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Contents

DELIVERING INJECTABLES: DEVICES & FORMULATIONS

ONdrugDelivery Issue N° 172, May 20th, 2025

This edition is one in the ONdrugDelivery series of publications. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field.

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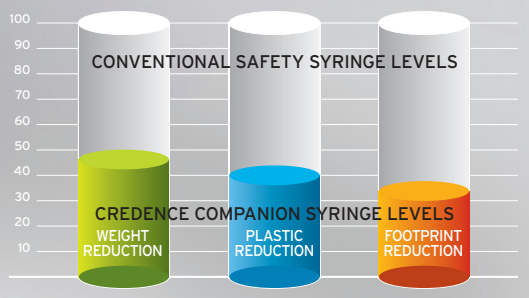

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Next-Generation Injection: Advanced Technologies & Novel Approaches

In this issue of ONdrugDelivery, we cover injectable drug delivery and the technologies that support it. The issue explores a diverse range of topics within this subject, from advanced delivery devices to industry partnerships and upcoming regulation. The injectables sector remains at the forefront of drug delivery technology, and, on the following pages, we highlight many of the areas in which progress continues to be made.

The opening article, from our Outstanding Sponsor, **Convatec** (Page 08), looks at the company's portable infusion set and how a partnership with AbbVie is making significant advancements in patient-centric care. Alongside Convatec, the issue also showcases advanced devices from across the industry, including **CCBio**'s product portfolio (Page 46), injection pens from **Nemera** (Page 56) and **Gerreshiemer** and **Midas Pharma**'s (Page 68) novel large-volume, high-viscosity autoinjector platform.

On a similar topic, **Ypsomed** and **BD** (Page 32) jointly present an article on the progress made on delivering high-viscosity formulations by combining the two companies' technologies.

Grand River Aspectic Manufacturing (Page 20) discusses the vital role that fill/finish partners play in supporting successful drug delivery device development, especially where novel primary containers are concerned, as highlighted by the company's partnership with **LTS**. Another key supporting technology for the industry is injection moulding, with **IGS GeboJagema** (Page 84) detailing a next-generation approach that has the potential to greatly enhance efficiency in the sector.

Vials, syringes and stoppers remain a core aspect of the injectables sector. Speaking to this, **Aptar Pharma** (Page 14) provides an enlightening interview on the upcoming UPS<382> regulation and how it will impact primary packaging developers. We also hear from **H&T Presspart** (Page 76) and **Stevanato Group** (Page 90) regarding their advanced primary packaging offerings.

As well as discussing specific technologies, this issue covers the myriad trends affecting the industry, with articles from **MGS** (Page 40) on sustainability, **PCI Pharma Services** (Page 49) on the transition from intravenous delivery to the intramuscular and subcutaneous routes, and **TTP** (Page 62) on the differences when using GLP-1s for weight management and other indications compared with diabetes. Also discussing these industry trends, are Evan Edwards and Mathias Romacker of **Kymanox** (Page 26) in an exclusive intervew with ONdrugDelivery's Guy Furness. They also introduce the first PDA Miniverse conference, an exciting new event for this sector, taking place in Indianapolis in June.

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ADVANCING SUBCUTANEOUS INFUSION THERAPY FOR PATIENTS THROUGH INNOVATION AND PARTNERSHIPS

Julien Vandewalle and **Clare Holden** of **Convatec** explain how the company's long-term partnerships with pharmaceutical and medical device companies are driving development in chronic care by introducing subcutaneous technologies that support the treatment of conditions such as diabetes and Parkinson's disease – showcasing Convatec's Neria™ Guard infusion set.

In 2024, a video of a 53-year-old man from the UK with advanced Parkinson's disease went viral. It was a before-and-after video that captured what he called the "extraordinary and life-changing" improvement from a new infusion therapy.[1] The two-minute video showed him preparing a cup of tea one-handed and with severe shaking. The film then cuts to the man smoothly scooping out his tea bag and walking to the kitchen dustbin to throw it away with ease – his progress gripped viewers and made headlines around the world, and rightly so.

Relief for this patient came through PRODUODOPA® (foslevodopa/foscarbidopa), a drug from Convatec's partner AbbVie, delivered via a portable infusion pump and Convatec's Neria™ Guard infusion set. The infusion set specifically provides continuous drug delivery, which helps to achieve stable symptom control, enabling patients to regain their independence.

This story is just one of the powerful examples of how Convatec is driving innovation in infusion sets and working with leading pharmaceutical partners to make a tangible and positive impact on people's lives worldwide.

CUSTOMER CENTRICITY AT THE CORE

More than one million people around the world rely on Convatec infusion sets every day (Figure 1). Convatec has long recognised the opportunity to provide

Figure 1: Neria™ Guard infusion set in use.

"CONVATEC SUPPORTS PHARMACEUTICAL COMPANIES IN BRINGING NOVEL SUBCUTANEOUS THERAPIES TO MARKET, EXPANDING TREATMENT OPTIONS FOR PEOPLE WHO MAY NOT TOLERATE ORAL MEDICATIONS EFFECTIVELY."

a better solution for patients with Parkinson's disease and other chronic conditions by developing an infusion set that works seamlessly with a pump to deliver medication in a controlled manner, featuring an easy-to-use design that supports high-quality care that can be delivered anywhere and everywhere.

Convatec collaborates closely with its partners to tailor solutions that align with the specific needs of their drugs and therapy areas. By prioritising user-centric development, Convatec ensures that its infusion sets meet the highest usability standards, optimising the patient experience and safety.

For Parkinson's disease and other chronic conditions, Convatec supports pharmaceutical companies in bringing novel subcutaneous therapies to market, expanding treatment options for people who may not tolerate oral medications effectively. These partnerships also help the company to expand its global reach.

Convatec's collaboration with AbbVie is one of the many examples of how pharmaceutical and medical device companies can work together to optimise subcutaneous drug delivery.

AbbVie's foslevodopa/foscarbidopa formulation is marketed in selected EU countries as PRODUODOPA® and is available for use with Convatec's Neria™ Guard infusion set. The drug has recently been approved by the US FDA as VYALEV™, where the Neria™ Guard infusion set is approved for subcutaneous infusion of medication.

This therapy is the first and only subcutaneous 24-hour infusion of a levodopa-based therapy for the treatment of advanced Parkinson's disease in the US.[2,3]

Convatec's Neria™ Guard infusion set, used together with a portable infusion pump and foslevodopa/foscarbidopa, plays a critical role in this therapy, ensuring a consistent drug delivery process.

A LEADER IN SUBCUTANEOUS INFUSION SETS

Guided by Convatec's vision – pioneering trusted medical solutions to improve the lives we touch – Convatec's infusion set technologies support patients who rely on subcutaneous therapies for conditions such as diabetes mellitus, Parkinson's disease, pain management therapy, primary immune deficiency and thalassemia.

Kjersti Grimsrud, President & Chief Operating Officer, Infusion Care at Convatec said, "At Convatec, we are focused on supporting people living with chronic conditions. Our pioneering subcutaneous infusion set technology, Neria™ Guard, is enabling a wide range of pharmaceuticals and medical device companies to extend access and improve the lives of people counting on us."

SUBCUTANEOUS DRUG DELIVERY DEVICES

The shift from intravenous infusion to subcutaneous administration is gaining momentum. In this evolving landscape, infusion sets can play a crucial role in optimising subcutaneous drug delivery by enhancing ease of administration, improving the patient experience and supporting the broader adoption of subcutaneous therapies.

For subcutaneous drug delivery, infusion sets can be flexible in drug volume and do not have volume requirement limitations, unlike other medical devices. Furthermore, infusion sets, in combination with a pump system, can be an ideal option for medications that require continuous delivery in a controlled manner. With so many potential scenarios and drug requirements, infusion sets with user-friendly features, such as easy insertion, are one of the ideal choices for subcutaneous drug delivery devices.

ALL-IN-ONE INFUSION SET

Neria™ Guard is an all-in-one infusion set with automatic inserter, designed to support simplicity for both at-home and outpatient treatment, with features such as automatic insertion with the touch of a button. The infusion set connects to a pump at one end and the user's body at the other end to deliver medication into the subcutaneous tissue continuously.

Studies indicate that Neria™ Guard's easy and intuitive insertion technique protects against user errors (internal company data), may help support at-home use and encourages independence in patients' everyday lives (Figure 2).[4]

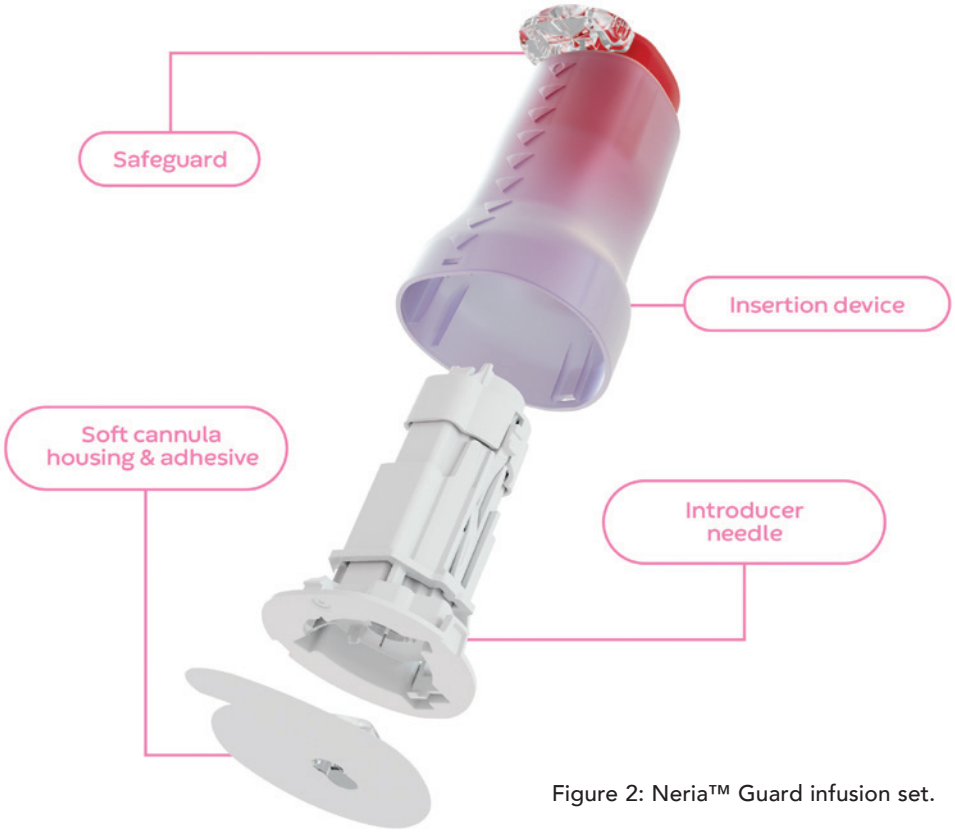

Figure 2: Neria™ Guard infusion set.

Convatec works with leading pharmaceutical and medical device companies to integrate its infusion products seamlessly into comprehensive drug delivery solutions. The company's capabilities and know-how, developed over more than 30 years, are highly transferable to other technologies and therapies, such as insertion technologies, fluid pathways, infusion cannulas, design for manufacturing and process knowledge for high-scale manufacturing.

"CONVATEC WORKS WITH LEADING PHARMACEUTICAL AND MEDICAL DEVICE COMPANIES TO INTEGRATE ITS INFUSION PRODUCTS SEAMLESSLY INTO COMPREHENSIVE DRUG DELIVERY SOLUTIONS."

Convatec's lasting relationships with existing partners and its commitment to quality are proof that the company is devoted to building strong partnerships, believing that transparency and proactivity are essential for productive relationships. Convatec's partners and collaborators include AbbVie, Beta Bionics (Irvine, CA, US), Medtronic (Minneapolis, MN, US), Mitsubishi Tanabe (Osaka, Japan), SOOIL (Seoul, South Korea), Tandem Diabetes Care (San Diego, CA, US) and Ypsomed (Burgdorf, Switzerland). Convatec believes that collaborating with more medical device and pharmaceutical companies will help people with chronic conditions to live more fulfilling lives.

REGULATORY REQUIREMENTS AND MARKET READINESS

Bringing a medical device to market requires strict adherence to regulatory requirements and standards to ensure patient safety, efficacy and drug-device compatibility. This is an increased focus area in the industry as shown by the EU's Medical Device Regulation (MDR) and the FDA's Center for Devices and Radiological Health.

The production of Neria™ Guard adheres to the ISO 13485:2016 quality standard, meeting industry benchmarks for subcutaneous drug delivery systems, guaranteeing reliability and precision. The infusion set already meets the new MDR requirements in the EU and is also approved in the US with a 510(k) as a Class II medical device. Convatec also has market approval for the Neria™ Guard in many other countries worldwide.

LARGE-SCALE MANUFACTURING AND CONTINUOUS INVESTMENT

Across its three infusion set manufacturing sites, Convatec produces approximately 130 million infusion set devices each year. Convatec's manufacturing capabilities include manual, semi- and fully

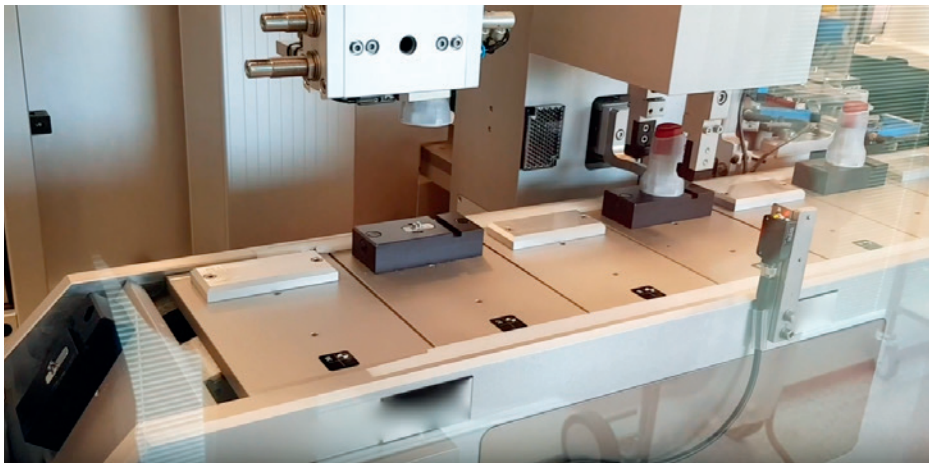

Figure 3: Neria™ Guard manufacturing.

automated manufacturing, as well as extrusion and injection moulding (Figure 3).

Convatec continues to invest in its manufacturing capabilities and footprint. In 2022, Convatec Infusion Care doubled the manufacturing capacity at its manufacturing site in Denmark, making it the most advanced manufacturing site in the overall Convatec network.[5] The company has continued to invest in its Infusion Care manufacturing, adding capacity to be able to meet demand, and it has more than doubled R&D investment in recent years[6] with the strongest innovation pipeline in its history.

DOING WHAT IS RIGHT FOR ALL STAKEHOLDERS

Convatec continues to invest in R&D to support innovation in infusion therapy, while integrating responsible business practices. The company's sustainability efforts seek to drive progress towards Convatec's vision, while generating value for stakeholders. For example, innovative infusion sets such as the Medtronic Extended infusion set, which is the first and only infusion set approved for up to seven days of wear (versus three days for standard sets), reduces the environmental footprint of plastic waste from insulin pump therapy. Developed in partnership with Convatec, this infusion set is estimated to reduce plastic waste by up to 50%.[7] Innovation like this is important for Convatec to reach its goal to achieve net zero by 2045.

Sustainability in the company's operations is also important. As of 2024, renewable electricity accounts for 100% of total electricity consumed at its manufacturing sites.[8] By minimising waste, expanding renewable energy and optimising manufacturing processes, Convatec seeks to continue delivering innovative solutions responsibly.

A FOREVER CARING PARTNER

Convatec's promise – forever caring – is core to its business. The company has revolutionised the field of subcutaneous infusion therapy for patients by tackling essential challenges encountered by both patients and healthcare professionals. Its solutions have made a notable difference in managing conditions such as diabetes mellitus, Parkinson's disease, pain, primary immune deficiency and thalassemia.

Convatec is more than an infusion sets manufacturer; it is a trusted partner on the journey towards better health and improved lives, and welcomes collaboration and strategic partnerships to bring impactful innovation to life.

"CONVATEC CONTINUES TO INVEST IN R&D TO SUPPORT INNOVATION IN INFUSION THERAPY, WHILE INTEGRATING RESPONSIBLE BUSINESS PRACTICES."

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Julien Vandewalle

Julien Vandewalle is Vice-President, Commercial & Strategy, Convatec Infusion Care business unit. He leads sales, marketing, strategy & business development teams for strategic commercial delivery and customer service. Mr Vandewalle joined the company in 2021, with an extensive background and profound business insights in the pharmaceutical and medical devices industry.

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Clare Holden, Vice-President, Research & Development, Infusion Care. Clare has been with the company since 2019 and has held a variety of leadership roles including in R&D for Continence Care and Ostomy Care.

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*Please refer to the Instructions for Use for information about medications that can be used with Neria™ Guard.

Interview: Understanding the Impact of USP<382> on Primary Packaging Development

Laure-Hélène Guillemot discusses the new USP <382> chapter coming into force on December 1st, 2025, which will significantly transform functional testing protocols for pharmaceutical companies. This new standard mandates that elastomeric components, such as stoppers and seals, meet stringent safety and efficacy criteria, including tests for container closure integrity, needle and spike access functionality, and the performance of plungers and stoppers. Here, Dr Guillemot explains the impact on pharmaceutical companies' product development approaches and how Aptar Pharma can support its customers from a functional testing perspective.

Q What is the objective of USP <382> compared with USP <381>, and how does it impact pharmaceutical companies?

A USP <381> "Elastomeric Components in Injectable Pharma Products Packaging" refers to the evaluation of elastomeric compounds individually, not considering them as part of a full system. As such, the stopper is evaluated without taking the potential impact of its interactions with the vial into account, the crimping cap and the drug product on its functional performances.

This USP chapter contains three sections – biological reactivity, functional tests and physical-chemical tests. The biological reactivity and physical-chemical tests sections apply to all elastomeric compounds, such as stoppers for vials and plungers for PFSs, whereas the functional tests only apply to elastomeric compounds meant to be pierced, such as stoppers for vials.

The objective of USP <382> "Elastomeric Component Functional Suitability in Parenteral Product Packaging/Delivery Systems" is to evaluate the functionality of the complete system instead of the individual elastomeric compounds alone. The novelty is that it includes not only stoppers but also plungers and needle-shields, so systems for injectable applications, such as vials, PFSs and cartridges, are therefore included. Pharmaceutical companies, being the stakeholders owning the complete packaging information, will therefore be responsible for checking the full compliance of its systems towards USP <382>.

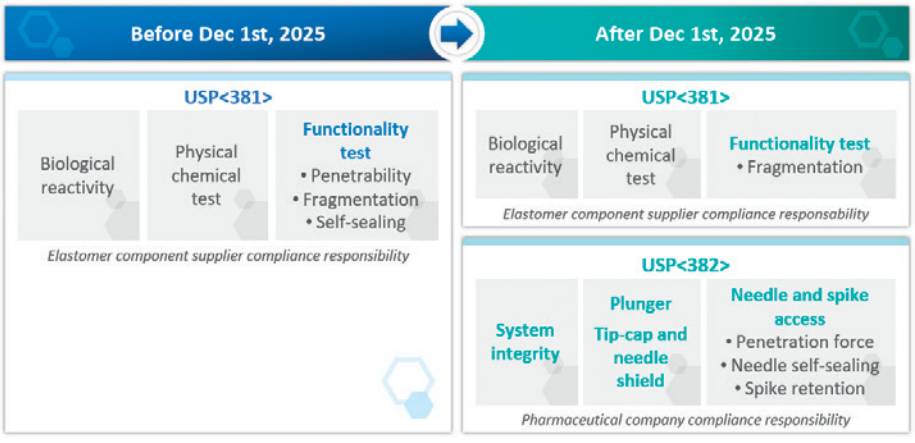

Figure 1: Implementation of USP <382> with regards to USP <381> and its impact for drug developers/pharmaceutical companies.

As of December 1st, 2025, USP <381> will remain the reference for biological reactivity and physical-chemical parts. Following the USP compendial notice published on April 25th, 2025, fragmentation testing will also remain applicable as described in USP <381>, while penetrability and self-sealing tests will be omitted from functionality tests of USP <381> to be included to USP <382> chapter (Figure 1).

Q Which new tests are required with USP <382> and which modifications are made to existing tests?

A The main recommendation from USP <382> is to evaluate the full system according to its final intended use. Pharmaceutical companies are responsible for setting acceptance criteria and developing testing methods that best represent their systems' real-life conditions of use. Although USP <382> does not impose specifications, it provides pharmaceutical companies with guidelines.

For infusion applications, the spike retention and sealability capacity test has been added as part of USP <382> to ensure that the spike does not slide out of the pierced rubber and that the solution does not leak at the stopper/spike interface. The penetration force and self-sealing capacity tests are not new, but have been reviewed to consider the product's final intended use.

As an example, for vial systems containing dry products that need reconstitution, USP <382> recommends

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Laure-Hélène Guillemot, PhD, has been Technical Product Manager within Aptar Pharma's Injectables division for its vials product line since the end of 2023. An engineering graduate of the Superior School of Chemistry Physics and Electronics (Lyon, France), Dr Guillemot also holds a PhD in Chemical Physics from CEA-Leti (Grenoble, France). Having worked for over six years in the construction products industry, she developed a strong expertise in glass chemistry and project management for product development. Dr Guillemot joined Aptar Pharma in 2020 as Project Manager for new product development, including Aptar Pharma's PremiumCoat® solutions.

evaluating self-sealing capacity using 30 stoppers pierced one time each with an 18G needle, then at least three times with a 21G needle. In comparison, USP <381> did not consider the need for reconstitution with an 18G needle and self-sealing tests only required 10 stoppers to be pierced 10 times with 21G needles.

For syringe barrel-plunger systems, USP <382> requires break-loose, extrusion force (also known as gliding force) and plunger seal integrity tests to be performed. These requirements are considered "new" as they were not previously described in the pharmacopeia, but such tests were already routinely performed by PFS and component manufacturers. This is also the case for the pull-off force and torque force tests now required for systems using tip caps or needle shields.

For both vials and PFS systems, USP <382> strongly recommends performing deterministic container-closure integrity testing rather than using a probabilistic method.

Q How will the drug development process be affected and what should pharmaceutical companies do to comply with the new requirements of USP <382>?

A Pharmaceutical companies and drug developers are the only stakeholders owning all information related to their drug and delivery systems. Under USP <382>, it is their responsibility to ensure the compliance of their complete vial system (stopper, vial, crimping cap and drug or placebo) or PFS system (barrel, plunger, tip closure and drug or placebo).

For products already on the market, there is no obligation to carry out these tests. However, starting December 1st, 2025, following changes for existing products, pharmaceutical companies will have to assess whether product functionality is affected and may be required to provide additional technical data to demonstrate compliance with USP <382>. For products in development phase, drug developers must include an evaluation according to USP <382> and all drug products submitted as of December 1st, 2025, will have to comply with this new regulation.

Q How can Aptar Pharma support drug developers in complying with USP <382>?

A Aptar Pharma has already performed a series of tests on its vial stopper market standards according to USP <382> guidelines. Results and documentation are available upon request and can help drug developers in making informed decisions when selecting their drug delivery system. Furthermore, as test methods must now represent the final condition of use of the drug product, Aptar Pharma's R&D specialists can work with drug developers to design situation specific tests and inform the choice of primary packaging.

Aptar Pharma has also performed a risk assessment and identified adjustments that need to be made to the quality documentation. For the latest stages of drug development and regulatory filing, drug developers may require assistance in functional testing to meet the requirements of USP <382>. Gateway Analytical, an Aptar Pharma company, offers GMP analytical and testing services.

In conclusion, Aptar Pharma's teams have been working to understand and anticipate the changes that will come into effect with the implementation of USP <382> on December 1st, 2025. The company's experts are ready to address pharmaceutical companies' concerns and support the seamless transition to this new regulatory landscape, so that they can focus on drug development and bring safer therapeutic options to patients around the world.

"FOR PRODUCTS IN DEVELOPMENT PHASE, DRUG DEVELOPERS MUST INCLUDE AN EVALUATION ACCORDING TO USP <382> AND ALL DRUG PRODUCTS SUBMITTED AS OF DECEMBER 1ST, 2025, WILL HAVE TO COMPLY WITH THIS NEW REGULATION."

