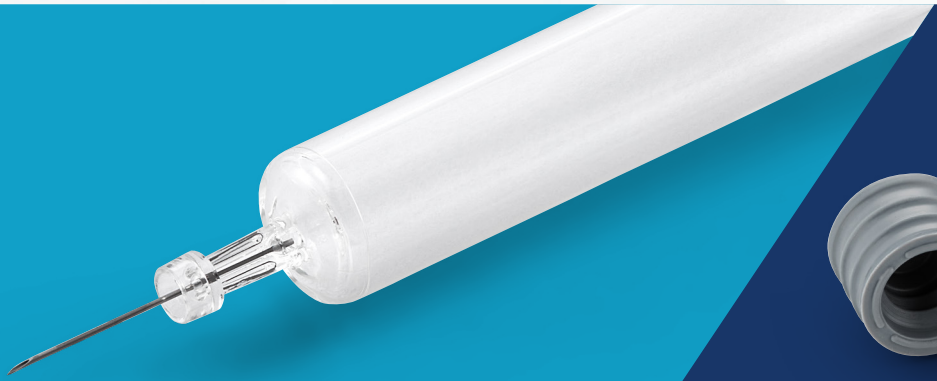
1. *"Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC". EUR-Lex, accessed Sep 2023.*
2. *Kelland K, Flynn D, "French breast implant fears spread around world". Reuters, Dec 22, 2011.*
3. *"Prefilled Syringes Market Size, Share & COVID-19 Impact Analysis, By Material (Glass and Plastic), By Closing System (Staked Needle System, Luer Cone System, and Luer Lock Form System), By Product (Complete Syringe Set and Components & Accessories), By Design (Single-chamber, Double-chamber, and Multiple-chamber), By End-user (Pharmaceutical & Biotechnology Companies, Contract Research & Manufacturing Organizations, and Others), and Regional Forecast, 2023-2030". Fortune Business Insights, Jul 2023.*

ABOUT THE AUTHORS

Victoria Morgan, Director Strategic Marketing, Biologics, has global marketing responsibility for West's biologics business, which strives to develop high-quality products and services to help pharma companies serve unmet patient needs with biologic molecules. She brings a wealth of knowledge about scaling drug development through to and beyond commercialisation, predominantly in injectable drug delivery products including vials and combination products. Currently, Ms Morgan has responsibility for West's global biologics strategy development and implementation. Throughout her tenures at West, Lilly and Sanofi, Ms Morgan has served in various functions across sales and marketing, and she earned her Bachelor's degree from the University of Wales, and her MBA from INSEAD Business School in Paris.

Stacy Gates-Rector, PhD, has worked as a chemist and material scientist for over 10 years and has a diverse background in analytical characterisation. At West, Dr Gates-Rector works as a Principal Scientist managing various aspects of component performance projects, using the technical data gathered from these projects to generate customer documents that help promote adoption of high-value products and services. Prior to joining West, Dr Gates-Rector worked as a senior scientist characterising crystal structures of drug product. She holds a Bachelor's degree in Chemistry and a PhD focused on material science, crystallography and diffraction.

The Highest Standards in Risk Mitigation.



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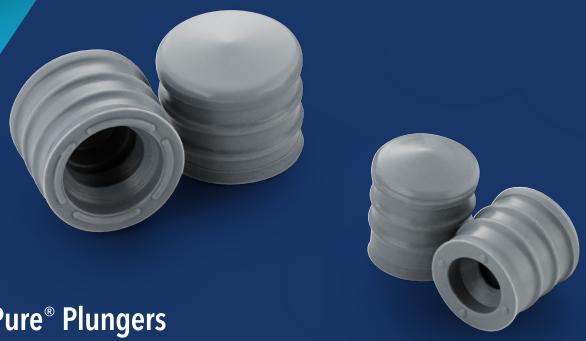
Break-resistant polymer of choice to protect sensitive biologics better than glass

Available in 1 and 2.25 mL sizes



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Superior quality plungers designed to optimize injection performance by reducing packaging variability

Available in 1 mL and 1-3 mL plunger sizes

At West, we've been a leading provider of innovative, high-quality injectable solutions and services for almost 100 years. Throughout our history, we have gone above and beyond to drive the kind of innovation necessary to keep up with emerging trends in life science and manufacturing. Nowhere is this more evident than in our NovaPure® components and in the Daikyo Crystal Zenith® Insert Needle Syringe system, both of which strive for the highest quality while mitigating risk.

To learn more about these breakthrough products, visit our website. You can also request samples and get a product recommendation from one of our Technical Customer Support (TCS) representatives by clicking on Support.

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