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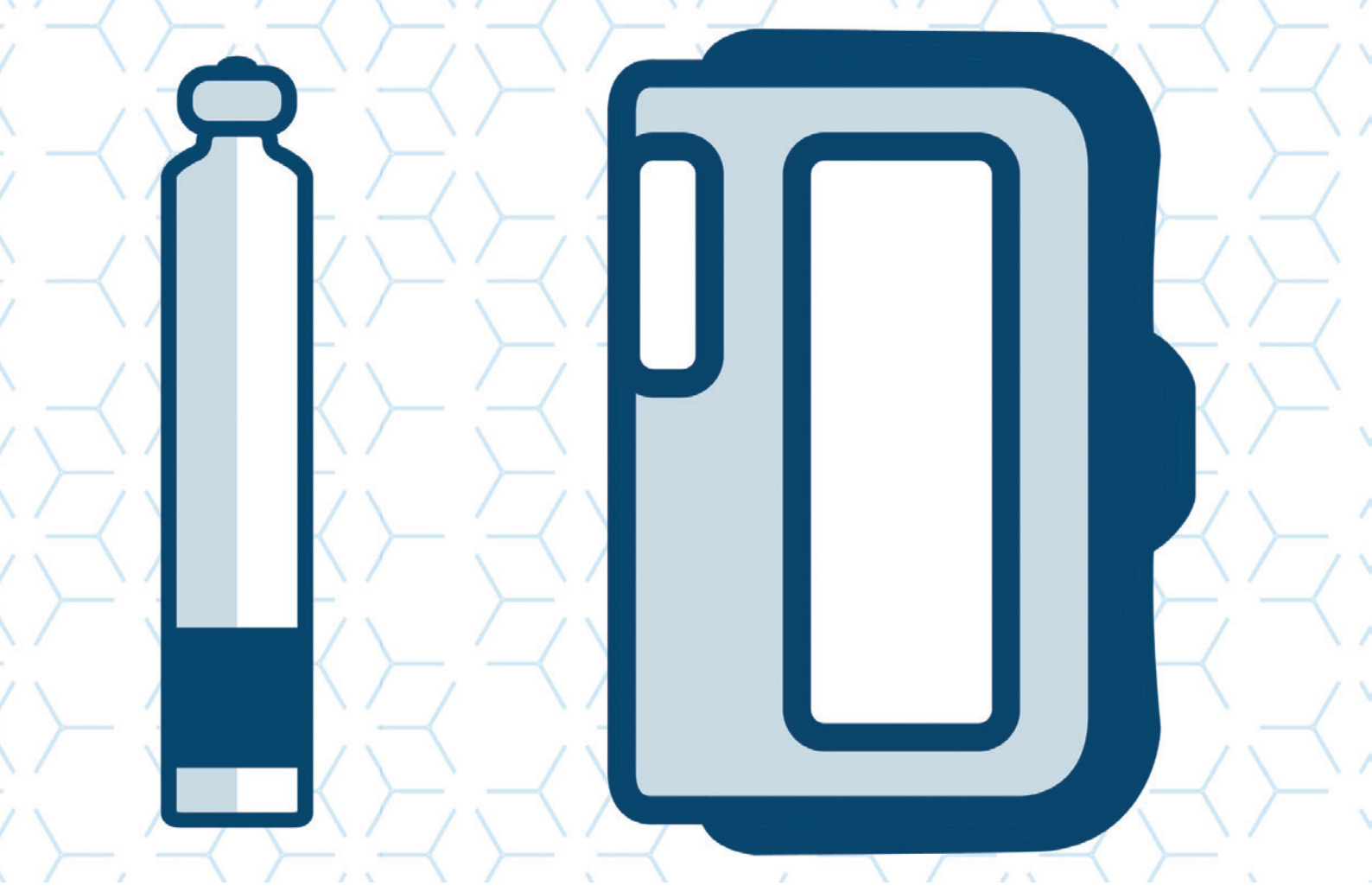

THE POWER OF PARTNERSHIP AND CLOSE COLLABORATION FOR FILLING ON-BODY INJECTORS

Mary Lou Glotzbach of **Grand River Aseptic Manufacturing** and **Dr Greg Moakes** of **LTS Device Technologies** consider the implications of the increasing demand for high-volume injections across the drug delivery industry, and how technologies such as wearable injectors are creating novel challenges for the fill-finish process due to the novel containers involved, making the case that it is only through clear communication and close collaboration between partners that these challenges can be met and surmounted.

A key frontier in today's drug delivery industry is biological therapeutics. These medicines hold great potential to treat indications previously out of reach and provide much needed treatment for multiple patient demographics. As a result, biologics now represent a major part of the drug delivery market and pharmaceutical pipeline, with drug formulators keen to capitalise on these medications and get patients the treatment they require.

However, biologics are notoriously difficult to deliver. The large proteins that comprise biologic therapeutics are fragile and prone to denature or agglomerate under adverse conditions, meaning that successfully storing and delivering them to patients is proving to be an ongoing challenge with no hard-and-fast solution. While many different approaches are in development, the broad consensus is that the injectable route is favourable for most biologics, as they tend towards liquid formulations and are prone to lose their therapeutic effectiveness if exposed to the gastrointestinal tract.

Injecting biologics is, of course, not without its own challenges. The large molecules lead to biologic formulations either being significantly more viscous than traditional small-molecule

"WHILE SOME DEVELOPERS ARE INVESTIGATING THE BOUNDARIES OF PATIENT TOLERANCE WITH AUTOINJECTORS, OTHERS ARE PIONEERING A NEW APPROACH – OBIs."

therapeutics or needing to be delivered in significantly higher volumes. While efforts have been made to deliver biologics with traditional autoinjectors, compromises have had to be made, either in injection time, needle gauge, increased volume or a combination of the three. However, while some developers are investigating the boundaries of patient tolerance with autoinjectors, others are pioneering a new approach – on-body injectors (OBIs).

THE DEMAND FOR LARGE-VOLUME INJECTIONS

A number of companies across the industry have dedicated significant resources to the development of OBIs, however, entrenched scepticism remains towards OBIs and the concept of large-volume injection more broadly. This is not unexpected, as the strict regulations surrounding pharma products naturally leads to a conservative mindset and a strong preference for established technology – formulators and regulators understand and trust autoinjectors, which is why efforts are ongoing to push the technology beyond its usual 1 mL and 2.25 mL standards into the realm of 5 mL autoinjectors.

When trying to push autoinjector technology to larger volumes, a number of challenges arise. A critical one has proven to be injection time – when using an autoinjector, the patient must hold the device at the injection site for the full duration of the injection, which is significantly longer than suggested limits for a 5 mL injection. While studies have demonstrated that patients are willing to hold an autoinjector in place for longer injections, 5 mL formulations of biologics are often viscous, presenting yet further challenges to autoinjector-based delivery.

THE POTENTIAL OF WEARABLE INJECTORS

This has led to the development of OBIs such as LTS's Sorrel platform. These devices represent an alternative path to solving the challenge of delivering biologics. As OBIs are worn on the body, holding an autoinjector in place ceases to be a consideration, which means injection times can be significantly longer and injections more comfortable for the patient. Furthermore, OBIs can handle volumes even greater than 5 mL, with some pushing up to 20 mL or more, unshackling formulators from the need to force their biologics into ill-suited established formats.

This is a critical factor in the modern drug delivery industry due to its intersection with another key trend – the drive to move care from the hospital to the home. Due to a wide array of factors, from ageing populations to sustainability concerns, healthcare systems across the world are under ever-increasing pressure. A key approach to alleviate this pressure is to facilitate patient self-administration at home, which both reduces the pressure on clinic hours and provides patients with greater agency over their own lives.

To achieve this paradigm shift in the way care is delivered, the issue of adherence must be addressed – for at-home treatment to be successful, patients must be able and willing to self-administer their medications successfully. This has required the drug delivery industry to adopt a mentality of patient-centricity in its design focus, putting the patient at the centre of its decision-making. OBIs are a key part of this, presenting a simple and effective treatment method for patients to self-administer complex, high-volume biologics that interferes with their daily lives as little as possible.

Figure 1: Grand River Aseptic Manufacturing cartridge filling for custom drug delivery innovations.

"AS IT EVOLVES, OBI DEVELOPMENT IS CONTINUING TO ACCOUNT FOR THE NEEDS OF FORMULATION DEVELOPERS, PATIENTS AND OTHER STAKEHOLDERS, WHICH HAS LED TO A VERSATILE PLATFORM APPROACH EMERGING AS A TREND."

However, OBIs come with their own design challenges. Given their relative novelty in the industry, there are currently no standards or conventions for their design, so device developers have taken often wildly different approaches to designing these complex devices, from form factor to drive mechanism to primary container (Figure 1). As it evolves, OBI development is continuing to account for the needs of formulation developers, patients and other stakeholders, which has led to a versatile platform approach emerging as a trend.

Versatility is a key feature of the Sorrel platform, with the device able to accommodate a range of volumes in either a vial or cartridge format. LTS is able to adapt the core chassis to fit the primary container that best suits the formulation in question and then tailor the injection profile using Sorrel's onboard electromechanical drive. This represents an excellent solution for LTS and its pharma partners, but presents a new challenge all of its own – with such a variety of primary containers available, how are they filled?

THE CHALLENGES OF FILLING NOVEL CONTAINERS

Fill/finish is a critical part of manufacturing any injectable product and one that requires specialist equipment and know-how. Grand River Aseptic Manufacturing (GRAM) is an expert in this field, with extensive experience in ensuring safety and quality when filling pharmaceutical products. The rise of biologics and shift towards patient self-administration has created challenges not only for device developers, but across the industry, including for fill/finish experts (Figure 2).

Large volume injectables, and OBIs in particular, have required fill/finish experts to step up. For more traditional injectables, such as vials and 1 mL long syringes, there are long-established industry standards for their dimensions. So, in tandem, filling lines have been adapted to accommodate these primary container formats with minimal friction – the line components are standardised along with the primary containers. However, there are no standards for larger formats, such as 5 mL and 10 mL cartridges or other, even more unusual primary containers used by some OBIs, so fill/finish experts such as GRAM have had to rapidly innovate and adapt to meet the demands of large volume injection devices.

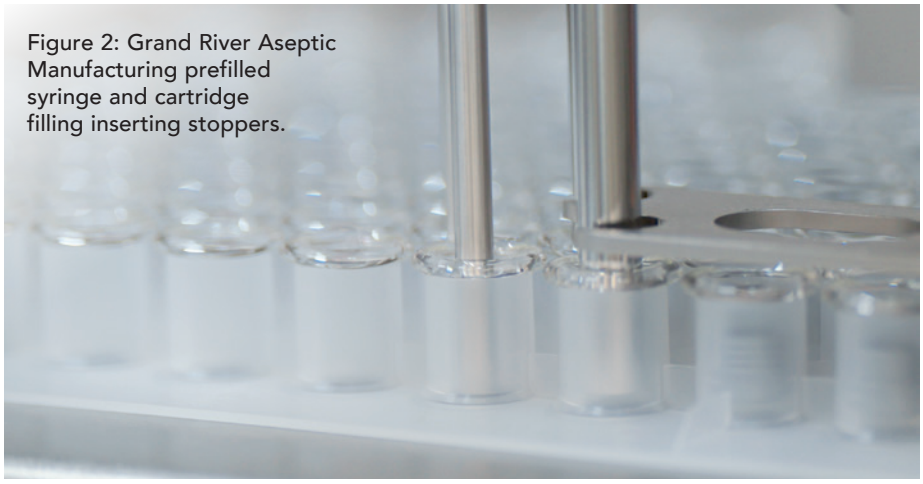

Figure 2: Grand River Aseptic Manufacturing prefilled syringe and cartridge filling inserting stoppers.

With many OBIs, device developers continue to iterate on their primary containers as their devices evolve in response to the needs of pharma partners and patients. For devices with a high degree of versatility in their primary containers, such as Sorrel, fill/finish partners need to be able to match that versatility to keep up with the rapid pace of development in this sector. With primary containers often being adapted to the needs of individual pharma partners, one 5 mL cartridge may not share dimensions with another, which places even greater demand on the fill/finish expert to be able to deliver top quality products throughout the development and commercialisation journey.

CLEAR COMMUNICATION AND THE POWER OF PARTNERSHIP

Meeting the demands of development and fill/finish for OBIs requires a wealth of expertise and experience from across the value chain. To be able to deliver a safe, efficacious product to patients and healthcare providers and stand up to the rigorous requirements of regulators, partners in this endeavour must engage in open and frank communication with each other. Inefficient or inaccurate communication can only lead to delays and unnecessary errors in the development process, which all parties should be eager to avoid.

An ideal example of this principle in action is the partnership forged between GRAM and LTS to deliver Sorrel OBIs to patients. In the process of partnering with GRAM to provide fill/finish services for its Sorrel device, LTS was sure to engage early in the process and foster trust through clear and open discussions around Sorrel's specifications and requirements. In doing so, GRAM and LTS have been able to keep up momentum throughout the development process, adapting to evolving needs and ensuring quality at all stages, thereby securing a position at the forefront of the OBI market.

Through frequent and transparent communication and engaging early on in the development process, GRAM and LTS have managed to circumvent several roadblocks and issues before they arose.

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Close collaboration has enabled the companies to combine their experience and expertise across device development, fill/finish and the supply chain to maximise Sorrel's competitive advantage and improve what Sorrel can offer to pharma partners.

Working together so closely has been possible for GRAM and LTS due to both companies sharing an understanding of the needs of the modern drug delivery industry; patient centricity and the culture that surrounds it is no longer only a concern for human factors specialists, it must be integrated into all aspects of the value chain. Clear communication has been key for ensuring that GRAM and LTS's values align and that the companies are working towards the same goal – better outcomes for patients.

CONCLUSION

The demand for large-volume injectors to meet the needs of novel biologic therapeutics is undeniable. As such, the drug delivery industry must rise to the challenges presented by these molecules and the needs of the healthcare sector so that patients can self-administer these life-changing medications. A key aspect of meeting this goal will be OBIs capable of delivering much larger volumes than traditional syringe-based injection devices in a patient-centric fashion. Novel large-volume devices also require an adaptive and innovative approach from fill/finish experts, who must meet the demands of filling primary containers in a fast-moving section of the industry with no established standards.

If this challenge is to be met, it will require close collaboration between partners across the value chain and a willingness to engage in open and frank communication to foster trust and co-operation. GRAM and LTS have achieved this with the Sorrel OBI, building up momentum in a rapidly evolving sector to offer pharma partners a versatile and adaptable OBI offering complete with fill/finish capacity. This collaboration enables GRAM and LTS to position Sorrel as a leading device in the OBI market and will allow patients to self-administer their biologics in a safe and effective manner, progressing healthcare towards a more patient-centric future.

"THROUGH FREQUENT AND TRANSPARENT COMMUNICATION AND ENGAGING EARLY ON IN THE DEVELOPMENT PROCESS, GRAM AND LTS HAVE MANAGED TO CIRCUMVENT SEVERAL ROADBLOCKS AND ISSUES BEFORE THEY AROSE."

Mary Lou Glotzbach

Mary Lou Glotzbach, Senior Business Development Manager at Grand River Aseptic Manufacturing (GRAM), has over 20 years of CDMO industry experience in managing pharma and biopharma alliances, primarily through aseptic manufacturing and packaging programmes. As part of the GRAM team since 2020, Ms Glotzbach managed the J&J and BARDA alliances while the organisations came together to successfully manufacture the covid-19 vaccine. Her new focus is in developing and executing strategic device partnerships. Prior to joining GRAM, Ms Glotzbach held various business development and marketing roles within the CDMO organisations at Abbott Laboratories, Hospira and Pfizer. Her experience in the healthcare market also includes the management of pharmaceutical and device sales teams while at Abbott and Hospira. Ms Glotzbach holds a BS in Biomedical Engineering from the University of Iowa (Iowa City, IA, US). She has completed multiple executive education programmes at the Kellogg School of Management (Evanston, IL, US) and The Wharton School (Philadelphia, PA, US).

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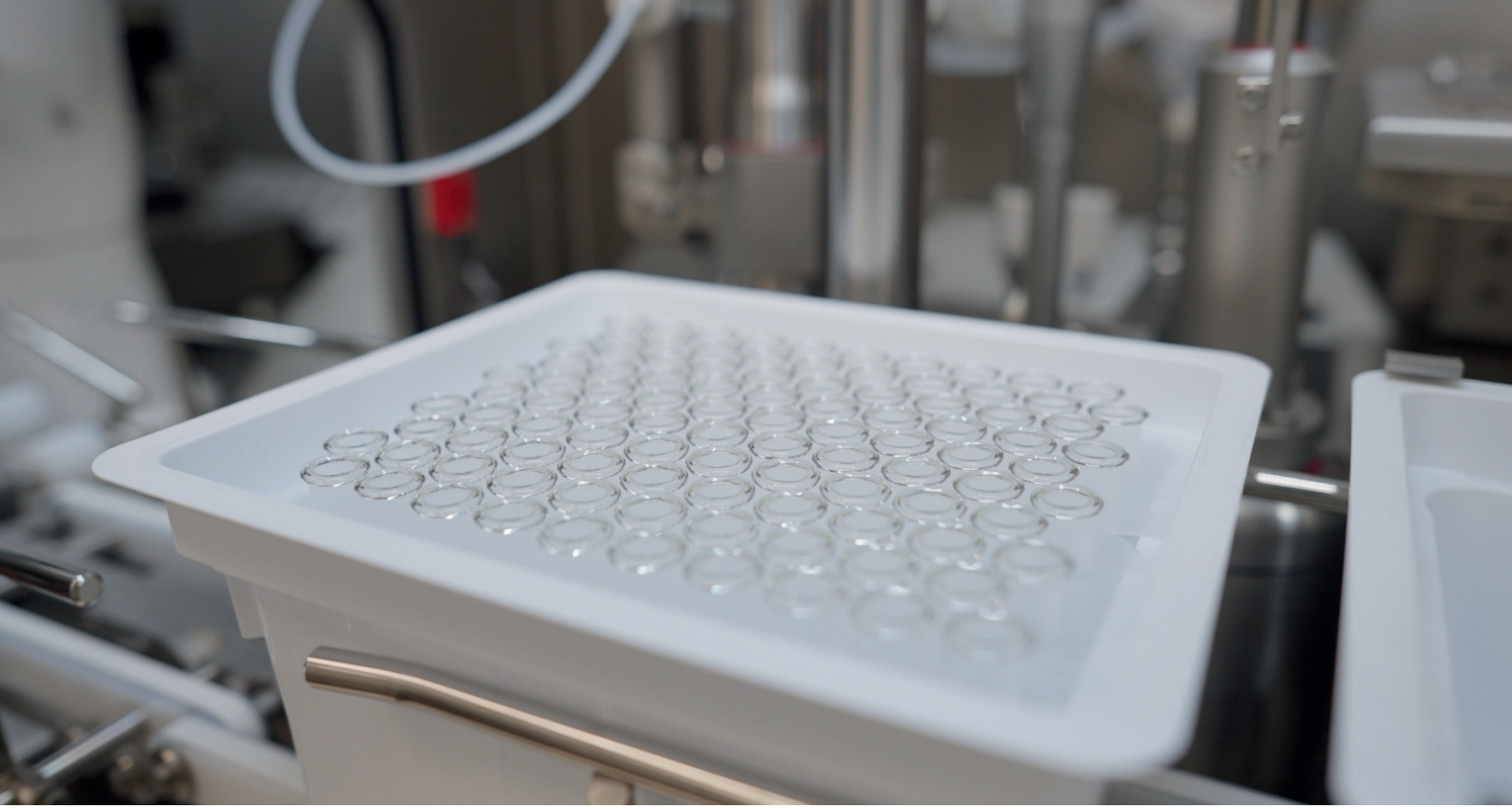
2025/26 Editorial Calendar

Each issue of ONdrugDelivery focuses 100% on one specific topic *within* drug delivery.

MAY/JUN 2025 Oral Drug Delivery DEADLINE PASSED	**JUN** Connectivity in Drug Delivery DEADLINE PASSED	**JUL** Industrialising Drug Delivery DEADLINE PASSED
SEP Wearable Injectors DEADLINE: **Aug 7, 2025**	**SEP/OCT** **NEW ISSUE TOPIC** Dual Chamber Delivery Systems DEADLINE: **Aug 14, 2025**	**OCT** Prefilled Syringes & Injection Devices DEADLINE: **Sep 4 , 2025**
DEC **NEW ISSUE TOPIC** Delivering Gene & Cell Therapeutics DEADLINE: **Nov 6, 2025**	**OCT/NOV** Sustainability in Drug Delivery DEADLINE: **Sep 18, 2025**	**NOV** Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 2, 2025**
JAN 2026 Prefilled Syringes & Injection Devices DEADLINE: **Dec 4, 2025**	**FEB** Skin Drug Delivery: Dermal, Transdermal & Microneedles DEADLINE: **Jan 8, 2026**	**MAR** Ophthalmic Drug Delivery DEADLINE: **Feb 5, 2026**
APR Pulmonary & Nasal Drug Delivery DEADLINE: **Mar 5, 2026**	**APR/MAY** Sustainability in Drug Delivery DEADLINE: **Mar 19, 2026**	**MAY** Delivering Injectables: Devices & Formulations DEADLINE: **Apr 2, 2026**



GRAND RIVER
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A patient-centric approach to fill-finish

As patients become more active participants in their healthcare, CDMOs can play a greater role in providing for the end patient. To do this, Grand River Aseptic Manufacturing has positioned itself as a strategic partner to help accelerate market entry for its customers.

The collaboration between the CDMO, drug delivery provider, and the pharmaceutical company is taking center stage when determining who will fill and finish a drug product. Partnerships characterized by transparency and mutual learning bring all parties towards a common goal and address challenges openly to create successful products.

By maintaining open communication and collaborating toward a shared goal, all parties can achieve success that ultimately benefits the patient.

Take a patient-centric approach **together.**

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Interview
PDA Miniverse and Trends in Injectable Drug Delivery

In this exclusive interview, **Mathias Romacker** and **Evan Edwards** of **Kymanox** talk with ONdrugDelivery's Guy Furness about the inaugural **PDA Miniverse: Medical Devices, Combination Products and Connected Health** conference in Indianapolis (IN, US), discussing the inspiration for the event and what delegates can expect at this smaller, more intimate companion to PDA's annual Universe of Pre-Filled Syringes & Injection Devices. Following on from Miniverse, the conversation broadens into a wider consideration of the topics and trends currently being felt across the injectable drug delivery industry.

Q The Parenteral Drug Association (PDA) "Miniverse" conference will take place in late June in Indianapolis. Mathias, as the event's co-chair, can you tell us more how this event came about?

MR It's fair to say that PDA's Universe of Pre-Filled Syringes & Injection Devices conference is the event of the year in terms of content, networking opportunity and just getting the injectable drug delivery industry together. The way it's currently structured is that it alternates each year between the US and Europe. This year it's taking place in Vienna, Austria, which makes it an off year for PDA Universe in the US. So, within PDA, we've been having conversations over the years about whether it would be beneficial if we were to offer a slimmed down version in the US during off-years.

"HOSTING THE EVENT IN INDIANAPOLIS IS ALSO AN EXCITING FIRST FOR US – IT'S AN INNOVATION HOTBED – AND, AS A BONUS, DELEGATES WILL BE GIVEN A TOUR OF STEVANATO GROUP'S LOCAL MANUFACTURING PLANT."

We eventually pulled the trigger early this year, and I think that we have a really great programme. Hosting the event in Indianapolis (Figure 1) is also an exciting first for us – it's an innovation hotbed – and, as a bonus, delegates will be given a tour of Stevanato Group's local manufacturing plant.

Q Evan, before we move on to discuss your role at Miniverse, can you give us some insights into your fascinating career and the journey that led you to your current role as President of Kymanox?

EE It's something of a unique story. My identical twin brother, Eric, and I grew up with severe allergies and, as a result, we invented one of the primary competitors to EpiPen (Viatris), an adrenaline (epinephrine) autoinjector

Figure 1: PDA Miniverse will take place in Indianapolis, Indiana, on June 24–26, 2025.

called AUVI-Q (Kaléo, Richmond, VA, US). So we spent 17 years working alongside some very talented leaders, developing Kaléo and inventing several drug delivery device platforms. Eventually, both my brother and I became fathers to children that were at risk of severe allergic reactions.

Our focus was on solving the challenges the industry faced back in the early 2000s – trying to identify unique ways of delivering injectables, for emergency use products in particular. Nowadays, you see all kinds of new drug delivery technologies, especially in the small-molecule space, even branching out into nasal administration. We're very proud of developing AUVI-Q, first for adults and then for paediatric applications. AUVI-Q 0.1 mg still remains the only autoinjector product on the market for infants.

The other thing that we then developed was the first out-of-hospital indication for naloxone. This was before the NARCAN nasal spray (Emergent Devices, Plymouth Meeting, PA, US) became readily available over the counter. At the time, naloxone was only administered by emergency medical technicians and healthcare providers. So we developed EVZIO (Kaléo), which was a naloxone autoinjector. That eventually transitioned off the market, but we used that technology to develop a 10 mg naloxone product for US soldiers in case of overdose of highly potent fentanyl or other opioids.

We spent a lot of time developing novel drug delivery platforms with Kaléo and, as a result, we worked with a lot of professional services firms. One of those companies was Kymanox, which is how I got to know Stephen Perry, the CEO and Founder. After I left Kaléo, I was blown away at the growth that Kymanox had achieved. I joined the company in 2020 as an adviser to help continue to build, scale and professionalise the organisation, starting with the human factors group, and the company has now grown to around 300 people.

Having spent most of my career in drug-device combination products, what really excited me about Kymanox was the opportunity to work with such a large number and variety of sponsors. Whether it's a small pharma, medtech or biotech company, all the way up to some of the largest pharma and biotech companies in the world, there's nothing quite like working alongside a wide variety of trusted partner companies; seeing what they're developing and helping them accelerate and advance those products through the regulatory authorities to get them into patients' lives is very rewarding.

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Mathias Romacker is a Kymanox Executive Advisor with more than 30 years of experience in the field of injectable drug delivery devices. He brings a deep understanding of prefilled syringes, handheld injection devices and on-body wearable devices, having been involved in multiple successful combination product launches. Mr Romacker was a co-chair for the PDA Universe of Pre-Filled Syringes and Injection Devices conference in 2013, 2017, 2019 and 2022, and received the PDA Edward Smith Packaging Science Award in 2018 for his contributions over the years.

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As an expert in the pharmaceutical and medical device industries, Evan Edwards serves as President of Kymanox. He was the Co-Founder of Kaléo and co-inventor of the AUVI-Q (adrenaline) autoinjector and Kaléo's drug delivery device technologies. He has extensive experience in drug-device combination products and is named on over 200 patents, issued and pending, both in the US and abroad. Mr Edwards is a subject matter expert in usability engineering, design controls, combination products, operations, industrialisation, quality systems, executive leadership, pre-approval inspection readiness, human factors, intellectual property strategy, and invention and design. He holds a BS in Mechanical Engineering and an MS in Systems Engineering with a focus on human factors engineering, both from the University of Virginia (Charlottesville, VA, US).

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Q Evan, you're one of the plenary speakers on day one of Miniverse, discussing the topic of risk mitigation and how to manage third-party resources. Can you talk about the relevance of this topic and give our readers a small preview?

EE When I was at Kaléo, we were a smaller company, so we had to rely on a lot of different third parties, including CDMOs and professional service firms like Kymanox. Now, at Kymanox, we're seeing increased use of third party and professional services for both the sponsor and the CDMO side within the industry. So I've seen the relationship from both sides; there are specific significant considerations when managing these resources.

We're also seeing CDMOs developing their own products internally, such as autoinjectors or other delivery platforms, which may not have been their core competency historically. As such, some of them are now trying to reach out to third parties to help them navigate how to identify and select the right partners, how to deal with the regulatory and quality management system considerations that they didn't have to before.

For me, it has a lot to do with risk. That can include quality control, regulatory concerns, supply chain issues, programme management and cybersecurity to name a few. All of these have significant impacts when you're trying to get products to market on time and on budget. Part of the topic I'll be exploring is how to mitigate these risks – what some of the key considerations are on both ends, especially for sponsors when they're looking to partner with a CDMO.

As an example, negotiating an appropriate master services agreement or quality agreement can take a significant amount of time. We've seen some of the sponsors we work with think that they're going to start this project in a month and, eight weeks later, they're still negotiating the terms of an agreement. So there are things that should be discussed to make sure that you're under-promising and over-delivering to your stakeholders, partners, leadership team and investors. I'm going to cover all of that, as well as some of the mitigation strategies on how to ensure that these companies are successful.

Q Mathias, you are a co-chair of PDA Miniverse this year. Can you talk about the programme and how Miniverse compares to the main PDA Universe conference?

MR As the name suggests, Miniverse will be slightly smaller than its Universe counterpart. It's still going to be a sizeable conference, but a bit more intimate than the main event, which I think is actually an upside for meeting people and networking. In my opinion, having a smaller crowd typically encourages people to speak with each other more freely.

In terms of programme, the theme for this year's Miniverse is "Integrated Innovation: Designing the Future of Injectable Drug Delivery", so you can see it still has a broad scope, with talks that will be relevant for most delegates in the typical Universe audience. In terms of topics, one key subject the talks will cover is the complexity of connected health, including cybersecurity. And, of course, they will cover how connected health is having an impact on clinical trials. Regulatory strategy is also always a very important topic to cover, especially with all the latest changes that have taken place this year in the US FDA, so we have a really good speaker lined up to cover it.

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Another topic that has been circulating for a while, which I think is really starting to take off, is large-volume systems, so I'm looking forward to the talks covering that subject. We also have some speakers that will talk about industry initiatives. To give some specific examples, we'll be hearing from the Subcutaneous Drug Development & Delivery Consortium (Beaverton, OR, US), with a presentation by one of their senior members from Halozyme.

Q Evan, there is a lot of uncertainty in the industry right now with changes occurring from the US administration, including layoffs at large companies and even the FDA. How are you all helping sponsors navigate these challenging times?

EE I think you hit the nail on the head that something we continue to hear about is uncertainty. What we've seen for the companies that we support is that it has increasingly been a challenge to raise money on the capital markets, especially for smaller companies. Most investors are trying to mitigate risk and, therefore, they want the companies they invest in to be further along the development journey, closer to the clinical or commercial stage than was the case even five years ago. Investors used to be willing to take on a bit more risk and invest in earlier-stage companies. So a key consequence is that we are seeing longer funding cycles for startups.

However, that comes with opportunity. You have to find trusted partners that can get you to that value inflection point as quickly as possible. It's been very beneficial for Kymanox to partner with these companies so that we can re-evaluate their programmes and find the least burdensome approach, putting them in a better position to raise capital.

For larger companies, the same thing is true, but in different way, with budgets tightening internally, layoffs occurring and the need for additional capacity support. Another factor is that larger companies are making more decisions to try to be careful and mitigate risk. For big pharma, a further consideration in their thinking is that there are several key drugs that are going off patent soon, so they need to be able to fill their pipelines.

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We've also seen that advanced therapies, such as cell and gene therapies, haven't picked up as quickly as industry analysts anticipated. We're still working alongside many sponsors in this space that have some incredible therapeutics and technology in the works, but overall progress has been slower than expected. CDMOs have been hit hard in this area in particular as well.

Of course, the FDA has also been strongly impacted by the new administration, and we've seen that start to cascade and begin affecting sponsors. An example of this would be longer response times when dealing with the agency. We are even seeing this affect manufacturing inspections on sites – the FDA does not have the capacity it used to because it has let go of several of the employees that were qualified to conduct those inspections. Naturally, this is having a negative effect on how quickly products are being approved.

I don't think that the true ramifications of everything going on have yet to be fully realised – there are still a lot of question marks. So, because of that uncertainty, people are being more cautious with the decisions that they make on commercial programmes. I do think that this means that there's an opportunity to have dialogue at events like PDA Miniverse where we can come together and share the challenges and discuss how we mitigate risk together as an industry.

I think we have to remain optimistic; this is an industry that has typically been able to navigate any headwinds that have arisen through external circumstances because, ultimately, patients need drugs. They need biologics. They need therapies. That ties into the other macro trend that we're seeing, which is that rare disease indications, oncology and glucagon-like peptide 1 (GLP-1) agonists are continuing to thrive. We have to focus on innovation and novel therapies that have significant promise.

Q You both keep your fingers on the pulse of the markets and trends within pharma, biotech and combination products. To round out our discussion, can you tell our readers what currently stands out most?

MR As a broad theme, I think many of the trends we were expecting to take off across the industry are moving slower than we thought they would. A major example of this is connected health, also large-volume systems. There's definitely something happening here, but I have the feeling that there's a discussion to be had first about how we navigate an environment that is still evolving before we see these ideas realise their full potential.

EE I'd agree with that, Mathias. Another thing we're seeing making steady progress is dual chamber syringes, including for lyophilised drugs and liquid-liquid technologies. Connectivity has always been a challenge – we've seen it have success in the clinical trial space, but I think from a payer and pharmacy benefit management perspective, it's been really hard to gauge the value of it – there hasn't been much enthusiasm to pay a premium for connected technology. That said, I do think that connectivity is coming and will gain support from a compliance standpoint in the future for certain therapies.

Of course, there are also GLP-1s. I think we're going to see them being applied to indication after indication after indication. They began as a therapy for diabetes, whereas, right now, obesity is the big thing, but that's just the surface. There are discussions happening across the industry about the enormous potential of these drugs, and I think we're going to see them at least investigated for a lot more therapeutic areas.

The other subject everyone is talking about is sustainability. When I went to Pharmapack Paris earlier this year, it was all about sustainability – a lot of European companies have put significant focus on it. Globally, the pharma industry is talking about carbon footprint, sustainability and manufacturing. There have been numerous talks and panels at conferences on developing sustainable drug delivery devices and how you minimise the overall environmental impact, from manufacturing glass all the way through to fill-finish and final packaging.

Packaging solutions is a big topic for sustainability, and it's not going away. However, the actual implementation of it and what it means is still a huge challenge. We're continuing to see sponsors struggle with how to extract value while committing to investments or certain targets, such as "We're going to reduce our carbon footprint by X% by 2030."

The actual implementation is still a real challenge because, at the end of the day, we're still working with standard container closure systems. We're still working with established manufacturing facilities and methods. Changing these represents significant infrastructure investment, and that's a time-consuming and expensive process. So what we're seeing is companies trying to go for the low-hanging fruit and minimise what emissions they can without too much investment. Personally, I think true change on the sustainability side is going to take a long time.

MR It seems clear to me that Europe is going to be leading the way over the US on sustainability. But, as Evan said, it's complicated and a lot of the low-hanging fruit has been already harvested.

Another trend I think we're definitely going to see more of is the transition of injectables from intravenous to subcutaneous formats. A big driver of this is moving healthcare from clinics to patients' homes, although that's not to say that if something moves from intravenous to subcutaneous it's always moving into self-injection. Subcutaneous injection is just more sustainable; it has so many advantages, and it's this part of the industry – combination products and drug delivery devices – that's done a lot of the work to make this transition possible. I think it's a

"SUBCUTANEOUS INJECTION IS JUST MORE SUSTAINABLE; IT HAS SO MANY ADVANTAGES, AND IT'S THIS PART OF THE INDUSTRY – COMBINATION PRODUCTS AND DRUG DELIVERY DEVICES – THAT'S DONE A LOT OF THE WORK TO MAKE THIS TRANSITION POSSIBLE."

really important shift in the way patients receive care, and I'm proud that PDA Miniverse can help facilitate part of that.

EE There's always an element where you need additional expertise as a part of lifecycle management. A lot of this is cost driven but, if patients have more options, it will drive down cost. The fact is that we have so many developers and CDMOs that fail to fully consider pricing and reimbursement. They think that if we just put a drug in a novel delivery device, someone would choose it over something else, but what we find time and again is that what drives behaviour, especially in the US, is the cost to the patient. So many companies are spending millions, sometimes billions, of dollars to come up with new drug-device combination products, but if they're not priced correctly, it doesn't matter that they have connectivity or a retractable needle. Sponsors are not getting rewarded for this differentiation, especially for small molecules that have several competitors on the market.

To summarise, the theme tying this whole discussion together is that patients deserve options, with treatment being able to take place in the clinic or at home being a major one. This is why we've seen companies, and regulators, put a bigger and bigger emphasis on human factors considerations. However, a lot of companies in the industry don't have that lifecycle management and strategic expertise in-house, so they have to rely on professional services firms like Kymanox to educate them and guide them. Overall, I'm really optimistic about where the industry is headed, and I'm looking forward to discussing these topics at PDA Miniverse next month.

PDA Miniverse: Medical Devices, Combination Products and Connected Health Conference will take place in Indianapolis, IN, US on June 24-26, 2025. For more information, visit the event website, here: www.pda.org/global-event-calendar/event-detail/pda-miniverse-medical-devices-combination-products-and-connected-health-conference-2025.

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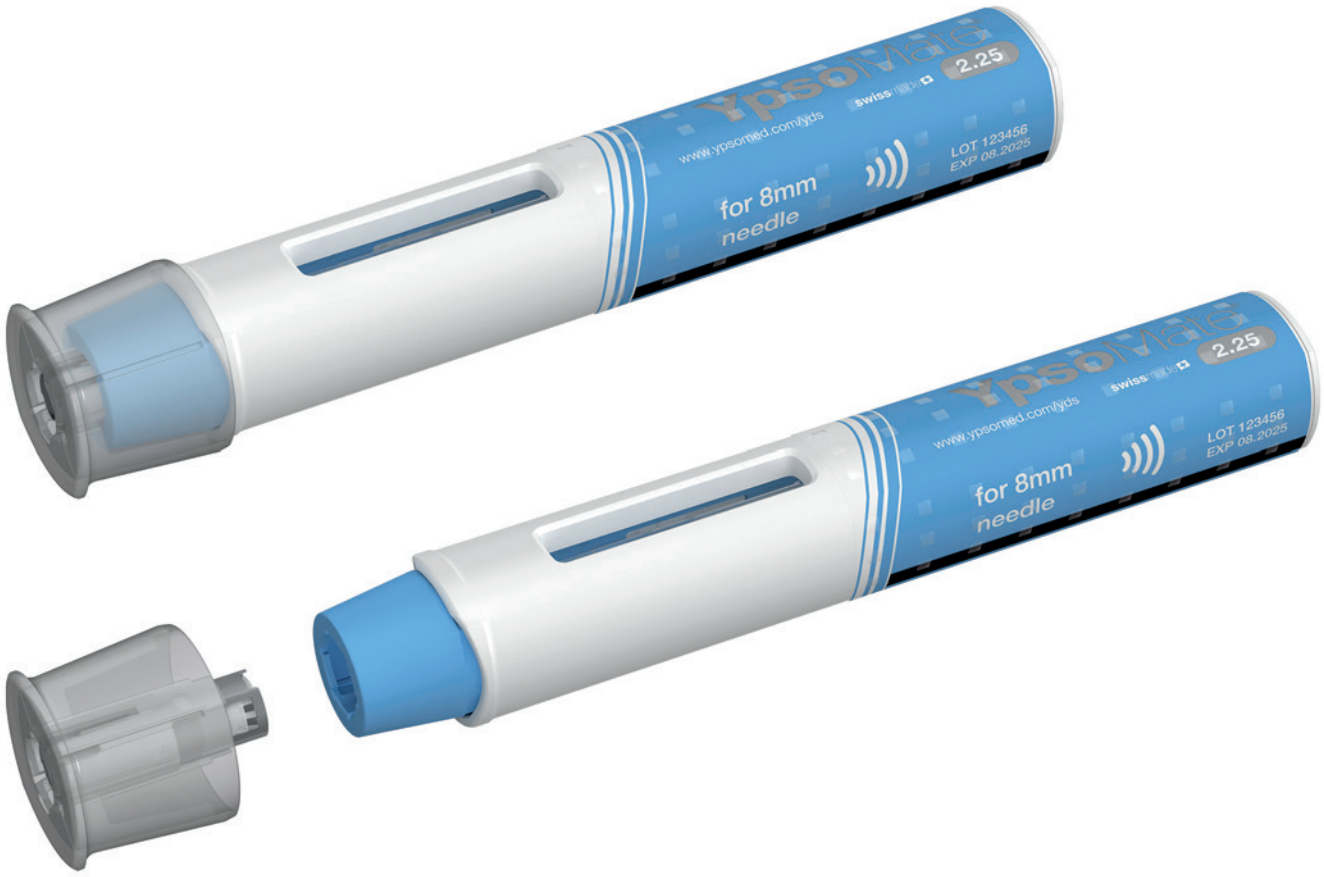


OPTIMISING HIGH-DOSE DELIVERY: SYRINGE-AUTOINJECTOR INTEGRATION, INJECTION TIME AND PERFORMANCE

Thomas Blaser of **Ypsomed** and **Dr Maëlle Douaire** of **BD**

explore how drug viscosity, autoinjectors and syringes affect the administration of injectable therapies, demonstrating the results of a study evaluating combined autoinjectors and syringes from the two companies that provide efficient and smooth delivery of high-dose therapies.

Delivering high-dose or high-concentration therapies via subcutaneous injection presents unique challenges, primarily due to increased viscosity. Biologics with high-viscosity formulations often exceed 15 cP, presenting challenges for injectability. Studies on immune globulin formulations have shown that protein concentrations above 200 mg/mL frequently exceed 20 cP, while 300 mg/mL formulations can reach viscosities as high as 128 cP.[1] These constraints highlight the need for optimised syringe and autoinjector designs that can accommodate high-viscosity drugs while maintaining usability and performance.

Higher viscosities increase injection force and may prolong injection time, leading to greater mechanical stress on autoinjectors and drug products. This can impact device usability, patient adherence and overall drug delivery experience. To maintain similar performance in the administration of high- and low-viscosity formulations, the syringe and autoinjector drive mechanism must be optimised together.

The ability to efficiently administer high-viscosity therapies depends mainly on needle design, fluid dynamics and autoinjector

drive mechanism. Each component plays a role in balancing injection time and required injection force, which may contribute to a preferred user experience. Understanding how these factors interact is essential for designing effective delivery systems.

Managing High-Viscosity Formulations in Subcutaneous Injection

Higher biologic concentrations increase viscosity, requiring advanced injection strategies to ensure controlled dose delivery within practical timeframes and patient comfort. As fluid resistance rises, greater injection force is needed to maintain acceptable delivery times. However, studies suggest that injections of up to 30 seconds for 2 mL volumes are well tolerated when supported by ergonomic autoinjector design and clear user guidance.[2]

The relationship between viscosity and injection performance is governed by fluid dynamics, where higher resistance requires increased pressure to maintain a constant flowrate. Needle length and, most importantly, needle inner diameter

"OPTIMISING SYRINGE AND AUTOINJECTOR DESIGN IS ESSENTIAL TO MAINTAINING INJECTION DURATIONS WITHIN THIS RANGE WHILE ENSURING USABILITY AND PATIENT COMFORT."

$$F = \frac{8\pi D_b^4 L_n}{D_n^4} \eta v_s + R_{(vs)}$$

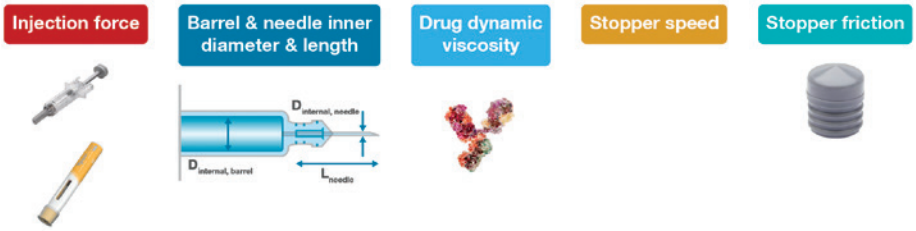


Figure 1: Fluid dynamic principles for modeling injection force and time. Considering an incompressible Newtonian fluid, a laminar flow and injection in air by application of Bernoulli theorem and Hagen Poiseuille law (including simplifications).

are dominant factors influencing injection force for the same injection time and a determined viscosity (Figure 1). Smaller inner diameter and/or longer needles can increase resistance, requiring greater force and/or extending injection time. Optimised needle-wall thickness, such as an ultra-thin wall (UTW) or extra-thin wall (ETW), results in wider needle inner diameter, which is the primary contributor to improving flow efficiency for staked needle syringes while maintaining a similar standard needle gauge profile, such as a 27G or 29G.

Beyond the needle and syringe, autoinjector drive mechanisms are essential to regulating injection performance. Spring force must be carefully adjusted – if too low, it may lead to excessively slow or incomplete injections, increasing the risk of early removal before the full dose is delivered. If too high, it may cause rapid fluid delivery, leading to discomfort and a higher likelihood of the autoinjector being removed too soon. Given the benchmark of well-tolerated injection times, optimising syringe and autoinjector design is essential to maintaining injection durations within this range while ensuring usability and patient comfort.

EVALUATING THE YPSOMATE 2.25 AND BD NEOPAK™ GLASS PREFILLABLE SYRINGE PLATFORM

Study Overview

To quantify how different syringe-needle configurations for a given autoinjector drive mechanism impact injection performance, a study was conducted using YpsoMate 2.25 paired with four BD Neopak™ glass prefillable syringe 2.25 mL platform needle designs (Figure 2) across five viscosity levels (Table 1).

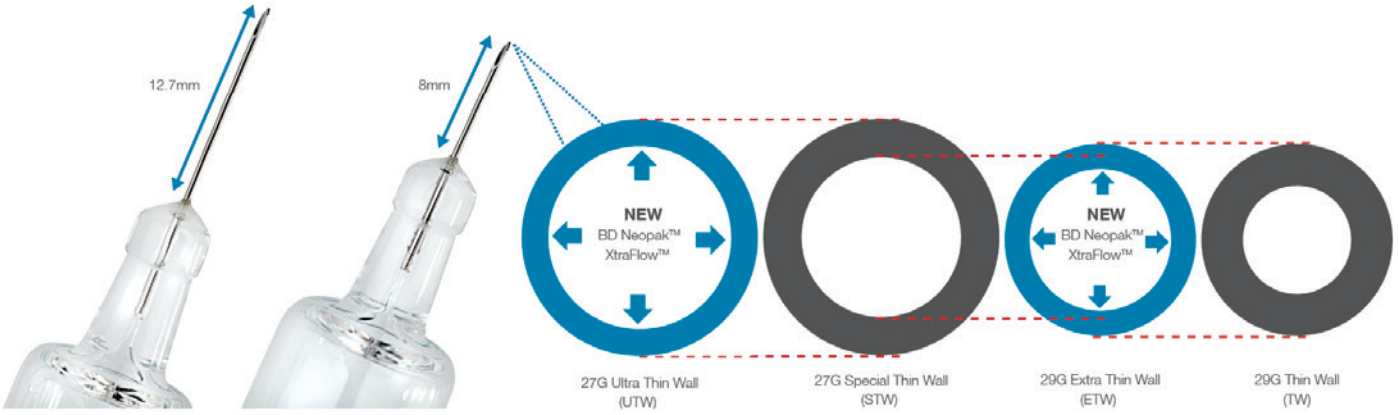


Figure 2: BD Neopak™ Glass Prefillable Syringe platform needle gauge offerings, including BD Neopak™ XtraFlow™ UTW and ETW 8 mm configurations.

Autoinjector	Needle Configuration†	Viscosity** 11cp	Viscosity** 23cp	Viscosity** 36cp	Viscosity** 53cp	Viscosity** 70cp
YpsoMate 2.25*	27G UTW 8 mm	n = 20	n = 20	n = 20	n = 20	n = 20
	27G STW 8 mm	n = 20	n = 20	n = 20	n = 20	n = 20
	27G STW 12.7 mm	n = 20	n = 20	n = 20	n = 20	n = 20
	29G ETW 8 mm	n = 20	n = 20	n = 20	n/a	n/a

*Autoinjector configuration was constant across different tested combinations. ** Viscosity at 21.5°C. †All syringes tested were a 2.25 mL BD Neopak™ or BD Neopak™ XtraFlow™ glass prefillable syringe, with varying needle configurations. UTW = Ultra-Thin Wall, STW = Special-Thin Wall, ETW = Extra-Thin Wall.

Table 1: Test overview.

The study assessed how syringe-needle configurations – including variations in needle gauge, length, and wall thickness – affect injection time when paired with the YpsoMate 2.25 autoinjector. By testing multiple syringe-needle combinations across different viscosities (Table 1), the objective was to analyse their impact on injection performance and provide insights into how these factors influence injection time into air.

The study focused on two main aspects:

1. Injection time across different needle-syringe configurations, evaluating whether dose delivery remained within a practical timeframe for various viscosities.
2. The interaction between autoinjector drive mechanism and syringe design, particularly at higher viscosities where increased resistance may influence injection performance.

Study Design and Methodology

The study was conducted under controlled laboratory conditions to replicate real-world injection performance. A high-speed camera (50 frames per second) tracked plunger rod movement, measuring injection time from activation to full dose expulsion. Autoinjectors were mounted in a vertical orientation, with all tests performed under standardised conditions to eliminate variability (Figure 3).

Four BD Neopak™ glass prefillable syringe platform needle configurations were tested with the YpsoMate 2.25 autoinjector: 29G extra-thin wall (ETW) 8 mm, 27G special-thin wall (STW) 12.7 mm (12.7 mm), 27G special-thin wall (STW) 8 mm and 27G ultra-thin wall (UTW) 8 mm. The YpsoMate 2.25 autoinjector configuration (injection force) was kept constant throughout the study.

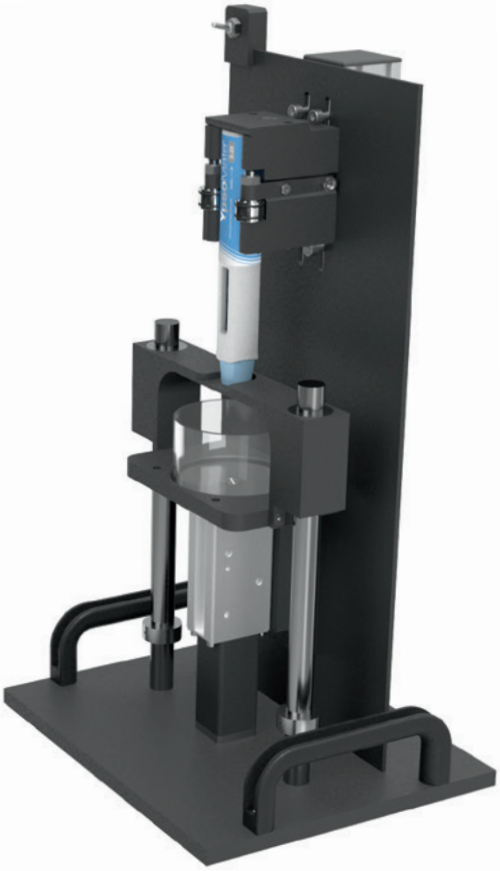
Each configuration was evaluated across up to five viscosity levels, reflecting a wide range of high-dose biologic formulations (Table 1): 11 cP, 23 cP, 36 cP, 53 cP and 70 cP.

Each configuration was tested with the autoinjector 20 times per viscosity level, ensuring statistically robust findings. The study analysed both mean injection time and variability (standard deviation and range) to assess injection consistency across configurations.

Figure 3: Schematic test set-up for injection time measurement.

Mechanical Interaction between Autoinjector and Syringe

Together, the syringe-needle configuration and autoinjector drive mechanism determine injection efficiency and consistency. The study confirmed that both shorter 8 mm needles and UTW designs improve injection times, with the 8 mm length reducing flow resistance compared with longer 12.7 mm needles, while UTW designs with increased inner diameters further optimise fluid flow without increasing needle gauge.



A well-adjusted autoinjector is essential to maintain consistent plunger movement and reliable dose delivery across viscosities. The YpsoMate 2.25 autoinjector applies controlled force, adapting to different syringe configurations while ensuring steady injection performance.

The study demonstrated how needle parameters and autoinjector drive mechanism robustness together influence injection time. The next section provides a detailed breakdown of injection time, showing the impact of needle-wall thickness and needle length across different viscosities for a given autoinjector configuration.

Performance Breakdown

The results confirmed that higher viscosity leads to longer injection times, with UTW needles and 8 mm lengths improving efficiency at higher viscosities by reducing flow resistance. Injection times ranged from 3.63 seconds at 11 cP (27G UTW 8 mm) to 37.45 seconds at 70 cP (27G STW 12.7 mm), demonstrating the impact of viscosity and needle selection on the injection time.

As viscosity increased, UTW designs consistently reduced injection time, while special-thin wall (STW) needles and longer needle configurations introduced greater flow resistance. However, the YpsoMate 2.25 maintained a steady and reliable injection performance across all configurations, demonstrating its ability to apply consistent force and ensure smooth plunger movement, regardless of syringe variations and viscosity levels (Figure 4).

At 11 cP, all syringe-needle configurations achieved efficient injection times, though differences were already measurable. The 27G UTW 8 mm needle injected in 3.63 seconds, making it the fastest among all tested configurations at this viscosity. The 27G STW 8 mm needle followed at 5.10 seconds (14% longer than UTW), while the 27G STW 12.7 mm needle took 6.08 seconds (40% longer than UTW) and the 29G ETW 8 mm took 8.13 seconds (124% longer than UTW).

For a given needle gauge, both needle-wall thickness and length influence injection time, with wall thickness playing the dominant role across all viscosities. Indeed, the Hagen Poiseuille equation shows that needle inner diameter has more weight than the needle length in the overall flow resistance of the needle. However, even at lower viscosities, a shorter needle length provided a measurable improvement in reducing injection time. All injection time measurements resulted in well-accepted ranges of injection times, regardless of the needle gauge.

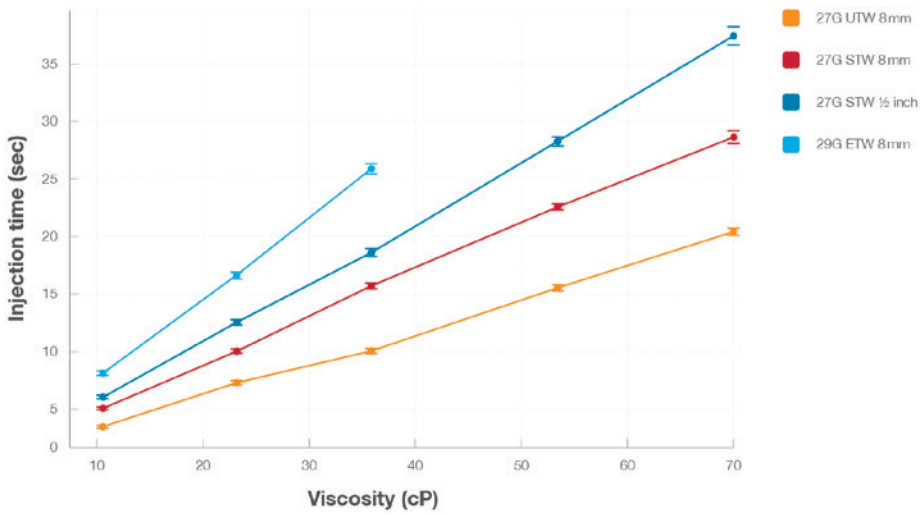


Figure 4: Injection time as a function of viscosity for different needle configurations. The 27G UTW 8 mm consistently demonstrated the shortest injection times across all viscosity levels, while longer and thicker-walled needles (27G STW 12.7 mm) resulted in significantly longer injection durations. Error bars represent standard deviation, indicating variability across 20 measurements per condition.

At 23 cP, the viscosity increase amplified the differences in injection time between configurations. The 27G UTW 8 mm needle injected in 7.30 seconds, confirming that thinner walls / larger needle internal diameters significantly reduce fluid resistance. The 27G STW 8 mm needle required 10.05 seconds (38% longer than UTW), while the 27G STW 12.7 mm needle took 12.57 seconds (72% longer than UTW) and the 29G ETW 8 mm took 16.63 seconds (128% longer than UTW), reinforcing that both wall thickness and needle length contribute to injection time reductions, even if all measured injections were within the preferred range.

At 36 cP, the efficiency of the UTW needle design became even more pronounced. The 27G UTW 8 mm needle injected in 10.10 seconds, maintaining superior performance as other configurations slowed significantly. The 27G STW 8 mm needle required 15.72 seconds (56% longer than UTW), while the 27G STW 12.7 mm needle extended to 18.61 seconds (84% longer than UTW). These results confirm that longer needles introduce greater flow resistance, but needle-wall thickness continues to have the most significant impact on reducing injection time. The 29G ETW 8 mm needle remained within the practical injection time range at 25.90 seconds. However, as viscosity increased, projected injection times exceeded the preferred range, leading to the decision not to evaluate this configuration at higher viscosities, reinforcing that needle gauge and bore size must be optimised for higher viscosities.

> "LONGER NEEDLES INTRODUCE GREATER FLOW RESISTANCE, BUT NEEDLE-WALL THICKNESS CONTINUES TO HAVE THE MOST SIGNIFICANT IMPACT ON REDUCING INJECTION TIME."

At 53 cP, injection time increased significantly across all configurations, with the 27G UTW 8 mm needle maintaining the shortest injection time at 15.57 seconds. The 27G STW 8 mm needle took 22.60 seconds (45% longer

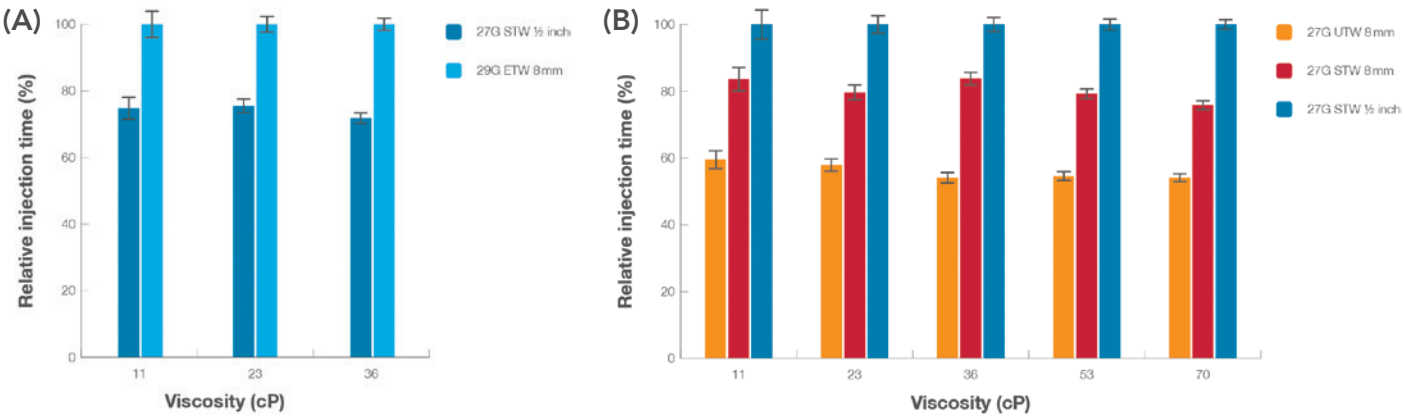


Figure 5: Relative injection time across viscosities, with the longest injection time at each viscosity set to 100%. A) Comparison between different needle gauges (27G STW 12.7 mm and 29 ETW 8 mm). B) Comparison between same needle gauge and different needle lengths and wall types (27G UTW 8 mm, 27G STW 8 mm, 27G STW 12.7 mm).

"THE STUDY DEMONSTRATED THAT INJECTION TIME IS PRIMARILY INFLUENCED BY THE COMBINATION OF NEEDLE-WALL THICKNESS AND LENGTH, WITH UTW DESIGNS AND SHORTER 8 MM NEEDLES TOGETHER PROVIDING THE GREATEST EFFICIENCY GAINS."

than UTW), while the 27G STW 12.7 mm needle required 28.29 seconds (82% longer than UTW). The gap between STW and UTW designs widened further, confirming that UTW optimisation is essential for efficient injection of high-viscosity drug formulations, such as biologics.

At 70 cP, injection times ranged from 20.42 to 37.45 seconds, varying by up to 83% between configurations. The 27G UTW 8 mm needle completed injection in 20.42 seconds, while the 27G STW 8 mm needle remained within the practical range at 28.63 seconds. The 27G STW 12.7 mm needle took 37.45 seconds (83% longer than UTW), confirming that longer, thicker-walled needles become increasingly inefficient for high-viscosity therapies. These results demonstrate that both shorter needles and thinner walls contribute to faster injection times, particularly as viscosity increases.

As shown in Figures 4 and 5, the error bars represent the standard deviation across 20 measurements per condition, illustrating the variability in injection times for each needle configuration. The data confirm that higher viscosities led to longer injection times, with error bars increasing slightly at higher viscosities, reflecting greater flow resistance and its effect on injection consistency. However, the overall variability remained within an expected range, with standard deviations across all conditions staying below 0.45 seconds, reinforcing the consistent and repeatable performance of the YpsoMate 2.25 autoinjector combined with the 2.25 mL BD Neopak™ glass prefillable syringe platform. These findings highlight the importance of optimising syringe selection and autoinjector drive mechanism to maintain predictable injection performance, even under varying viscosity conditions.

Industry Impact

The study demonstrated that injection time is primarily influenced by the combination of the needle's wall thickness and length, with UTW designs and shorter 8 mm needles together providing the greatest efficiency gains. For high-viscosity formulations

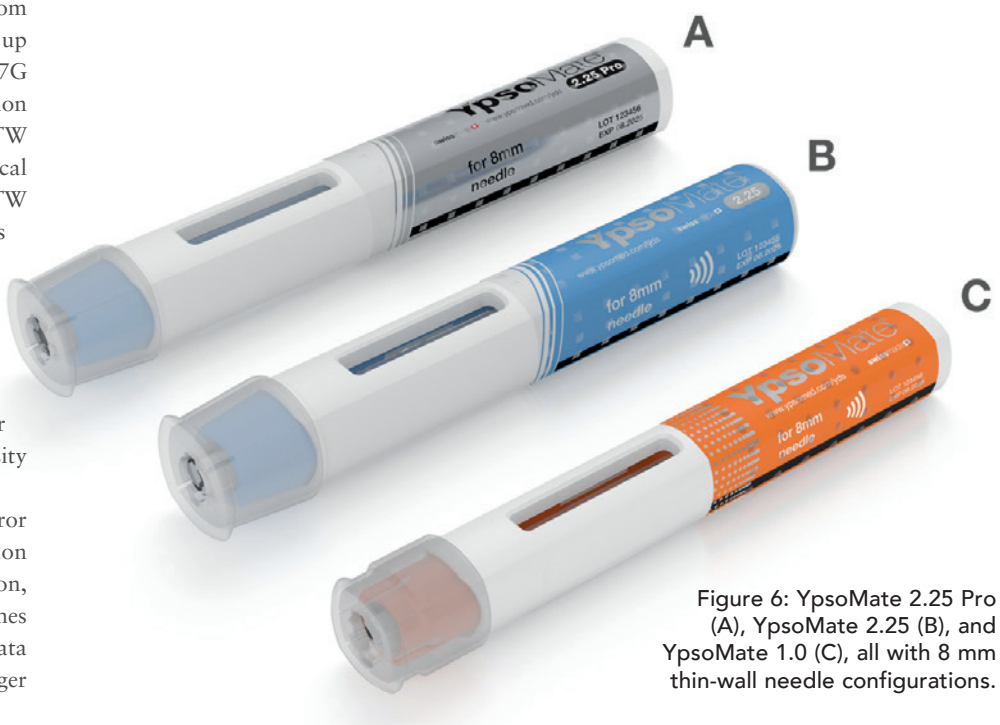


Figure 6: YpsoMate 2.25 Pro (A), YpsoMate 2.25 (B), and YpsoMate 1.0 (C), all with 8 mm thin-wall needle configurations.

"ACROSS ALL VISCOSITY LEVELS, THE YPSOMATE 2.25 AUTOINJECTOR MAINTAINED CONTROLLED INJECTION SPEED AND SMOOTH PLUNGER MOVEMENT."

above 36 cP, the impact of needle selection becomes even more pronounced, as flow resistance increases significantly. The study showed that UTW needles and 8 mm lengths provided the greatest efficiency gains at these viscosities, keeping injection times within a preferred range while ensuring dose accuracy.

Across all viscosity levels, the YpsoMate 2.25 autoinjector maintained controlled injection speed and smooth plunger movement, ensuring consistent force application and reliable dose delivery, with injection time variability remaining very low (0.45 seconds) across all conditions. The results confirm that optimising both syringe selection and autoinjector drive mechanism is essential for achieving predictable injection times, usability and performance consistency in high-dose drug delivery.

CONCLUSION

Through their partnership, Ypsomed and BD are advancing self-injection solutions by enabling integration of the YpsoMate autoinjector platform with the BD Neopak™ XtraFlow™ glass prefillable syringe (Figure 6). This collaboration provides pharmaceutical and biotech companies with flexible options to select the optimal syringe configuration for their formulation needs, balancing injection time and delivery consistency. By combining the expertise in syringe and needle technologies from BD with the leadership in autoinjector design from Ypsomed, the partnership ensures reliable and user-friendly self-injection systems, even for high-viscosity and complex formulations.

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Thomas Blaser

Thomas Blaser has been working as a Mechanical Engineer, Autoinjectors, in Product Development at Ypsomed since 2024. He is a trained polymechanic and studied mechanical engineering in Switzerland. His main responsibilities include the technical support of existing products, with a focus on handling market complaints, conducting root cause analyses and implementing design changes. He also performs verification activities and prepares development-related documentation in accordance with internal processes. With his technical expertise, he contributes to maintaining product quality and driving continuous improvement throughout the product lifecycle.

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Maëlle Douaire, PhD, is the R&D Segment Lead for the Biologics Prefillable Syringe platform at BD. With extensive experience in both academic and industrial research, Dr Douaire has worked on diverse areas including food formulation engineering, colloids and emulsions, microfluidic devices and rheology. She holds a PhD in Engineering from the University of Toulouse (France), which, combined with her industrial experience, has provided her with a broad scientific and technical understanding of complex systems. Her expertise spans multiple disciplines, enabling her to tackle challenging problems with innovative solutions. Having joined BD in 2021, her focus is on portfolio development activities, with a key element being the expansion of the system approach to streamline the integration of prefillable syringes in combination products.

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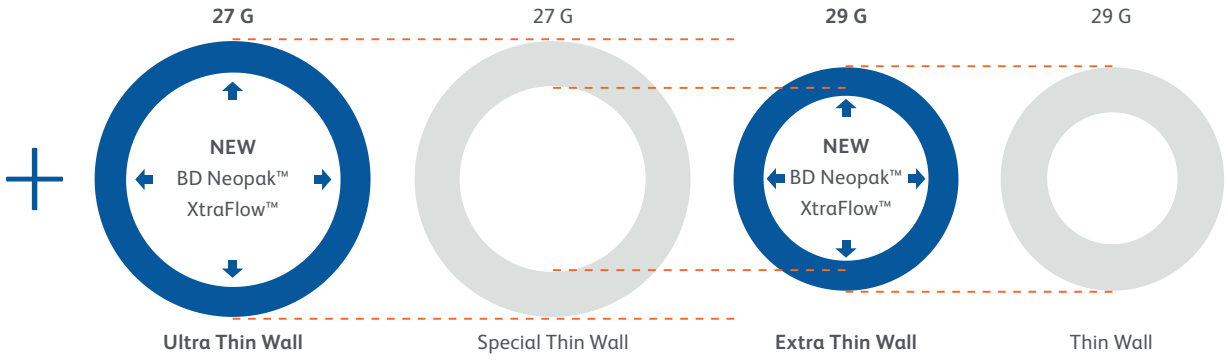

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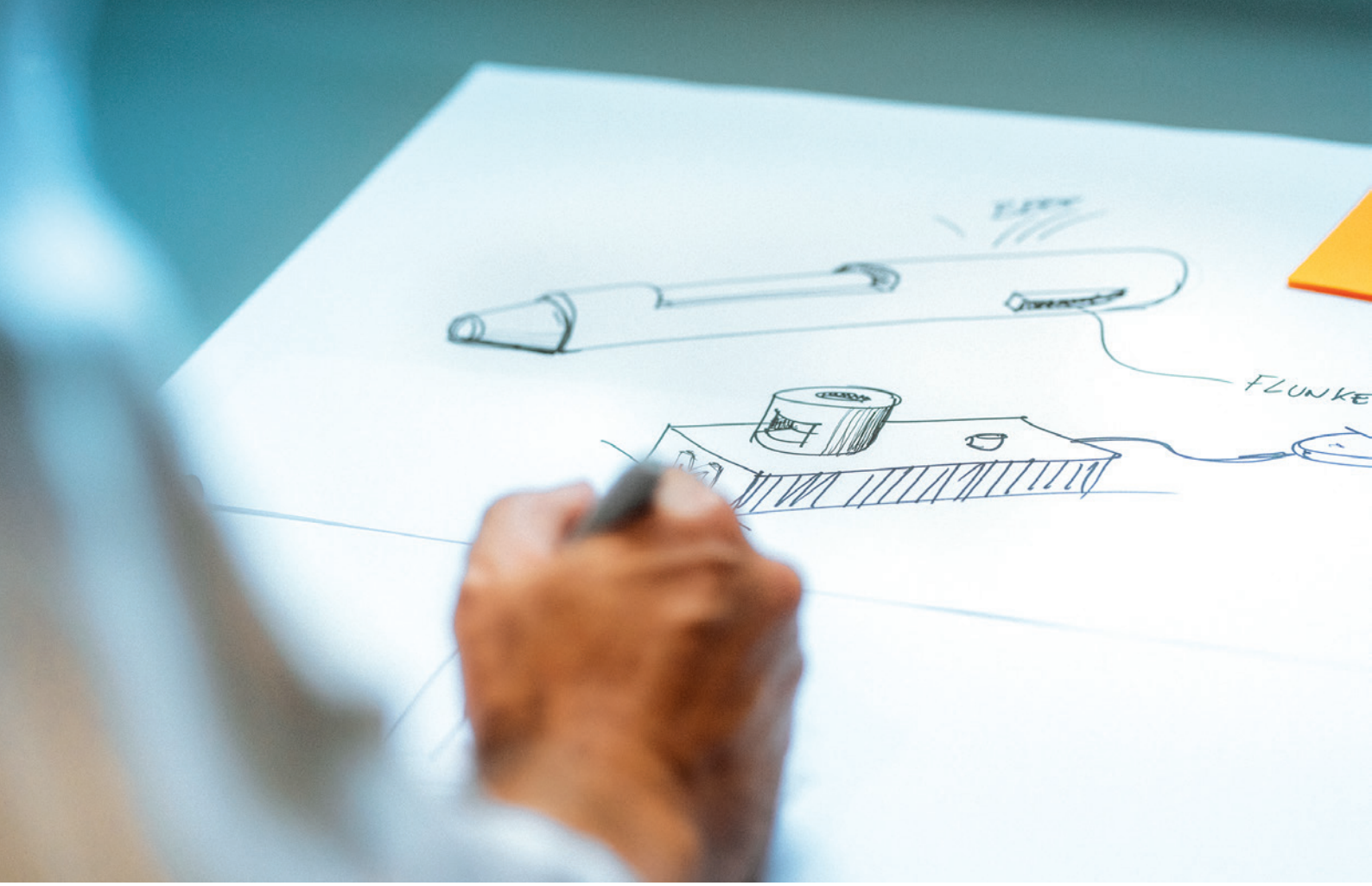

DRIVING SUSTAINABILITY IN DRUG DELIVERY DEVICE DESIGN AND MANUFACTURING

Martin Høier Thomsen of **MGS** discusses the need for the pharma industry to rise to the challenges of meeting its sustainability goals, explaining how MGS' expertise and established practices to drug delivery device design and manufacture present a forward-thinking approach to achieving this aim.

MEETING THE PHARMA INDUSTRY'S SUSTAINABILITY CHALLENGE

Sustainability is now a critical objective for the pharma industry, one that extends beyond drug formulation and into the design, production and lifecycle management of drug delivery devices. As regulatory agencies tighten environmental standards and consumers increasingly favour eco-conscious products, pharma manufacturers must find ways to align their sustainability goals with patient safety, therapeutic efficacy and global compliance.

In fact, the healthcare sector, which includes the pharma industry, accounted for 4.4% of global carbon emissions in 2014,[1] a figure that has only grown alongside rising demand for advanced treatments and the widespread adoption of complex drug delivery systems. These systems, ranging from autoinjectors to inhalers, prefilled syringes (PFS) and intravenous (IV) delivery components, all play a critical role in modern medicine but also significantly contribute to environmental impact due to their material composition, manufacturing energy needs and end-of-life disposal challenges.

At the intersection of these environmental and regulatory pressures, pharma companies are seeking new strategies to reduce the carbon footprint of their devices without compromising patient outcomes or regulatory compliance. This is where MGS comes in. By applying a robust eco-design methodology (Figure 1) and employing vertically integrated

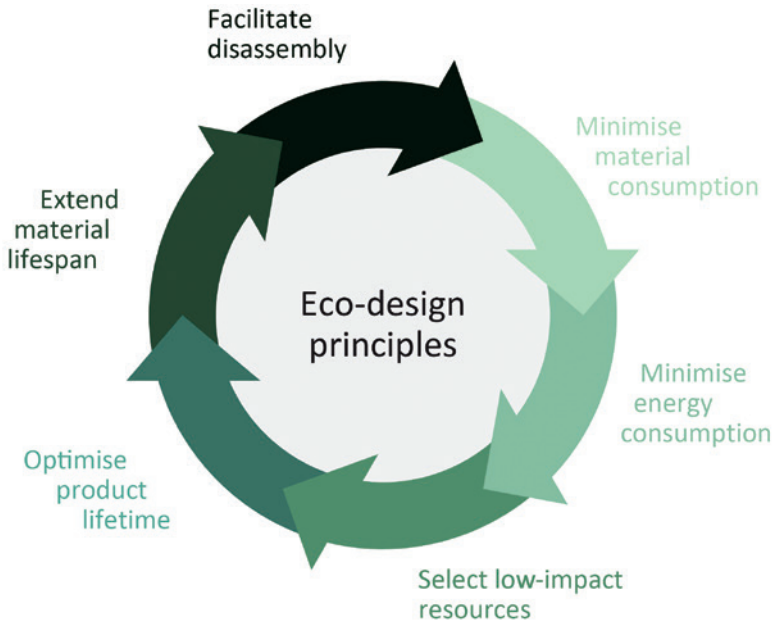

Figure 1: The six eco-design principles implemented in MGS' product development model.

manufacturing capabilities, MGS helps its pharma partners minimise waste, improve efficiency and future-proof drug delivery devices.

WHY STRATEGIC COLLABORATION IS ESSENTIAL

Pharma companies developing drug delivery devices are in a unique position. They operate in one of the most heavily regulated sectors globally, upholding the highest standards of quality, while simultaneously managing consumer and healthcare provider demands for environmental responsibility.

Working with a specialised manufacturing partner for drug delivery devices offers key advantages in navigating this complex landscape. By collaborating with experts in sustainable device design and production,[1] pharma firms can gain access to:

- **Leading Expertise and Dedicated Support**: Partnering with MGS means working with a team of industry-leading engineers, designers and regulatory experts who are fully committed to customer and patient success. The company's specialists bring decades of experience in drug delivery device development, ensuring that every project benefits from cutting-edge innovation and a patient-centric approach.
- **Specialised Product Development and Engineering Resources**: Expertise in balancing eco-design principles with strict pharma regulatory requirements, such as ISO 13485, US FDA 21 CFR and the EU MDR.
- **Faster Time to Market**: Streamlined design for manufacturing processes that reduces the need for costly reworks and accelerates commercialisation timelines.
- **Greater Supply Chain Control**: Vertical integration across manufacturing processes – product design and development, tooling, automation, manufacturing – enables comprehensive oversight of quality and sustainability metrics from concept through production and post-market support.
- **Reduced Risk**: A partner like MGS can help to mitigate common challenges related to product design, material selection, manufacturing efficiency and regulatory audits.

With a proven track record in drug delivery device design, engineering and manufacturing, MGS empowers its partners to meet rising global sustainability expectations while developing safe, high-performing and compliant combination products.

SIX ECO-DESIGN PRINCIPLES FOR SUSTAINABLE MANUFACTURING

MGS follows a structured, six-principle eco-design framework that optimises drug delivery devices for sustainability without sacrificing functionality or patient safety.

Designing for Material Reduction

Material selection is one of the most impactful levers available in sustainable device design. Using fewer materials and minimising their volume has cascading benefits throughout the supply chain, from reducing raw material demand and simplifying moulding processes to enhancing recyclability at a product's end-of-life.

MGS encourages its customers to strategically balance critical performance attributes, such as durability, biocompatibility and sterilisation compatibility, with sustainability indicators such as carbon footprint, energy consumption and recyclability. For instance, polypropylene (PP) is a single-type polymer that offers excellent recyclability compared with more complex copolymers, while still meeting many pharma-grade requirements.

Additionally, MGS employs advanced engineering techniques such as:

- **Topology Optimisation**: Using computer-aided design to distribute material only where it is structurally necessary, creating lightweight, resource-efficient components (Figure 2).
- **Moulding and Filling Simulations**: These simulations optimise wall thickness, gating locations and cooling pathways, significantly reducing material waste and supporting leaner production cycles.

Through thoughtful material reduction and optimisation, pharma partners can easily develop components and products that are lighter, more sustainable and more cost-effective to produce.

"MATERIAL SELECTION IS ONE OF THE MOST IMPACTFUL LEVERS AVAILABLE IN SUSTAINABLE DEVICE DESIGN."

Figure 2: Evaluating a topology-optimised prototype – designing with material efficiency in mind supports lighter, more sustainable drug delivery devices.

Lowering Energy Consumption at Every Stage

Energy efficiency is critical to a drug delivery device's overall environmental footprint. From manufacturing to end use, reducing energy demand leads to measurable carbon reductions.

MGS integrates energy-saving strategies throughout its vertically integrated manufacturing operations, including:

- **Servo-Electric Injection Moulding:** This technology consumes significantly less energy than traditional hydraulic systems.
- **Advanced Cooling Systems:** Conformal cooling channels, thermally balanced moulds and insulated tooling reduce cycle times and limit energy consumption.
- **Optimised Assembly Lines:** Applying design for manufacturing and assembly principles, MGS engineers simpler device designs that reduce assembly complexity and energy input during production.

Additionally, MGS works with its pharma partners to design drug delivery devices that are compatible with energy-efficient sterilisation and maintenance processes, such as low-temperature sterilisation methods, further reducing a device's lifecycle impact.

Prioritising Sustainable and Low-Impact Materials

Material selection extends beyond volume reduction to include sourcing and processing. MGS helps its pharma clients identify and incorporate low-impact materials, such as bio-based polymers and recyclable resins, into device designs where appropriate. While regulatory constraints currently limit the direct use of recycled resins and many bio-based polymers in drug delivery devices, there are still ways to integrate sustainability, such as selecting materials with lower environmental footprints or improving recyclability through mono-material design.

Beyond just recommending eco-friendly materials, MGS leverages lifecycle screenings (LCS) to assess a product's environmental footprint early in the development process (Figure 3). LCS provides data-driven insights into the environmental impacts of material choices, enabling companies to make informed decisions that consider both regulatory requirements and sustainability goals.

For instance, selecting a simpler, mono-material polymer over a blend not only reduces energy during material processing but also facilitates future recycling and reduces regulatory complexity associated with waste handling and disposal.

Designing for Longevity

The pharma industry faces unique challenges when choosing between single-use and reusable devices. Single-use

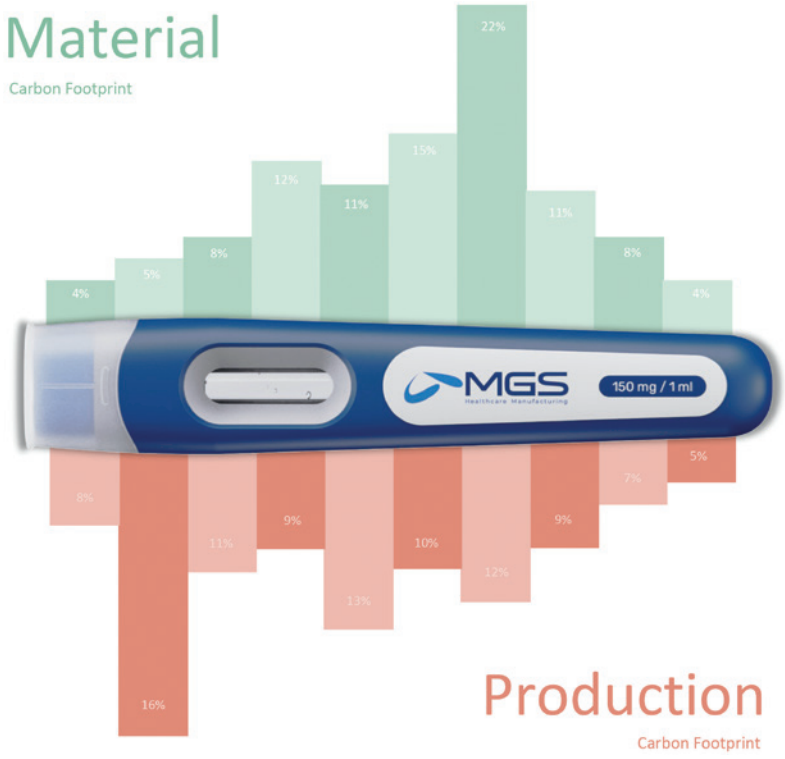

Figure 3: LCS are used to calculate a product's carbon footprint to support design decisions.

devices, such as PFS, IV bags and infusion tubing, must be lightweight and minimise waste at the end of their lifecycle. In contrast, reusable components, such as surgical devices or certain autoinjector housings, should be engineered for long-term performance, repairability and durability.

MGS helps its pharma customers carefully define device lifespans and tailor designs to meet their specific use-case scenarios while avoiding overengineering. The company employs strategies that include:

- **Robust Design Principles:** Simplifying mechanical features and reducing component count without sacrificing reliability.
- **Modular Components:** Creating devices with replaceable or serviceable parts to extend product lifespan where appropriate.
- **Material Durability:** Selecting high-performance materials that withstand repeated use, sterilisation cycles and transport handling.

By aligning design intent with actual product use requirements, pharma companies can reduce the environmental impact of both single-use and reusable devices.

Promoting Proper Recycling of Pharmaceutical Devices and Materials

Unlike consumer goods, pharmaceutical devices often cannot incorporate recycled materials due to the strict health and safety regulations that govern them. However, proper disposal and recycling of these devices remain crucial in reducing their environmental impact (Figure 4). A few ways to extend material lifespan include:

- Designing devices that use single-type polymers, such as PP, to simplify recyclability
- Co-operating with material processing companies to establish take-back programmes to ensure responsible end-of-life processing of devices
- Advising on sustainable packaging solutions such as bio-based or recyclable packaging that reduce overall waste.

While closed-loop recycling for pharma-grade materials is still emerging, these strategies position leading pharma innovators to meet regulatory and corporate sustainability objectives today, while also preparing for future advancements in material recovery.

Enabling Easy Disassembly for Improved Recycling

Ease of disassembly is a key factor in facilitating the recycling of drug delivery devices, particularly those used in clinical or at-home care settings where healthcare providers and patients handle disposal.

Figure 4: Important design decisions to extend material and product lifetime are made in the early development phases. The goal is to prioritise reuse and, when that's not feasible, to ensure recyclability wherever possible.

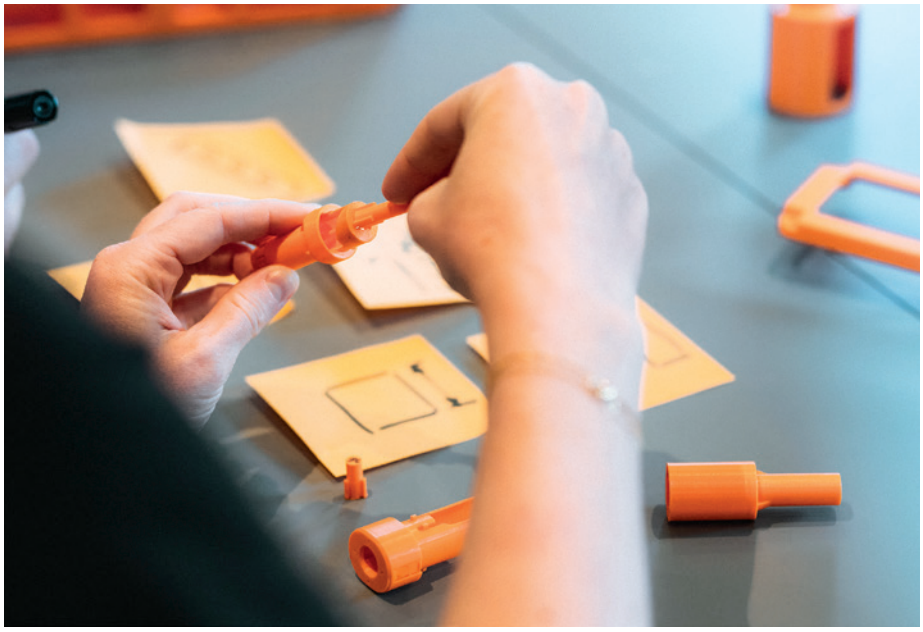

Figure 5: Hands-on evaluation of a device prototype with modular components – designing for easy disassembly supports more efficient recycling and sustainable end-of-life processing.

MGS integrates features into device designs that enable easier material separation post-use (Figure 5), including:

- Snap-fit connections and interlocking components that allow for manual or mechanical disassembly
- Break lines or fracture points that enable controlled breakage, which aids in separating materials for recycling
- Crush-separation designs for single-use devices that will be processed in industrial recycling facilities.

By engineering for disassembly, MGS makes it easier for healthcare facilities, recycling centres and even patients to engage in sustainable disposal practices, helping pharma companies meet their environmental commitments.

WHY SUSTAINABLE DESIGN PROVIDES A COMPETITIVE EDGE

Eco-design isn't just about environmental stewardship; it also offers significant business benefits:

- **Operational Cost Savings:** Leaner material use, shorter cycle times and reduced energy consumption help to lower production and operation costs.
- **Regulatory Resilience:** Early adoption of eco-design principles can help to future-proof products against tightening global environmental regulations.
- **Enhanced Market Trust:** Sustainability is increasingly a key purchasing factor for healthcare providers and patients alike.

By integrating sustainability into their device design and manufacturing strategies, pharma companies can position themselves as forward-thinking, responsible organisations in a competitive and evolving marketplace.

THE FUTURE OF DRUG DELIVERY DEVICES

As industry expectations shift towards greater environmental accountability, sustainability will become a baseline standard, not a differentiator. Pharma companies that proactively embrace eco-design principles will be better positioned to meet evolving regulatory frameworks and changing market demands.

MGS is committed to staying at the forefront of this transformation. The company is well positioned to help its pharma partners create next-generation drug delivery devices that deliver both clinical performance and environmental responsibility. Sustainable drug delivery device design is a necessity for modern pharma companies that are committed to environmental stewardship and regulatory excellence. By prioritising eco-design, pharma can deliver safer, greener products that help patients, providers and the planet.

"EASE OF DISASSEMBLY IS A KEY FACTOR IN FACILITATING THE RECYCLING OF DRUG DELIVERY DEVICES, PARTICULARLY THOSE USED IN CLINICAL OR AT-HOME CARE SETTINGS WHERE HEALTHCARE PROVIDERS AND PATIENTS HANDLE DISPOSAL."

MGS: A STRATEGIC PARTNER FOR SUSTAINABLE INNOVATION

MGS works with leading pharma companies to embed sustainability into every stage of device development and manufacturing. The company's approach includes:

- End-to-end integration of eco-design principles, ensuring that sustainability is built in from concept through commercialisation
- Vertically integrated capabilities, giving its pharma customers direct access to product design and development, tooling, automation and manufacturing to drive efficiency and reduce supply chain complexity
- A continuous improvement mindset, with ongoing investments in green technologies, sustainable materials research and process optimisation.

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Martin Høier Thomsen

Martin Høier Thomsen is a Senior Development Engineer on MGS' product design and development team. He is a skilled engineer with a Masters in Engineering from Aalborg University (Denmark) and has more than a decade of experience in medical device development. He has a passion for transforming ideas into market-ready products, directing the process from imagination to realisation. Mr Thomsen spent six years as a line manager at LEO Pharma where he built in-depth knowledge of the pharmaceutical industry and what matters most to pharma innovators. He is also certified in Scaled Agile Framework (SAFe), specialising in product management and agile methodologies.

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Product Showcase

DELIVERING INJECTIONS: CCBIO'S INJECTOR PLATFORM PRODUCTS

THE IMPORTANCE OF SELF-INJECTION

There is clear evidence to suggest that self-injection is an effective strategy for improving adherence to medication in gastrointestinal therapies. This is largely because pen injectors, compared with traditional injections administered in a clinical setting, reduce discomfort and enhance user-friendliness (Figure 1).[1]

The self-injection process has evolved over time to meet the demands of a variety of medications, resulting in the development of cartridge-based designs with variable dosing and multidose capabilities, as well as designs based on single-use prefilled syringes (PFS). Medications that require frequent daily injections and make use of self-injection devices include insulin, human growth hormone, follicle-stimulating hormone, adrenaline (epinephrine), glucagon-like peptide 1 (GLP-1) and parathyroid hormone.

Future advancements will likely focus on the sustainability and reusability of self-injection pens. Reusable injection pens were first introduced in 2000, primarily targeting insulin and the diabetes market. Today, over 12 million reusable pens and more than 1.7 billion prefilled pens are sold annually, with GLP-1s driving additional growth in the demand for injection pens.

Figure 1: CCBio's portfolio of self-injection products.

Property	Flora	Felice Dose	Quick Dose	Ianus
Device Type	Electronic-assisted autoinjector	Electronic-assisted on-body injector	Electronic-assisted on-body injector	Two-drug autoinjector
Usage	Mutidose; reusable	Single dose; disposable	Mutidose; reusable	Single dose; disposable
Dose Volume	0.01–1 mL	0.1–40 mL	0.01–40 mL	0.1–3 mL
Injection Needle	User installs PFS or cartridge with 32G needle	Hard needle: 27G Soft needle: 25G	Hard needle: 27G Soft needle: 25G	Two 27G

Table 1: CCBio's injector platform products.

Figure 2: CCBio's portfolio of advanced injector platform products.

Figure 3: CCBio's cartridge-based pen injectors.

CCBIO'S SELF-INJECTION PRODUCT PORTFOLIO

From initial design to practical market applications, CCBio has developed a suite of innovative injector platform products based on patient-centric usage patterns for self-injection devices (Figure 2). These injectors, both autoinjectors and on-body injectors, are designed to provide pharmaceutical partners with superior solutions, offering enhanced convenience and functionality (Table 1).

Cartridge-Based Design

CCBio also provides an array of cartridge-based injection pens (Figure 3). The primary container format for these devices is a 3 mL glass cartridge (Table 2), which provides a reliable and versatile solution for storing and delivering injectable drugs via the subcutaneous administration route.

Property	Kratos	Aurora	Castor	Pollux
Device Type	Manual pen	Spring-assisted pen	Manual pen	Manual pen
Usage	Fixed 0.08 mL dose; disposable	Mutidose; disposable	Mutidose; disposable	Mutidose; reusable
Dose Volume	0.08 mL	0.01–0.8 mL	0.01–0.6 mL	0.01–0.6 mL

Table 2: CCBio's cartridge-based design injector platform products.

PFS-Based Design

Completing its product portfolio, CCBio offers two single-use autoinjectors (Figure 4). The primary container format for these devices is either a 1 or a 2.25 mL PFS (Table 3), which provides a reliable and versatile solution for storing and delivering injectable drugs via the subcutaneous administration route.

CCBIO'S AUTOMATED ASSEMBLY LINE FOR SELF-INJECTION PRODUCTS

CCBio is proud to be a fully Taiwan-based company, taking full advantage of Taiwan's strong advantages in semiconductors, metal processing

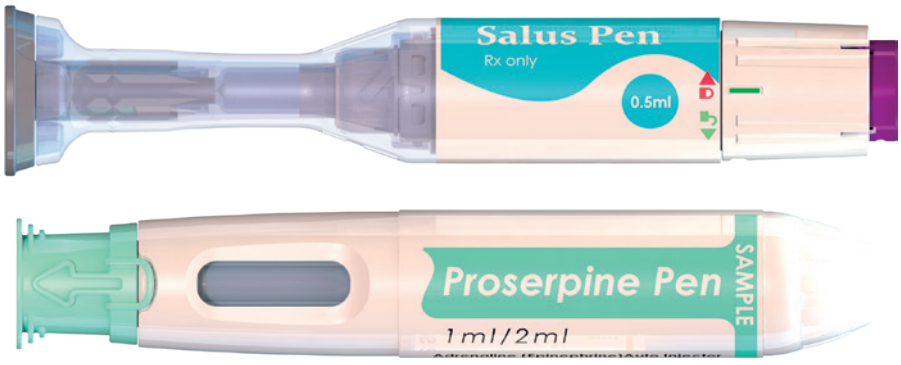

Figure 4: CCBio's PFS-based pen injectors.

Property	Salus	Proserpine
Device Type	27–29G autoinjector	27–29G autoinjector
Usage	Single dose; disposable	Single dose; disposable
Dose Volume	0.5–0.75 mL	0.3–2 mL

Table 3: CCBio's PFS-based injector platform products.

Figure 5: CCBio's automated assembly line.

and automation. The company offers a fully integrated service, applying top-tier craftsmanship to its products and manufacturing processes (Figure 5). As a trusted supplier, CCBio ensures that its customers receive comprehensive, high-quality solutions tailored to their requirements.

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TRANSFORMING PARENTERAL DELIVERY: KEY CONSIDERATIONS FOR SC AND IM FORMULATION DEVELOPMENT

Jeff Clement of **PCI Pharma Services** looks at the changing landscape of parenteral delivery, considering the pros and cons of intravenous, subcutaneous and intramuscular formulations and considers how new technologies are reshaping the drug delivery landscape.

The pharmaceutical landscape is constantly evolving as patient-centric care and innovative drug delivery methods reshape treatment paradigms. Among these advancements, the transition of many traditional intravenous (IV) therapies to subcutaneous (SC) and intramuscular (IM) formulations stands out as a pivotal development. A report by Roots Analysis has estimated that the global subcutaneous biologics market for approved drugs will reach US$233 billion (£176 billion) by 2035, with this significant growth bringing tangible benefits for patients, healthcare systems and manufacturers.

THE IMPERATIVE FOR TRANSITION: WHY SHIFT FROM IV TO SC AND IM?

The change from IV to SC or IM administration is driven by multiple factors, including patient centricity and self-administration to aid convenience, the increased availability and wider acceptance

> "SC AND IM FORMULATIONS, HOWEVER, CAN BE SELF-ADMINISTERED OR ADMINISTERED IN OUTPATIENT SETTINGS, REDUCING HOSPITAL VISITS AND IMPROVING PATIENT QUALITY OF LIFE."

of drug delivery devices, a focus on reduced healthcare resource use and costs, and an overall objective to improve therapeutic adherence for better patient outcomes.

Traditional IV therapies often require prolonged infusion times in controlled clinical environments, imposing a logistical burden on patients and healthcare providers. SC and IM formulations, however, can be self-administered or administered in outpatient settings, reducing hospital visits and improving patient quality of life.

For pharmaceutical companies, SC and IM formulations extend product lifecycles and intellectual property (IP), enhance market differentiation and align with value-based care models. Notably, the exponential growth of glucagon-like peptide-1 (GLP-1) therapies has accelerated interest in alternative patient-centric delivery mechanisms, highlighting the importance of decentralised care.

When transitioning from IV to SC or IM administration, it is important to consider the advantages and limitations of each delivery technique, as well as the need to balance pharmacokinetics, patient comfort and operational feasibility. Tables 1 and 2 show the advantages and disadvantages of each type of administration.

	Intravenous (IV)	Intramuscular (IM)	Subcutaneous (SC)
Use Case	For administration of drug products in emergency situations and drugs with poor oral absorption	Useful for formulations needing sustained release	Suitable for vaccines, biologics and patient self-administration therapies
Onset of Action	Rapid onset exposure	Moderate onset, typically 15–30 minutes	Slower onset due to absorption through subcutaneous tissue, can be 30 minutes to several hours
Bioavailability	100% bioavailability due to direct systemic delivery	High bioavailability, although slightly lower than IV	High but variable bioavailability depending on tissue perfusion
Pharmacokinetics	Rapid systemic absorption with consistent plasma concentration profiles	Depot effect possible for slow, sustained drug release	Slower uptake enhances duration of therapeutic effect
Volume	Minimum constraints, volumes can be up to litres	Moderate volumes (2–5 mL)	Typically small volumes (1–2 mL)
Dose Control	Optimised management of therapeutic concentration and titration parameters	Suitable for drugs requiring prolonged or sustained release	Allows for gradual drug absorption and sustained therapeutic effect
Patient Adherence	Healthcare administration ensures compliance	Can be administered by healthcare providers or in some cases self-administered	Easily self-administered by patient, enhancing compliance

Table 1: Advantages of IV, SC and IM administration.

	Intravenous (IV)	Intramuscular (IM)	Subcutaneous (SC)
Skill Required	Requires trained healthcare personnel	Requires knowledge of specific points on the body to avoid nerve damage	Easier to perform, but clear instructions for use and training needed
Formulation Challenges	Requires aqueous and sterile formulations compatible with blood	Sterile formulation should be well-tolerated and optimised for intramuscular uptake	Limited by volume, solubility and viscosity; must minimise local irritation
Stability Concerns	Maintains solution stability, with degradation risk introduced during administration	Stability for depot formulations may require advanced formulation strategies	Stability of proteins and biologics must be ensured over time
Convenience	Requires clinical setting and monitoring	Requires healthcare provider oversight	Ideal self-administration, increasing patient convenience and adherence
Cost	High cost due to hospital setting administration and required equipment	Lower cost than IV but more expensive than SC	Cost-effective for long-term treatments and self-administration

Table 2: Limitations of IV, SC and IM administration.

"SC TISSUE TYPICALLY HAS LOWER BLOOD FLOW COMPARED WITH MUSCLE, RESULTING IN SLOWER DRUG ABSORPTION, WHILE IM INJECTIONS CAN PROVIDE A FASTER ONSET OF ACTION DUE TO RICHER VASCULARISATION."

SCIENTIFIC CONSIDERATIONS IN FORMULATION DEVELOPMENT

Pharmacokinetic and Pharmacodynamic Profiles

Developing an SC or IM version of an existing IV formulation requires a thorough understanding of its pharmacokinetic (PK) and pharmacodynamic (PD) profiles. SC and IM administration introduce variability in absorption rates, which can impact drug bioavailability, time to peak concentration and therapeutic effect duration. Formulation scientists must evaluate:

- **Drug Solubility and Stability in Various Delivery Matrices:** For biologics, such as monoclonal antibodies, the molecular size can significantly affect diffusion through interstitial tissues and lymphatic absorption, necessitating tailored formulation approaches.
- **Targeted Tissue Absorption Characteristics:** SC tissue typically has lower blood flow compared with muscle, resulting in slower drug absorption, while IM injections can provide a faster onset of action due to richer vascularisation. Formulators must carefully design studies to model these pharmacokinetic differences and assess their clinical implications to ensure therapeutic equivalence.
- **Impact of Injection Site Variability on Systemic Exposure:** Physiologically based pharmacokinetic modelling is increasingly used to predict drug behaviour following SC or IM administration. Such models integrate several key parameters, including drug physicochemical properties, tissue composition and lymphatic transport. This predictive approach helps to refine formulation design and supports regulatory submissions by offering mechanistic insights into absorption kinetics.

Excipient Selection and Compatibility

Excipients play a crucial role in stabilising the formulation and modulating drug release. In SC and IM formulations, excipients must support drug stability while minimising injection site reactions. Common excipients include:

- Viscosity modifiers to facilitate diffusion
- Buffers to maintain pH, tonicity and stability
- Preservatives, where applicable, to ensure microbial safety.

Each excipient must meet regulatory standards for biocompatibility and safety while maintaining drug efficacy over the intended shelf life. Furthermore, excipients must be chosen to account for the physiological properties of the injection site. For example, osmolarity-adjusting agents are crucial for preventing local irritation. The choice of surfactants can also impact protein stability in biologics while minimising aggregation and immunogenicity.

Excipient compatibility testing should include forced degradation studies to identify potential interactions under stress conditions. Additionally, comprehensive extractables and leachables testing is required to ensure no adverse effects arise from the chosen container-closure system.

"ADVANCED FORMULATION STRATEGIES SUCH AS MICRO-EMULSIONS, LIPOSOMAL ENCAPSULATION AND NANOPARTICLE CARRIERS CAN ENHANCE DRUG SOLUBILITY AND REDUCE INJECTION VOLUME."

Volume and Viscosity Constraints

Unlike IV administration, which allows for larger infusion volumes, SC and IM delivery are volume-limited. Generally, SC administration is restricted to 1–2 mL per injection with the exception of some recent higher volume autoinjector systems in development, while IM injections may accommodate 2–5 mL. In high-concentration biological formulations, the antibodies or proteins "stick together" and can be very viscous, proving difficult to produce and administer with a syringe, impeding administration ease and patient comfort, therefore necessitating formulation optimisation. Techniques to address these challenges include:

- Concentrating the API
- Using viscosity-reducing excipients
- Exploring technologies for sustained release.

Additionally, advanced formulation strategies such as micro-emulsions, liposomal encapsulation and nanoparticle carriers can enhance drug solubility and reduce injection volume. Enzyme-based permeation enhancers, such as recombinant hyaluronidase, are also used to facilitate the diffusion of larger molecules through dense tissues, improving bioavailability.

Rheological profiling is essential for characterising the viscoelastic properties of high-concentration protein formulations. Optimising syringeability and injectability ensures that the formulation is compatible with available delivery devices and does not exceed acceptable injection forces.

Stability and Shelf Life

Maintaining stability throughout the product lifecycle is a significant challenge when transitioning from IV to SC or IM. Stress testing under various conditions is essential to evaluate the degradation pathways specific to the new delivery format. Proteins and biologics are particularly susceptible to denaturation

and aggregation during storage and administration. Critical areas to monitor include:

- Physical stability (e.g. precipitation, phase separation)
- Chemical degradation (e.g. oxidation, hydrolysis)
- Storage conditions (e.g. temperature sensitivity).

Innovative stabilisers, such as trehalose, can mitigate stability challenges and enhance the shelf life of temperature-sensitive formulations.

Analytical methodologies must be robust and validated, incorporating size-exclusion chromatography for aggregation detection and differential scanning calorimetry to evaluate thermal stability.

REGULATORY CONSIDERATIONS

Bridging Studies and Bioequivalence

Switching from IV to SC, or even from vials to device-based delivery, constitutes a major regulatory event. Regulatory authorities therefore require robust evidence demonstrating bioequivalence or comparable efficacy and safety between the new SC or IM formulation and the existing IV product. Bridging studies are designed to evaluate the pharmacological and clinical impact of transitioning between formulations while ensuring consistent therapeutic outcomes. Key elements of a bridging study include:

- **PK Comparisons**: Evaluate parameters such as peak plasma concentration (C_{max}), area under the curve and time to peak (T_{max}) to ensure similar drug exposure between IV and SC or IM routes.
- **PD Assessments**: Where applicable, analyse biological markers or clinical endpoints to confirm that the therapeutic effect remains unchanged.
- **Immunogenicity Evaluations**: For biologics, assess the potential for increased immunogenicity with the new route of administration, as altered absorption kinetics may impact immune responses.
- **Local Tolerability Studies**: Examine injection site reactions, pain, erythema and patient-reported outcomes to ensure acceptable tolerability.
- **Dose Conversion**: Evaluate appropriate dose adjustments accounting for absorption differences to maintain therapeutic efficacy.

Regulatory agencies may allow streamlined clinical programmes if sufficient similarity is demonstrated through PK and PD data and bridging study results, reducing time-to-market for new SC and IM formulations.

Device Integration and Human Factors Engineering

SC and IM formulations often require advanced drug delivery devices such as autoinjectors or prefilled syringes. Human factors engineering ensures device usability aligns with patient capabilities and regulatory expectations. Factors such as ease of handling, convenience and patient comfort are evaluated to determine which container and device type may be preferred by end-users.

"HUMAN FACTORS ENGINEERING ENSURES DEVICE USABILITY ALIGNS WITH PATIENT CAPABILITIES AND REGULATORY EXPECTATIONS."

With patient-centric focus, the interaction between users and the product as received is paramount. Understanding how patients and healthcare professionals interact with the packaging, instructions for use (IFU), and the device itself is vital for optimising usability, minimising user errors, and enhancing overall safety, efficacy and adherence for improved outcomes.

Conducting usability studies and incorporating human factors considerations early in the design process can help to identify potential issues and inform design modifications. Human factors and usability engineering is an integral component of regulatory submissions and essential for demonstrating the product's usability and user comprehension. Key design considerations include:

- **Needle Gauge and Length**: Optimised to balance drug viscosity, injection speed and patient comfort while ensuring appropriate tissue penetration.
- **Injection Force and Speed**: Device mechanisms must accommodate high-viscosity formulations without compromising injection time or causing undue patient discomfort.

- **Ergonomics and Usability:** Devices should be designed for ease of handling, especially for patients with limited dexterity or chronic conditions.
- **User Training and IFU:** Clear, comprehensive instructions must be developed and tested to ensure patients and caregivers can safely and effectively use the device.
- **Device Robustness and Reliability:** Ensuring consistent performance under varied environmental conditions and across multiple use scenarios.
- **Safety Features:** Incorporation of needle shielding, dose counters and error prevention mechanisms to enhance user safety.

DRUG-DEVICE STRATEGY CONSIDERATION

Considering the target product profile or quality target product profile, decisions can be made on whether there is a unique need for device innovation tailored to specific patient populations, or whether traditional, readily available platforms would be suitable. Selecting established platforms that have received regulatory approval as part of a drug-device combination product previously, may be deemed lower risk for a new programme. Table 3 shows the advantages and disadvantages of established versus proprietary programmes.

STRATEGIC BUSINESS ADVANTAGES OF SC OR IM TRANSITION

Transitioning from IV to SC or IM delivery offers a range of strategic business advantages for biopharmaceutical companies, spanning clinical development, commercial success, market differentiation and patient engagement, ultimately enhancing both competitive positioning and operational efficiency.

- **Improved Patient Experience and Adherence:** SC and IM delivery enables self-administration or fewer clinic visits, improving convenience for patients with chronic conditions, thereby enhancing treatment adherence and persistence, especially for long-term therapies.

	Advantages	Disadvantages
Established Platform	• Lower upfront costs • Use of existing capital infrastructure • Smoother regulatory path • Robustness of device uses currently in the market	• Limited product differentiation • Higher unit costs • Coemption of supply for popular devices
Proprietary Platform	• Product differentiation – competitive advantage • Custom design for specific applications • Extend IP life of the product • Lower unit costs when scale is achieved	• Higher upfront costs, including design, IP, capital, technology • Complex regulatory path

Table 3: Advantages and disadvantages of established versus proprietary platforms.

- **Reduced Healthcare Costs:** The transition to patient-centric, self-administered formats facilitates outpatient or at-home administration, minimising the need for infusion centre resources, nursing time and healthcare facility overheads – reducing overall treatment cost for payers and providers.
- **Faster Time-to-Market with Lifecycle Management:** Reformulating approved IV therapies for the SC or IM routes can extend product lifecycles, gain additional IP and support differentiation in crowded therapeutic areas. Transitioning enables bridging studies rather than full clinical programmes, accelerating development timelines.
- **Enhanced Competitive Differentiation:** SC and IM formulations offer a competitive edge in crowded biologics markets where multiple IV options exist. It differentiates products based on patient convenience, dosing frequency and administration route, which can influence prescriber and payer preference.
- **Broader Market Access and Global Reach:** Simplified self-administration enables deployment in resource-limited settings and global markets where infusion infrastructure may be limited, thereby increasing accessibility and enhancing commercial reach.
- **Manufacturing and Supply Chain Efficiencies:** Transitioning to SC or IM administration can reduce manufacturing and logistics costs associated with infusion services. Prefilled syringes, autoinjectors and long-acting injectables often have smaller fill volumes, enabling higher batch yields. SC and IM formats can also reduce cold chain complexity for some formulations and support more efficient logistics and packaging.

FUTURE OUTLOOK AND INNOVATIONS

As the pharmaceutical industry continues to evolve, a wave of innovative technologies are reshaping the landscape of SC and IM drug delivery, paving the way for more effective, patient-friendly and precision-guided therapies. Examples of some such emerging technologies accelerating SC and IM development include:

- **Nanoparticle and Liposomal Carriers:** These cutting-edge drug delivery systems are designed to encapsulate APIs, improving their pharmacokinetic and pharmacodynamic profiles by providing improved solubility and prolonged systemic circulation.
- **Long-Acting Injectables:** Formulations that slowly release drug product over extended periods, often weeks or months, are growing in relevance, as they improve chronic disease management with fewer administrations, maintain stable drug concentrations and reduce fluctuations that might lead to side effects.

As precision medicine advances, customisation of patient-specific formulations will become increasingly feasible, further enhancing therapeutic outcomes. Together, these developments are transforming SC and IM delivery from a traditional route into a dynamic, patient-centric platform for next-generation therapeutics.

CONCLUSION

Transitioning IV formulations to SC or IM delivery represents a transformative opportunity for pharmaceutical progress. While the path involves complex scientific, regulatory and operational challenges, the rewards include enhanced patient outcomes, market expansion and sustained product viability. By adopting a holistic development approach, pharmaceutical companies can drive meaningful advancements in drug delivery and shape the future of patient-centric care.

Jeff Clement

Jeff Clement joined PCI Pharma Services in 2014. In his current role of Executive Director, Technical Sales – Drug Development and Manufacturing, he provides technical drug product development and manufacturing support to PCI's global business development teams. Mr Clement has over 25 years in the biotech and pharmaceutical industries and his career includes experience in the pharmaceutical discovery sciences, high-throughput automation, clinical formulation development, and cGMP analytical and manufacturing contract services. All his business development experience is in the aseptic manufacturing and analytical fields. Prior to his current role, Mr Clement was the Director of Global Business Development at Curia (Drug Product). Mr Clement received a BS in Biology from Keene State College (Keene, NH, US) and an MS in Quality Systems from The New England College of Business (Boston, MA, US).

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YES, PEN INJECTORS CAN ACCOMMODATE MORE THAN JUST INSULIN

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Cécile Gross and **Mark Tunkel** of **Nemera** explore the benefits of pen injectors, highlighting their versatility and ease of use, and introduce the company's novel platforms and how they can be adapted for a wide range of indications, enhancing treatment options and the patient experience.

In anxiety-inducing social environments, the increasing burden of disease or widespread pathologies may be perceived as unhelpful. However, increasing awareness of pharmaceutical progress and technical solutions to assist patients daily can be beneficial (Figure 1).

According to WHO data from 2022, there are approximately 1.71 billion individuals in the world with musculoskeletal conditions, making these conditions the leading cause of disease or disability, closely followed by obesity (890 million) and diabetes (830 million). The number of individuals with diabetes is expected to increase fourfold over the next 30 years.

Harder to quantify, but not to be undervalued, is the number of children and young people suffering from growth deficiency, which affects between one in 3,000 and one in 10,000 people. Last but not least, infertility is estimated to affect 42–180 million people worldwide.

How are those conditions addressed? In the context of drug delivery devices, the insulin pen injector for diabetes comes to mind. Launched in the 1980s, it served

"INCREASING AWARENESS OF PHARMACEUTICAL PROGRESS AND TECHNICAL SOLUTIONS TO ASSIST PATIENTS DAILY CAN BE BENEFICIAL."

two purposes – to ensure accurate dosing and to provide a comfortable injection. In both cases, the objective was to improve on vials and syringes. Since then, its use has spread across other pathologies, such as obesity, growth disorders, bone disorders and fertility issues. This device is still relatively new in the grand scheme of things, but its use is expected to increase in the coming years.

ADVANTAGES OF USING A PEN INJECTOR

Access to diagnostics and treatment availability remain a challenge for health authorities, with several factors causing this globally prevalent issue. However, with treatments available in injectable form and drugs being increasingly adapted for self-administration via pen injectors, promoting their widespread adoption could help to alleviate the burden for patients.

When discussing injections, it is essential to consider needle phobia. Advances in insulin delivery have resulted in pen needles being very short and very thin, making injections less traumatic than those administered with a standard syringe. In the same way, needlestick injuries are very rare with this type of device. The risks associated with dealing with vials and syringes are also minimised by the ready-to-use cartridge already integrated in the pen injector. Patients do not need to manipulate the drug container, except in the case of reusable pen injectors; however, such containers are safe enough not to pose risks for patients.

Figure 1: Awareness of pharmaceutical progress and technical solutions to assist patients daily can be beneficial.

"NEMERA HAS DEVELOPED EACH DEVICE BASED ON ITS PLATFORMS, MEANING THAT A SINGLE DEVICE CAN BE USED FOR MULTIPLE PURPOSES, AND DIFFERENT PATIENT GROUPS AND POPULATIONS."

Lack of trained personnel, necessary equipment and infrastructure can sometimes lead to poor patient care. Pen injectors, which resemble writing pens, are very intuitive in their use and can be used independently by patients.

Nemera has developed various pen injectors to accommodate the drugs needed to treat patients suffering from one of the main pathologies mentioned above. All of its pen injectors can accommodate insulin, glucagon-like peptide 1 (GLP-1), follicle-stimulating hormone, parathyroid hormone and human growth hormone, as well as their analogues and new chemical entities. From the patient perspective, Nemera can address any need through various technical solutions, including reusable or disposable devices, manual or spring-assisted injections and variable or fixed doses (Figure 2).

Figure 2: Nemera's pen injector platforms to cover any indication.

PEN INJECTOR PLATFORMS TO MEET PHARMA REQUIREMENTS

Nemera has developed each device based on its platforms, meaning that a single device can be used for multiple

purposes, and different patient groups and populations. The main advantages of platforms are the optimised time to market, with a technical solution already validated and market proven; broad compatibility with available cartridges; cost effectiveness – especially for a drug pipeline; and derisking benefits when it comes to manufacturing. The platforms still offer opportunities for differentiation and customisation.

For patients, having a month's treatment available in a single device instead of four separate devices makes it less cumbersome, eases portability when travelling or going to work, and fosters familiarity with the device through longer use of the same device. Some of Nemera's devices even have a dose counter to facilitate treatment monitoring, and the company can add connectivity to ease tracking. Pen injectors are also beneficial in terms of sustainability, as they are multi-use, so they can be reused until the cartridge is empty. Reusable pen injectors can be reused for several years.

PenDIA: Variable Dose Spring-Assisted Platform for GLP-1

Focusing on high-volume doses requiring frequent but not daily injection, Nemera developed a spring-assisted feature for a smooth injection experience (Figure 3). Volumes to be injected are larger than the "standard" insulin doses, therefore, using a spring to assist the patient helps to guarantee low force and a constant speed. This is especially helpful for patients who may not be as familiar with multiple daily injections as people with diabetes. The risk of misdosing is reduced, as there is no possibility of overdosing during the 4-week period – the dose to be administered is in the same device, rather than a separate one with a higher dosage.

"Autoinjector-Like" PenSET for Novel Drugs

Similarly, for this platform, Nemera kept the spring-assisted feature for a smooth injection while combining the advantages of the multidose capability of pens with the fixed-dose feature of autoinjectors (Figure 4). Patients do not need to be concerned about accurate dosing or associated risks, as everything is controlled by the device itself. The dose is pre-set, which means that the dose is accurate by default – it is not possible to alter it and therefore there is no risk of under- or overdosing. Additionally, several doses remain in the device, making it more sustainable.

Figure 3: PenDIA – a spring-assisted pen injector for seamless GLP-1 administration.

Usage steps are labelled very clearly so that patients know which step they are at, such as before an injection, priming or administering a dose. One interesting feature is priming – it is a one-time process that occurs until the device is completely used. If the patient forgets whether the priming has been performed, it is not an issue because the device will not allow administration of a dose until priming is complete.

The capabilities of Insight by Nemera – the company's independent development and consulting team within its services business unit – were called upon to create this modern design, selecting a cylindrical form with rounded ends and integrating the anti-roll feature subtly by flattening the surface. Special attention was given to the dose window, which only displays symbols – no numbers – to signal the device's status. It is a circular design, with a gloss finish to create a visual highlight. The push button features a concave finger placement to makes the spring-assisted injection more comfortable.

INTEGRATED SERVICES AND MANUFACTURING CAPABILITIES TO SUPPORT THE DRUG-DEVICE COMBINATION

For specific customer applications, Insight by Nemera can support any pen-platform-based combination product from registration through to commercialisation. Nemera's suite of consulting services provides this support, and is able to address every aspect of combination product development. With a proven track record in helping customers to achieve regulatory approvals in over 50 countries,

Figure 4: PenSET – a fixed-dose spring-assisted pen injector for an injection experience similar to an autoinjector.

Nemera created customised strategies to meet the unique needs of each programme with the following services:

- **Functional/Analytical Lab Testing and Design Verification:** Nemera's state-of-the-art facilities and customised methodologies ensure that products meet safety, quality and compliance standards. Nemera supports performance and functionality testing, analytical testing (including stability and biocompatibility) and design verification for final combination products. Nemera's processes align with ISO and US FDA requirements, supporting a wide range of administration routes beyond parenteral.
- **Human Factors Management and Design Validation:** Nemera ensures devices and combination products are safe and effective for target users while enhancing patient experiences and adherence. The company can support human factors strategy development, risk analyses, usability testing (formative and summative) and preparation of regulatory documentation.
- **Instructional Materials and Secondary Packaging Development:** Nemera creates tailored instructions for use, value-added packaging and integrated digital assets that improve the user experience, increase adherence, boost engagement and support platform value.
- **Regulatory Strategy and Registration Support:** Nemera's team navigates the complexities of global regulatory processes and standards from strategy and pre-market activities to registration and post-market support. The company develops strategies, engages with regulatory bodies and prepares submission-ready materials to ensure compliance with global requirements.

These services can be augmented by preclinical, clinical and small series device supply, accelerating development timelines while deferring capital expenses. This ensures a cost-effective and streamlined process. A holistic approach to these activities is crucial for success.

With the aim of providing a fully automated industrial line to its partners, Nemera has invested in a new plant, offering its capability to produce prototypes, small series for clinical batches, as well as large-scale automated volumes. Gathering state-of-the-art equipment from moulding to assembly and quality control testing, this brand-new facility includes an ISO 8 clean room and complies with Building Research Establishment Environmental Assessment Methodology (BREEAM) recommendations. For example, heat is recovered from the process line, and the facility also segregates and sorts all waste, aiming for 100% recycling of waste (Figure 5).

Figure 5: State-of-the-art manufacturing facility, hosting cleanrooms compliant with BREEAM recommendations.

By combining its comprehensive service offerings with its global manufacturing facilities and a commitment to sustainability, Nemera delivers unmatched value to its customers. Its holistic approach ensures that every aspect of combination product development is seamlessly integrated.

> "BY COMBINING ITS COMPREHENSIVE SERVICE OFFERINGS WITH ITS GLOBAL MANUFACTURING FACILITIES AND A COMMITMENT TO SUSTAINABILITY, NEMERA DELIVERS UNMATCHED VALUE TO ITS CUSTOMERS."

BENEFITS OF PARTNERING WITH AN INTEGRATED PRODUCT AND SERVICE PROVIDER

Partnering with Nemera means working with a proactive, integrated partner capable of delivering comprehensive solutions from proven pen platforms, development, manufacturing and consulting to support its partners' combination products from concept to market. Insight by Nemera's experience with pen platforms streamlines project onboarding and execution, ensuring efficient progress and on-track programmes. At every stage, Nemera's development and consulting excellence is dedicated to driving improved outcomes for patients and delivering confidence to its customers.

Nemera eliminates the need to co-ordinate multiple specialised partners. By simplifying the process, reducing complexity and risk, and accelerating regulatory approval and market access, Nemera's agile and integrated approach allows customers to focus on their core business while managing combination product development to ensure a safe, effective and differentiated result.

To conclude, the aforementioned pathologies are by no means exhaustive. Ongoing clinical trials aimed at expanding indications for existing drugs are expected to lead to treatment advances and an increase in the number of patients receiving care. Nemera strongly believes that the pen injector journey is warranted even more now than ever before!

Cécile Gross

Cécile Gross is Marketing Global Category Manager – Parenteral/ICO at Nemera, focusing on parenteral devices. She oversees the product portfolio strategy, development and lifecycle for safety system, pen injector and on-body injector platforms. Ms Gross has more than two decades of experience in the medical device industry, marketing business-to-business technological products and implementing product lifecycle management for various kinds of devices. A graduate in International Business, she completed her initial training with a master's degree in Marketing and Management in the Healthcare Industry at the IMIS Institute (Lyon, France).

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ONE PEN AT A TIME

Nemera
we put patients first

Expert View

RETHINKING GLP-1 DELIVERY DEVICES: DESIGNING FOR USERS BEYOND DIABETES

Dan Lock of TTP explores how the experiences and motivations of individuals using glucagon-like peptide 1 drugs for weight loss may differ from those managing diabetes or heart disease. Focusing on behavioural insights and understanding the specific challenges faced by people using these therapies for weight management can lead to more tailored drug delivery solutions that could enhance user engagement and adherence, and even disrupt the market leaders.

Glucagon-like peptide 1 (GLP-1) drugs are revolutionising weight management – but with more than half of users discontinuing their treatment within months,[1] are current drug delivery solutions failing them? By rethinking the drug delivery devices used with GLP-1s, is it possible to improve adherence and unlock the full potential of GLP-1 therapies?

The first injection pens, such as the NovoPen (Novo Nordisk) launched in 1985, were designed to deliver insulin to people with Type 1 diabetes (T1D). The design of these pens is the result of years of iteration, including human factors research focusing on the needs of users with the greatest accessibility challenges across a diverse user population that ranges from children – who may need help from caregivers – to elderly adults with conditions such as arthritis, neuropathy or visual impairments.

People with diabetes depend on these devices for survival, and the devices have been optimised accordingly for their ease of use, safety and reliability. However, as GLP-1s – originally intended to treat Type 2 diabetes (T2D) and often delivered with injection pens developed for insulin – are increasingly used to treat obesity, perhaps it is worth rethinking the basis of these designs to accommodate a user group that may have different requirements. Could poor adherence to GLP-1 drugs among those using it for weight loss (30% stop within four weeks without achieving clinically meaningful weight loss[2]) be explained, in part, by a user experience that does not cater to the specific needs of this population?

"AS GLP-1s – ORIGINALLY INTENDED TO TREAT TYPE 2 DIABETES (T2D) AND OFTEN DELIVERED WITH INJECTION PENS DEVELOPED FOR INSULIN – ARE INCREASINGLY USED TO TREAT OBESITY, PERHAPS IT IS WORTH RETHINKING THE BASIS OF THESE DESIGNS TO ACCOMMODATE A USER GROUP THAT MAY HAVE DIFFERENT REQUIREMENTS."

MARKET TRENDS IN GLP-1 USAGE

Recent market data suggest that around 5% of US adults (approximately 12.5 million people) have used or are currently using GLP-1s for weight loss alone.[3] This is higher than the 7.4 million[4] people (both adults and children) using insulin and equal to the 5% who have used or are currently using GLP-1s solely to treat

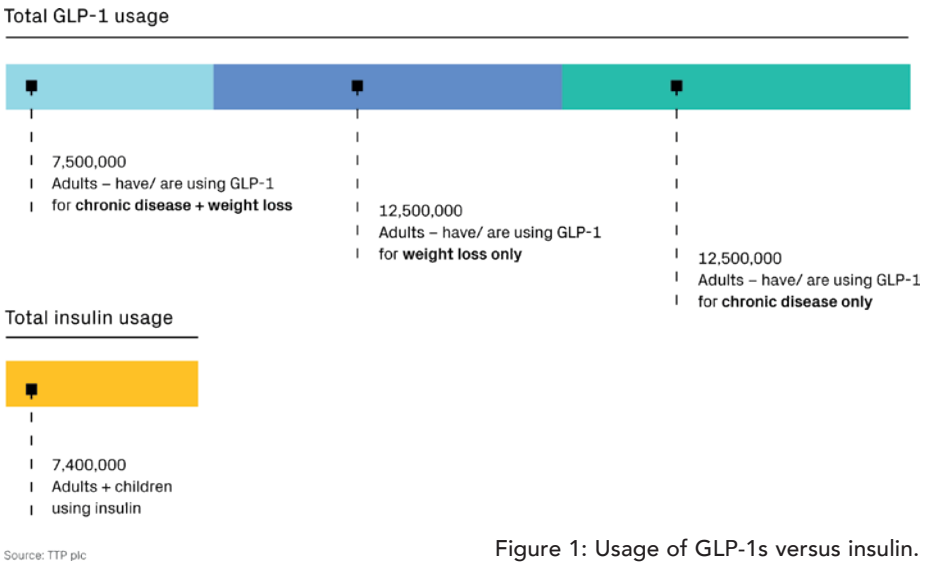

Figure 1: Usage of GLP-1s versus insulin.

a chronic condition such as diabetes or heart disease – approximately 3% are using GLP-1s to both treat a chronic condition and to lose weight. The comparative uptake of GLP-1s and insulin among US adults is shown in Figure 1.

As T2D is often associated with having a high body mass index, one would be forgiven for assuming that the needs of people who use GLP-1s for weight loss and those using it to treat diabetes would be very similar, but recent market research suggests a number of significant differences:[5]

- The majority of people using GLP-1s for weight loss are in their 30s to 50s (often as part of a wider strategy to be proactive about their health), whereas those using GLP-1s for diabetes control are more likely to be over 60.
- People using GLP-1s for weight loss are twice as likely to have a high income, whereas those using GLP-1s for diabetes control tend to be less well-off on average.
- A greater proportion of those using GLP-1s to target a weight loss of <7 kg are younger (teens to 30s) compared with those using GLP-1s to target a weight loss >7 kg.
- Of those targeting a weight loss of <7 kg, two-thirds already actively manage their health in some way, compared with only half of those targeting a higher amount.

User profile	GLP-1 for weight loss	GLP-1 for diabetes control
Average age	30s to 50s	60+
Average income	Twice as likely to be high-income earners	Tend to be less well-off
Health management mindset	More proactive – GLP-1 is often part of a broader self-care strategy	More reactive – GLP-1 is used to manage a chronic condition

Table 1: Differences in user profiles.

These differences in user profiles are outlined in Table 1, and the trends are accelerating – the percentage of users prescribed GLP-1s exclusively for weight loss grew from 10% in October 2022 to 43% in October 2023. Yet, in many countries the devices being used to deliver GLP-1s are the same for both the weight loss and T2D populations and, in many cases, were originally designed for delivering insulin, such as Novo Nordisk's FlexTouch pen (Wegovy, semaglutide) or Eli Lilly's KwikPen (Mounjaro, tirzepatide) outside the US.

UNIQUE REQUIREMENTS

Designing effective GLP-1 delivery solutions requires a deep understanding of the people who use them. While regulatory standards ensure safety and functionality, addressing the unique needs of GLP-1 users for weight loss offers an opportunity to go beyond compliance, creating solutions that are not only practical but also deeply engaging.

This user group presents distinct challenges and opportunities for design. Unlike patients with diabetes, many of whom are well-acquainted with managing complex medication regimens, GLP-1 users for weight loss are often new to injecting and may have different levels of medical literacy, motivations and expectations. By tailoring the user experience to their specific profiles, it is possible to improve adherence, support better outcomes and position these devices as tools for health empowerment.

By developing a user-engagement framework[6] that can be used to generate ideas for behavioural interventions at all stages of a task, it is possible to ensure that products resonate on a practical, emotional and aspirational level (Figure 2).

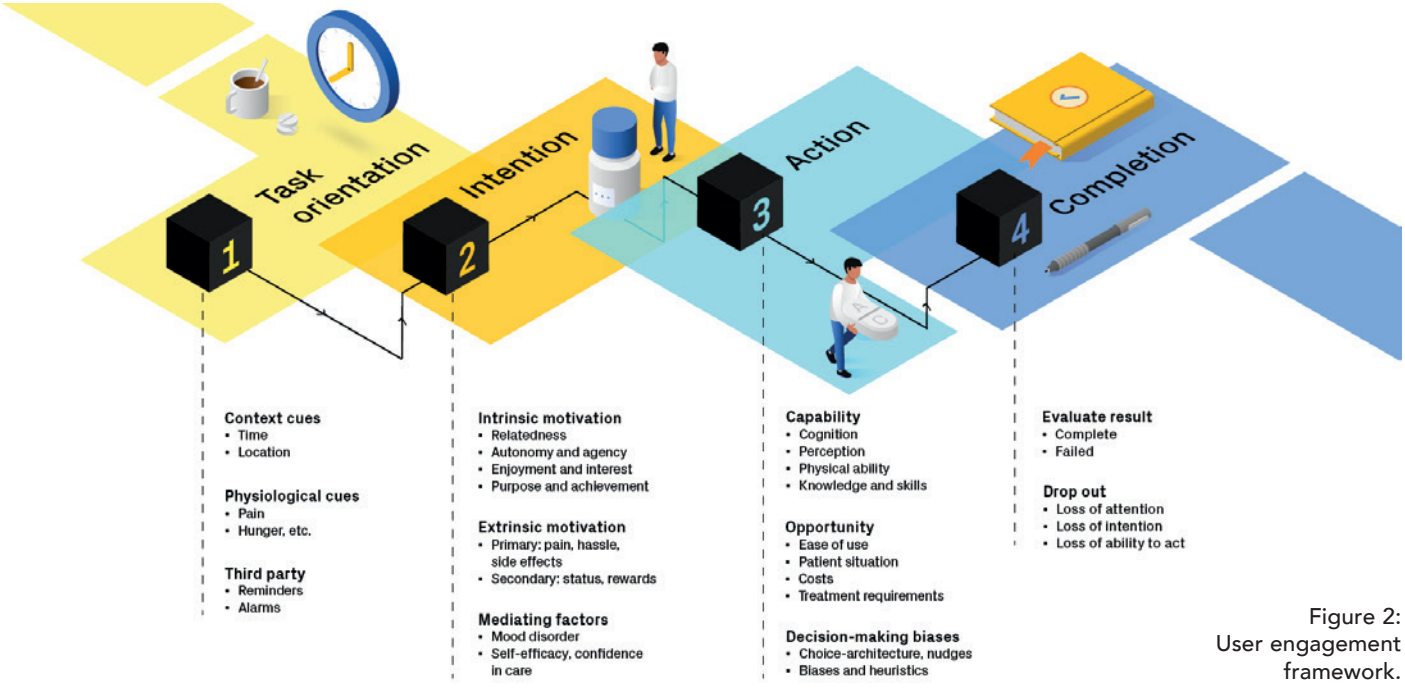

Figure 2: User engagement framework.

Challenges	Opportunities
Greater anxiety around injections	Lower need for portability
Poor adherence levels	Fewer comorbidities affecting capability
Users lack medical literacy	Users have a goal-oriented mindset

Table 2: Challenges and opportunities for GLP-1 drug delivery devices.

This approach, grounded in behavioural science, addresses real-world barriers to medication adherence by mapping engagement touchpoints to drivers of motivation, providing a tool for design teams to think through problems and create solutions that not only function well but also encourage user participation. The challenges presented by using GLP-1s for weight loss – and the opportunities that solving those challenges offer – are summarised in Table 2.

CHALLENGES

Greater Anxiety Around Injections

People with diabetes often become familiar with managing complex medication regimens due to the ongoing need for blood glucose control. Frequent injections – sometimes four to five times a day – can lead to a level of routine and familiarity with the process, shaped by frequent exposure. For some, the level of comfort even extends to injecting through clothing or in public settings, practices that have been studied for safety. In fact, some diabetes associations no longer emphasise the use of alcohol wipes before injection as part of standard practice.[7]

However, for those on a weekly injection schedule, such familiarity may be harder to achieve. The less frequent need for injections can mean that users do not develop the same level of comfort or routine, which may influence their overall experience and adherence. GLP-1 users are often new to injecting and may feel anxious or reluctant about the process. As GLP-1s have moved towards weekly dosing, users are less likely to experience the desensitisation that comes from repeated exposure.

One way to tackle the issue is to reduce exposure by making injections even less frequent. Companies are investing in GLP-1 formulations and devices that allow for a lower injection frequency, such as quarterly injections. Developing devices that manage higher dose volumes, increased viscosity and larger needle diameters represent engineering challenges that are the subject of a great deal of ongoing research.

"THE LESS FREQUENT NEED FOR INJECTIONS CAN MEAN THAT USERS DO NOT DEVELOP THE SAME LEVEL OF COMFORT OR ROUTINE, WHICH MAY INFLUENCE THEIR OVERALL EXPERIENCE AND ADHERENCE."

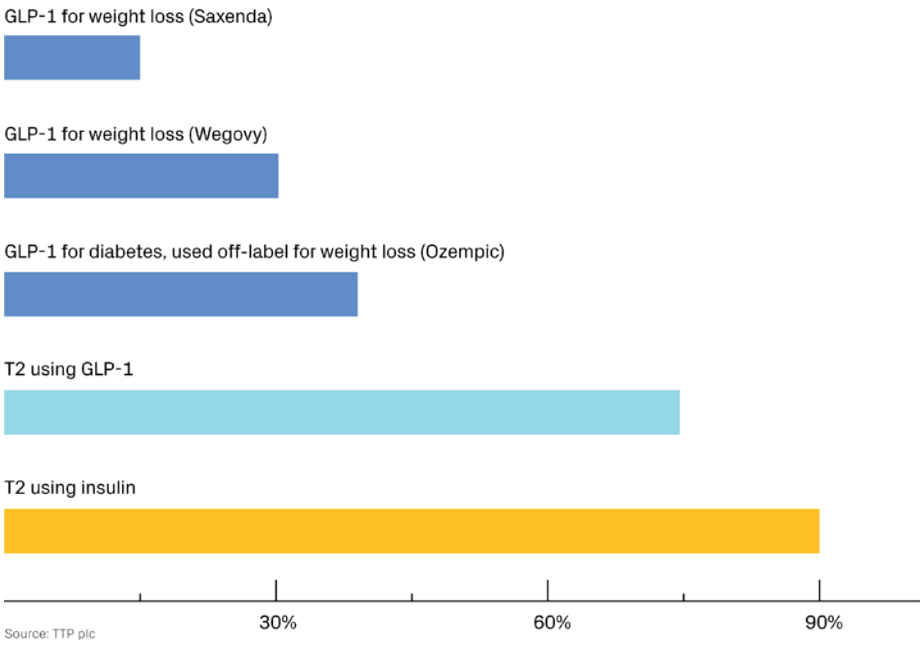

Figure 3: Adherence rate.

However, there are also ways to help anxious users feel in control while maintaining the current injection schedule. A review of posts by users on social media indicates that needle phobia is not necessarily as straightforward as not wanting to see the needle, as one Reddit user commented: "I am so scared to take my first shot because I can't see the needle. Ozempic needles I can see, so I have control. I have a fear of needles so I'm having major anxiety." For many, the uncertainty, tension and sudden release of an autoinjector is more anxiety inducing than injecting with an exposed needle. This need to be in control, or "autonomy", is the most essential driver of intrinsic motivation.[8]

The challenge, therefore, is to design a drug delivery solution that maximises that sense of autonomy while also maintaining the simple workflow that autoinjectors offer. There are a number of concepts that could be explored, such as adding a retractable window that allows the user to see the needle only if they want to or reworking the trigger mechanism to ramp up smoothly rather than the current characteristic "snap".

Poor Adherence Levels

For people with diabetes, insulin injections are critical. A study comparing adherence between people with T2D that use insulin

and those using GLP-1s found that insulin users had an adherence level of around 90% compared with around 74% for those using GLP-1s (both oral and injectable versions).[9]

For those using GLP-1s for weight loss, injections are a choice. As a consequence, levels of adherence are lower than for people with diabetes, as demonstrated by another study that applied the same metric of adherence to people using GLP-1s to treat obesity: 40.1% for Ozempic (semaglutide, Novo Nordisk), 31.5% for weekly injectable Wegovy and just 15% for daily injectable Saxenda (liraglutide, Novo Nordisk).[10] This suggests that greater expectation management is required to maintain users' faith in the value and purpose of what they are doing. These differences in adherence rates across various medications and use cases are illustrated in Figure 3.

Adherence is generally affected by a combination of capability (strength, dexterity, cognitive powers), opportunity (complexity, cost, availability) and motivation (intrinsic drivers, rewards, general mood).[11] Based on this, it is possible to calculate relative differences in likely adherence with a quantitative analysis of typical disease impact, patient demographics, drug effects and device operating principles.[12] By systematically analysing a drug delivery solution, it is possible to identify opportunities for improvement and determine the cost-benefit of investing in a wide range of design features.

Lacking Medical Literacy

People with diabetes have a steep learning curve upon diagnosis but, over time, many develop a deep understanding of their condition and the way their bodies respond to carbohydrates, insulin, exercise and other factors. Training courses for patients diagnosed with T1D are practically oriented and emphasise the critical importance of proper nutrition and recognising and managing the signs of both low and high blood sugar.

GLP-1 users may not have such earnest study and medical knowledge thrust upon them. They are less likely to rely on authoritative sources of medical information and more likely to make risky medical choices based on opinions and experiences shared online. For example, "stacking" different brands of GLP-1 medication, using more than the prescribed dose or changing dosing intervals without reference to a medical professional – as one Redditor commented: "I did 10 my first shot, then 12. I just now gave myself 15 for week 3. If all goes well, I'll up it to 20 next week. I'm impatient and this is too expensive to be overly cautious."

A balance must be struck between creating a comfortable experience – such as minimising medical aesthetics and any stigmatising elements – and ensuring that users fully understand their treatment and approach it with the seriousness it requires. A companion app that helps to guide new users through the first few weeks of learning the device and titrating the dose and that explains what to expect, what to look out for and what kind of weight loss is reasonable, may be one way to help to manage expectations and keep users safe. Another might be electronically preventing non-standard dosing schedules or quantities.

The problem is also partly driven by cost. Many users find branded GLP-1s are not affordable and turn to lower cost sources, such as getting semaglutide made up by a compounding pharmacy (often requesting additions to the formula such as vitamin B12) – a practice that is not recommended by the US FDA.[13] This may decrease as the first generic versions of GLP-1 drugs become available, which started to get FDA approval in late 2024. While there are typically serious limitations to what changes can be made to the method of operation for drug delivery devices, there may also be an opportunity for competing products to differentiate themselves through access to high-quality patient support materials and moderated forums.

OPPORTUNITIES

Less Need for Portability

Insulin pens for rapid-acting insulin must be portable so that users can easily carry them throughout the day. In contrast, pens for long-acting insulin, used once or twice daily, have fewer portability requirements, although similar devices are often used for both.

GLP-1 treatments for weight loss are typically injected at home once daily or weekly, meaning that portability is even less critical unless users are travelling. Reduced portability requirements allow for designs that are more engaging, supportive and ergonomic, with more premium aesthetics driven by a consumer health mindset.

"BY CONDUCTING USER PREFERENCE STUDIES BEFORE DETAILED ENGINEERING BEGINS, DESIGNERS CAN LEARN THE ACCEPTABLE LIMITS FOR DEVICE SIZE AND CAN MAKE INFORMED TRADE-OFFS IF INTERNAL COMPONENTS REQUIRE ADJUSTMENTS."

By conducting user preference studies before detailed engineering begins, designers can learn the acceptable limits for device size and can make informed trade-offs if internal components require adjustments. This approach ensures that the final product closely matches user expectations and, in subsequent user evaluations, is more likely to be significantly preferred over alternatives.

However, sometimes improvements to user experience come from combining devices with digital technologies, such as smartphone apps, without changing the injection device itself. Providing better support, especially in the initial phase of treatments such as GLP-1s, can greatly improve the user experience, reduce anxiety and help users adhere to their treatment plans.

Fewer Comorbidities Affecting Capability

People with diabetes are more likely to suffer from peripheral neuropathy (29.1% of T1D, 42.2% of T2D) and retinopathy (28.4% of T1D, 23.8% of T2D),[14] among other things. Devices must include high-contrast labels and tactile features for those with visual or dexterity impairments. Those using GLP-1s for weight loss may deal with obesity or hypertension but are less likely to have severe visual or dexterity issues. This means

that designers may have a little more leeway and flexibility on aesthetic aspects of design.

Donald Norman coined the concept of "Emotional Design",[15] which proposes that users engage with products at three levels:

- **Visceral:** The instinctive level comprising gut reactions driven by evolutionarily derived aesthetic preferences.
- **Behavioural:** The purely utilitarian level that is focused on functionality and ease of use.
- **Reflective:** The intellectual level that incorporates cultural status, meaning, sentimental value and so on.

Medical device development focuses, correctly, on what Norman called the "Behavioural" level. However, there is also strong evidence that products with aesthetic appeal lead to enhanced usability,[16] perhaps because users are more inclined to invest their time in learning how to use it. Often, when designers cannot understand the popularity of a product, it is because they have neglected to consider one of these levels.

Having the freedom to invest in designs that tap into each level, particularly the "Reflective" level, could help with engagement. One could envisage ways in which this freedom could be used to create something more personal, or even a range of options to cover the design needs of different user segments and cultures.

Given the success of consumer-oriented wellness products and services, adopting a less medical "feel" for the experience and tuning in more to the aesthetics and sensibilities common to lifestyle products could improve user adoption. Taking inspiration from fitness and wellness products, such as Strava, Whoop and Noom, devices could bolster users' self-identity as someone proactively managing their health, fostering a sense of empowerment and engagement.

Goal-Oriented Mindset

People with T2D are typically prescribed GLP-1s to stimulate their pancreas and to ward off worsening symptoms that may lead them to require using insulin down the line. They anticipate chronic use of the drug – at least until more intensive treatment becomes necessary.

"A WEIGHT-LOSS FOCUSED GLP-1 DEVICE SHOULD EMPHASISE PROGRESSION AND MOVEMENT TOWARDS A GOAL, WHICH MAY DIFFER FROM DESIGNS FOR T2D USERS."

In contrast, people using GLP-1s for weight loss may be more focused on achieving a specific goal: they hope to resolve an issue – obesity – rather than simply maintaining or prolonging their current health status. Their motivations can vary, driven by concerns such as health (50%), appearance (35%) or mood (15%).[17] As a result, they may not perceive their need as strictly medical and so may be put off by products with overtly medical aesthetics. Additionally, weight loss is generally seen as having a definitive endpoint, leading users to (rightly or wrongly) expect that their treatment can be tapered down or discontinued once their goal is achieved. This goal-oriented approach brings a different psychological perspective compared with managing other chronic conditions.

A weight-loss focused GLP-1 device should emphasise progression and movement towards a goal, which may differ from designs for T2D users. Targeting specific segments – such as health, appearance and mood – could further refine device positioning. For example, athlete-focused glucose monitors have been successfully adapted to prioritise performance optimisation over strictly medical functionality, offering a tailored approach that is distinct from those designed for diabetes management, although careful analysis and testing are needed so as not to undermine safety critical elements of the design or workflow.

CONCLUSION

By addressing the unique requirements of people using GLP-1s for weight loss, device teams can develop solutions that support better adherence and create a positive, engaging user experience. It is clear that the early integration of engagement strategies can lead to devices that resonate with users as tools for health empowerment.

While this article has focused on the differing requirements for people using GLP-1s for weight loss, the list of proposed indications for GLP-1s grows seemingly on a daily basis, with research currently ongoing in neurodegenerative disease, chronic kidney disease and liver disease. Each of these patient groups will have unique needs, underscoring the importance of designing a diverse range of devices tailored to the specific requirements of each segment.

ABOUT THE COMPANY

TTP is a technology and medical device development consultancy that provides end-to-end design and engineering services for drug delivery devices. The company supports pharmaceutical and medtech clients across the full development lifecycle – from early concept development and feasibility studies to design for manufacture and commercial-scale production support. Its multidisciplinary drug delivery team combines expertise in engineering, human factors and applied science to develop robust and scalable drug delivery systems, including injectors, wearable devices and inhalation platforms. TTP's work spans both novel and established drug formats, with a focus on improving therapeutic delivery and patient usability in complex clinical and regulatory environments.

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GREATER FORMULATION FREEDOM WITH A NOVEL AUTOINJECTOR PLATFORM THAT EXTENDS VOLUME AND VISCOSITY LIMITS

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Prof Sigrid Saaler-Reinhardt and **Dr Andrea Lennerz** of **Midas Pharma**, along with **Moritz Mond** and **Marie Stockton** of **Gerresheimer**, discuss how the Gx Inbeneo® autoinjector overcomes the limitations of prefilled syringe-based autoinjectors to provide effective, safe administration of large-volume, high-viscosity formulations.

The market growth of approved biotherapeutics, particularly monoclonal antibodies (mAbs), has driven demand for self-injection devices, such as autoinjectors.[1] These devices, designed for subcutaneous (SC) or intramuscular (IM) injection, encountered challenges when required to deliver protein-based formulations. Limited delivery volume of standard autoinjectors can require higher concentrations to achieve therapeutic efficacy resulting in higher viscosity, or the need to dilute, which increases volume.[2]

In addition to mAbs with immediate-release profiles, there is a growing development pipeline of long-acting injectables with advanced delivery systems, such as nano-suspensions, emulsions, liposomes and microspheres,[3,4] some of which can exhibit very high viscosities.[5] Administering these complex formulations effectively and comfortably necessitates specialised delivery devices.[6]

The Gx Inbeneo® autoinjector, developed by Gerresheimer and Midas Pharma, addresses these challenges through a novel pre-pressurised cartridge-based design with a double-ended needle system.[7] This enables delivery of larger volumes and higher viscosities while also supporting patient adherence through user-centric design and tolerable injection times. The Gx Inbeneo® overcomes the limitations of prefilled syringe (PFS)-based autoinjectors in terms of viscosity, volume and injection time. Formulations scientists thus have greater flexibility when developing biologic drug products for SC self-administration.

CHALLENGES IN FORMULATING BIOLOGICS FOR SC ADMINISTRATION

High Concentration and Viscosity Considerations for Stability and Manufacture

Sensitive biotherapeutics, such as mAbs, are vulnerable to aggregation, which may lead to a loss of biologic functionality. Transitioning from intravenous (IV) to SC self-administration often requires higher concentrations to achieve the necessary therapeutic dose within a manageable injection volume, leading to higher viscosity.[8] This complicates delivery via standard syringes formats, as higher forces and larger needle gauges are needed to achieve acceptable injection times for patients.

Water-based immunoglobulin G (IgG) solutions, which include mAbs, are generally relatively low viscosity and exhibit Newtonian behaviour up to approximately 230 mg/mL. However, above 300 mg/mL, viscosity increases dramatically due to intermolecular interactions, such as self-association between molecules, causing protein aggregation and potentially resulting in non-Newtonian shear-thinning behaviour.[9] This can lead to negative consequences, such as functional inactivation.[10]

Although mAbs are IgG molecules, they vary in behaviour according to their physico-chemical properties.[11] Maintaining protein stability and preventing aggregation in mAbs during storage and transportation often requires adding excipients or adjusting salt composition and pH,[8] which can further increase viscosity. Highly concentrated viscous formulations also complicate manufacturing, particularly during filtration and filling.[12,13]

Most marketed mAbs are in the range of 100–200 mg/mL, generally maintaining viscosities under 30 cP, though some reach 40–100 cP.[11,14] Above 200 mg/mL, viscosity can reach up to 200 cP, and may exhibit non-Newtonian behaviour.[9]

High-viscosity formulations require either longer injection times or larger needles, negatively impacting patient comfort and ease of administration, which may affect patient adherence.[15] Maintaining stability and optimal viscosity remains a major challenge in SC biologic formulations.

"SC SELF-ADMINISTRATION IS INCREASINGLY PREFERRED, AS IT FACILITATES GREATER PATIENT INDEPENDENCE AND REDUCES THE BURDEN ON HEALTHCARE SYSTEMS."

Self-Administration Challenges

SC self-administration is increasingly preferred, as it facilitates greater patient independence and reduces the burden on healthcare systems. Autoinjectors offer patient usability and safety advantages, such as needlestick protection, but they also present challenges:

- **Patient Comfort:** High-injection forces can cause pain, necessitating finer needles.[16]
- **Adherence:** Extended injection times and complex handling may reduce adherence, particularly for patients with conditions that impact dexterity, such as rheumatoid arthritis.
- **Efficacy:** Ensuring complete dosing within an acceptable timeframe is crucial for therapeutic effectiveness.[17]

THE LIMITATIONS OF PFS-BASED AUTOINJECTORS

Most conventional autoinjectors that rely on a PFS face several limitations when handling high-viscosity and large-volume formulations.

Such autoinjectors employ a staked-needle PFS combined with a compressed spring held in place with a locking mechanism. This must then be reliably released at the moment of injection, which can cause high-impact forces[18] that place stress on components. The higher spring force required to deliver drugs in large volumes or high viscosity can be particularly problematic and may lead to misfiring.[19]

Due to these design limitations, PFS-based autoinjectors can typically handle up to a maximum volume of 2.25 mL. The combination of spring force and needle gauge also restricts their ability to deliver high-viscosity formulations without unacceptably long injection times.

Another disadvantage of a staked-needle PFS when handling viscous biologic drug products or suspensions is the risk of clogging during storage. Aggregation caused by migration of silicone oil droplets is another challenge that is significantly reduced by employing a cartridge with baked-on siliconisation.[20]

OVERCOMING BOUNDARIES WITH A CARTRIDGE-BASED, DOUBLE-NEEDLE DESIGN

The Gerresheimer Gx Inbeneo® autoinjector platform was specifically developed to overcome the boundaries of traditional PFS-based systems, enabling delivery of volumes up to 3 mL and very high-viscosity formulations.

Cartridge-Based and Pre-Pressurised

The use of a glass cartridge as the primary container in the Gx Inbeneo® facilitates many of its advantages. The novel design is pre-pressurised and employs the cartridge as the force barrier, which eliminates the need for an additional spring-locking mechanism. Stronger springs can therefore be used – enabling the delivery of higher viscosities and avoiding a pressure spike – for a steady delivery profile. An

"THE GERRESHEIMER GX INBENEO® AUTOINJECTOR PLATFORM WAS SPECIFICALLY DEVELOPED TO OVERCOME THE BOUNDARIES OF TRADITIONAL PFS-BASED SYSTEMS, ENABLING THE DELIVERY OF VOLUME UP TO 3 ML AND VERY HIGH-VISCOSITY FORMULATIONS."

additional benefit of the pre-pressurised design is the reduction or elimination of a gas bubble according to Henry's Law, which may otherwise cause aggregation in sensitive drugs.[21] Functional and usability testing of the Gx Inbeneo®, which confirms efficacy and patient acceptance, is outlined in an ONdrugDelivery article from October 2024.[22]

Platform Provides Freedom to Choose Needle Options

As the Gx Inbeneo® needle is separated from the primary cartridge until the moment of injection, the risk of the biologic drug molecules or excipients clogging the needle during storage is eliminated. The Gx Inbeneo® platform concept provides pharmaceutical customers with the freedom to not only select the appropriate cartridge size and spring force but also the appropriate needle for their specific drug formulation. Customisation of the needle can include outer needle diameters, inner diameters, thin/ultra-thin walls and specific tip geometries. However, the optimal choice is the Gx Inbeneo®'s unique double-ended needle system (Figure 1).

Advantages of a Double-Ended Needle

In typical autoinjectors, selecting a needle gauge involves a trade-off between flow rate and patient comfort. To accelerate drug delivery, a larger diameter needle can be chosen, but it may increase injection pain. Conversely, a thinner needle is gentler for the patient but can lead to slow injection times or higher injection forces. The Gx Inbeneo® helps to resolve this conflict by employing a double-ended needle system with two different needle gauges in one integrated assembly.

On the cartridge side of the needle, a larger internal diameter is used to pierce the cartridge septum, enabling higher flow rates for viscous solutions and significantly reducing flow resistance. This allows the drug to pass quickly through the needle even when dealing with elevated viscosities or larger injection volume. The needle diameter on the patient end is deliberately smaller to minimise discomfort.

The double-ended needle concept directly addresses one of the biggest challenges in delivering large volumes or highly viscous formulations subcutaneously by reducing the compromise between flow rate and patient comfort.

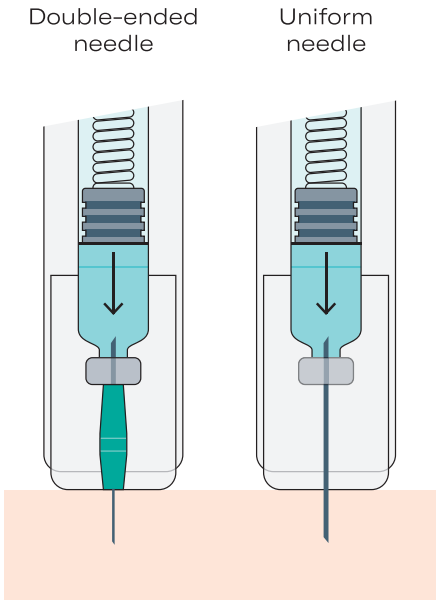

Figure 1: The double-ended needle design optimises flow dynamics due to different diameters of the needle for piercing the patient's skin and septum.

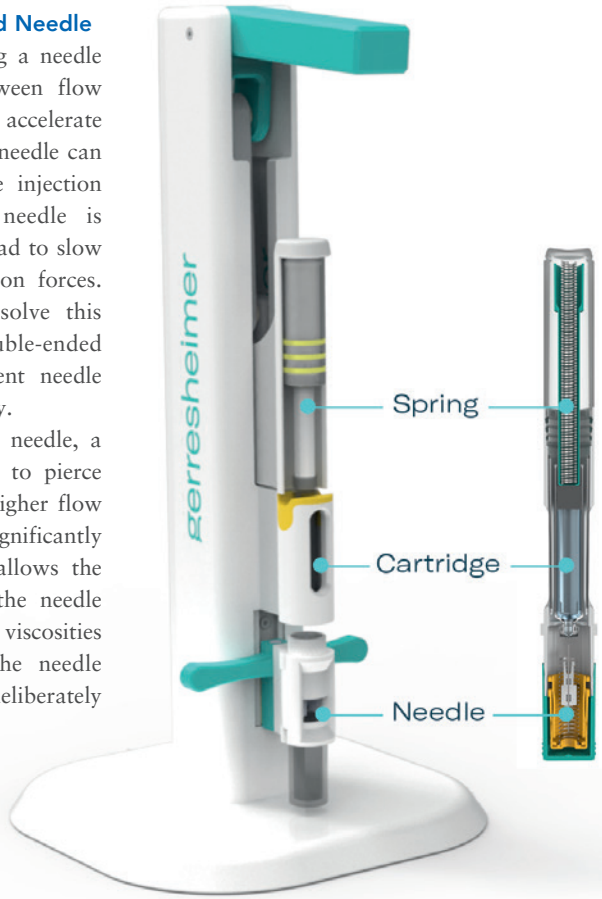

Figure 2: The Gx Inbeneo® platform simulator correlates to the autoinjector platform and enables a tailored assembly of spring force, needle size and ISO-cartridge volume for testing.

TESTING THE LIMITS

Gerresheimer and Midas Pharma recently conducted comprehensive testing of the Gx Inbeneo® autoinjector to evaluate its capability to deliver highly viscous drug formulations and large volumes. Testing was carried out with the Gx Inbeneo® platform simulator, which mimics the autoinjector platform, enabling different combinations of spring force, needle gauge and volume. The simulator can, therefore, provide real-life results, substantiating theoretical calculations using Hagen-Poiseuille's law. Formulation scientists can use the simulator to test injection times for their specific formulation at different stages of development (Figure 2).

The test series was conducted with both 1.5 and 3.0 mL ISO glass cartridges, paired with 45 and 90 N spring power units, respectively. In addition, 25G and 27G double-ended needles were tested, as well as a 25G uniform needle for comparison. Glycerol and distilled water were mixed in varying viscosities according to weight percentages calculated using an established viscosity calculation script. The cartridges were filled and sealed by carefully mounting the plunger with a thin steel implement to minimise air entrapment. Strict protocols were followed, with every measurement repeated five times at a temperature of approximately 21°C. The described results give the mean value of each test.

Large-Volume Delivery

To evaluate the full capacity of the Gx Inbeneo®, 3 mL ISO cartridges were filled with glycerol solutions of varying viscosities and combined with 25G and 27G double-ended needles. Several key results demonstrated the success of the design.

Using a 27G double-ended needle, a viscosity of 20 cP could be expelled in less than 15 seconds, and up to 40 cP in approximately 26 seconds (interpolated).

"ANOTHER INTERESTING FINDING, PARTICULARLY WHEN CONSIDERING PATIENT COMFORT, IS THAT THE 27G DOUBLE-ENDED NEEDLE SHOWED COMPARABLE RESULTS WITH A 25G UNIFORM NEEDLE."

By increasing the needle diameter to 25G, 75 cP could be expelled in 10 seconds and viscosity exceeding 160 cP could be delivered within 20 seconds (Figure 3).

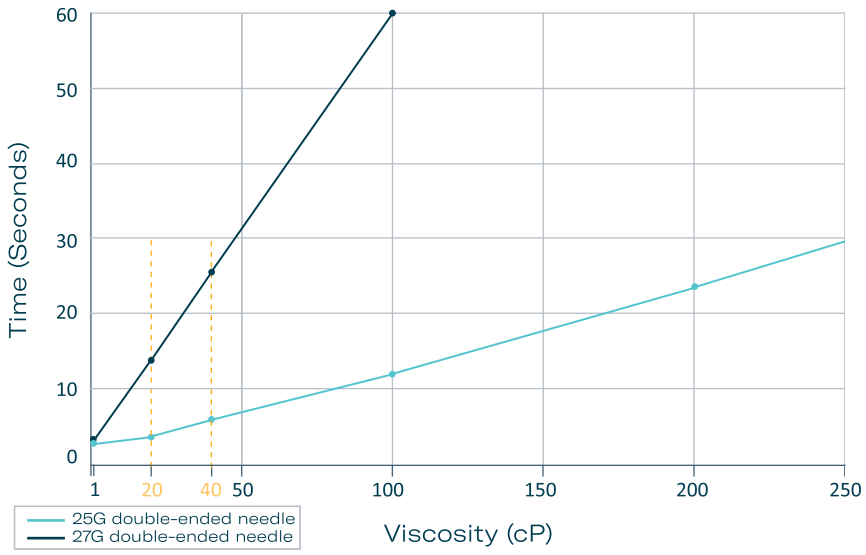

Figure 3: Comparison of injection times with 25 and 27 G double-ended needles for 3 mL of liquid of different viscosities.

Proven Advantage of a Double Needle

Direct comparison between standard and double-ended needles revealed a significant difference in injection time. The double-ended needle expelled a liquid of 20 cP approximately 10 seconds faster than a uniform needle. With the increase in viscosity, this improvement became ever more apparent, with a five-fold decrease in injection time recorded with the double-ended needle compared with a uniform needle under the same conditions. When reaching a viscosity of 200 cP, the double-ended needle was able to expel 3 mL in approximately 23 seconds. Even with very high viscosities of 500 cP and a volume of 1 mL, the delivery time remained under 30 seconds with the double-ended needle (Figure 4).

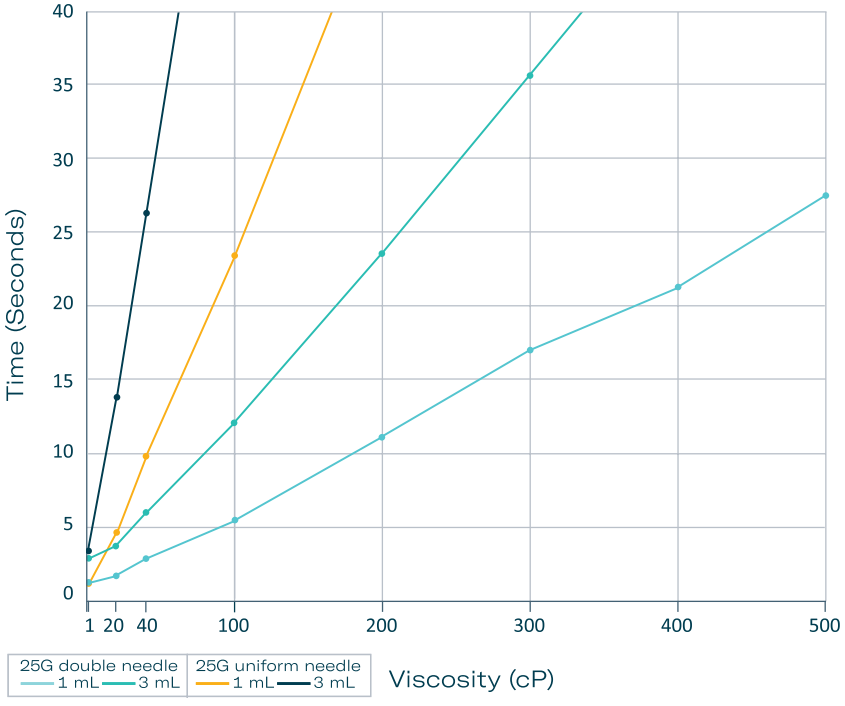

Figure 4: Comparison of injection times with 25 G uniform and double-ended needles and volumes of 1.0 and 3 mL.

Another interesting finding, particularly when considering patient comfort, is that the 27G double-ended needle showed comparable results with a 25G uniform needle (Figures 3 and 4).

Efficacy at Very High Viscosity

At extremely high viscosity and lower volume, the Gx Inbeneo® also proved its efficacy. At viscosities >1200 cP, 0.5 mL could be delivered in less than 30 seconds. When the volume increased to 1 mL, viscosity as high as 500 cP was still achieved in less than 30 seconds (Figure 5).

The results demonstrate the superior performance of the Gx Inbeneo® over traditional syringe-based autoinjectors, which can handle less volume and often struggle to deliver above 50 cP within a tolerable injection time.[23,24]

ADVANTAGES FOR FORMULATION SCIENTISTS

For formulation scientists, the Gx Inbeneo® platform provides significant advantages:

- **Greater Flexibility in Drug Concentration:** The ability to deliver higher viscosities subcutaneously without excessive dilution means biologics, as well as long-acting complex formulations, can be formulated at more optimal concentrations without impacting efficacy.

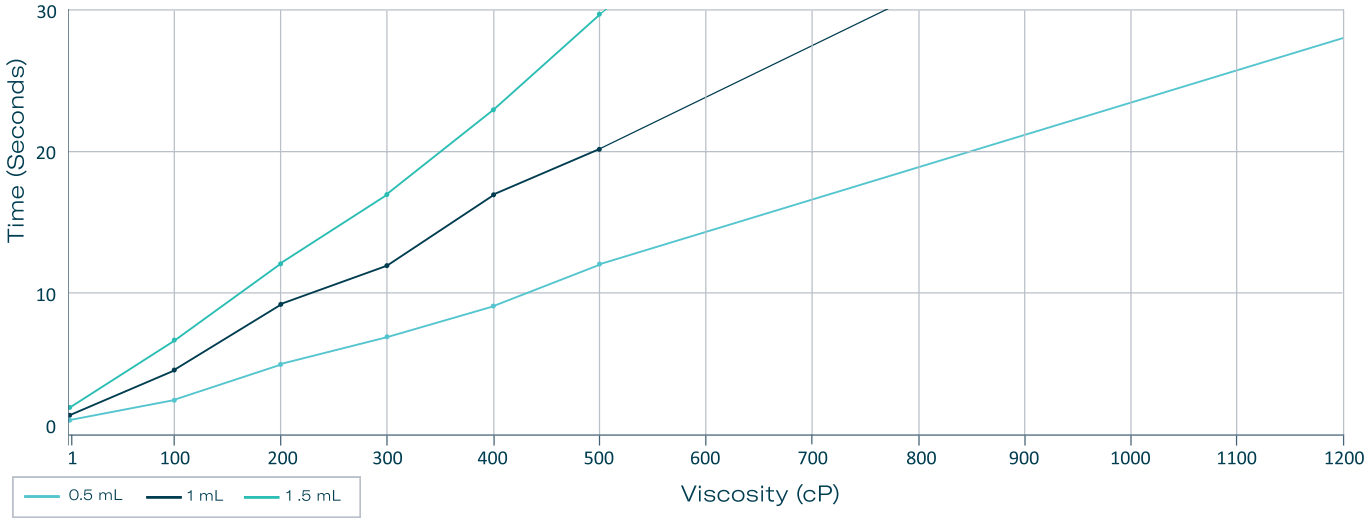

Figure 5: Measurement of maximum viscosities delivered with a 25 G double-ended needle in 30 seconds at volumes of 0.5, 1 and 1.5 mL in a 1.5 mL ISO cartridge.

- **Reduced Need for Excipients:** Avoiding unnecessary excipients that lower viscosity can enhance stability and reduce potential immunogenicity risks.[8]
- **Larger Volumes Made Possible:** Injection times are a critical factor. The tests demonstrate that Gx Inbeneo® can deliver larger doses without longer injection times compromising patient comfort.
- **Compatibility with Next-Generation Biologics:** Many pipeline biologics, including bispecific antibodies and antibody-drug conjugates, have inherently higher viscosities due to their inclination to form aggregates. The Gx Inbeneo® accommodates these formulations more effectively than traditional autoinjectors.

PATIENT-CENTRIC DESIGN SUPPORTS ADHERENCE

The benefits of the Gx Inbeneo® platform design not only include greater formulation flexibility but it is also user-centric – something that is at the core of all product development at Gerresheimer. Faster injection times for high-viscosity formulations enable a broader range of high-viscosity drugs to be administered in a clinically acceptable and tolerable injection time. Reduced injection force due to optimised needle dynamics improves usability and may also reduce pain. A unique transparent top casing allows the patient or healthcare professional to visually track injection progress, and the needle remains hidden before and after injection, reducing needle phobia and risk of needlestick injury. Such features enhance user experience and safety and may aid patient adherence.

CONCLUSION

The Gx Inbeneo® platform represents a breakthrough in SC biologic drug delivery by enabling the safe, effective administration

Prof Sigrid Saaler-Reinhardt

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of large-volume, high-viscosity formulations using an autoinjector. Its cartridge-based design provides formulation scientists with the flexibility to develop stable and effective biologics while ensuring patient comfort and adherence. The innovative design has not only demonstrated efficacy and user-centricity through extensive testing but was also awarded a prestigious Red Dot Design Concept award in October 2024.

As the market for biologics continues to expand, innovative drug delivery systems, such as the Gx Inbeneo®, will play a crucial role in helping to achieve treatment outcomes that, ultimately, enhance patient quality of life.

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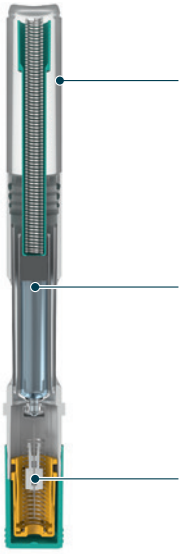
reddot winner 2024

Gx Inbeneo®

Autoinjector for biopharmaceuticals



Patient-friendly design

— Push-on-skin activation for ease of use
— Double-ended needle shortens injection time

Created for biologic drugs

— Dry needle prevents clogging in storage
— Cartridges with baked-on siliconization

Quick customization

— Platform concept reduces time-to-market
— Volume up to 3 mL & very high viscosity

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VYTAL – ONE STEP INTO THE FUTURE OF CONTAINER-CLOSURE SYSTEMS

H&T PRESSPART

Ana Isabel Gutierrez at **H&T Presspart** looks at advancements in sterile and aseptic filling methods in the pharmaceutical industry, introducing the company's Vytal® snap-fit container-closure system, which is designed to meet the growing regulatory demands of the pharmaceutical industry.

The biopharmaceutical industry is experiencing significant transformation driven by technological advancements and the emphasis on specialised therapies. There is an increasing demand for specialised biological products, including biologics and biosimilars. According to a Global Biologics Market Research Report by Insight Ace Analytic, the global biologics market was valued at US$402 billion (£313.6 billion) in 2023 and is predicted to reach $717 billion by 2031, at a 7.76% compound annual growth rate. This growth is fuelled by the expiration of patents on major biologics and the necessity for innovative treatments for complex diseases.

Advancements in sterile and aseptic filling methods are essential for maintaining product sterility. Robotics and automation significantly reduce the risk of contamination, while advanced isolator technologies enhance sterility assurance and operational efficiency. These innovations enable manufacturers to meet strict regulatory requirements and deliver high-quality products, which accelerate drug development timelines and enhance the accuracy and efficacy of therapies, thus promising significant improvements in patient care.

Ready-to-use (RTU) containers play a crucial role in improving production efficiency and sterility. These containers are pre-sterilised and are prepared for aseptic filling, minimising contamination risks. Snap-fit closure systems facilitate rapid assembly without additional equipment, preserving the sterile barrier. These systems are essential in environments where high

precision in required, such as in the production of monoclonal antibodies or messenger RNA-based drugs. They allow for design flexibility to meet diverse product needs, which is crucial for customisation.

The integration of RTU systems with snap-fit closures is revolutionising the industry by reducing costs, improving production efficiency and enhancing product safety. As regulatory demands increase, these systems provide solutions to meet global quality and safety standards, enabling rapid delivery of safe and effective biopharmaceutical products to the market.

RTU SNAP-FIT CLOSURE SYSTEM: INNOVATION WITH VYTAL

Vytal Snap-Fit Technology

To meet increasing regulatory demands and the stringent requirements of the pharmaceutical industry, H&T Presspart has introduced Vytal, a new snap-fit container closure. Vytal effectively handles biologics and complex drugs, is compliant with ISO13485 and GMP Annex I, and is compatible with multiple sterilisation methods.

Single-Step Vytal System Advantages

Vytal offers a single-step design that optimises sealing with three security areas, reduces residual volume, and features tamper evidence and laser marking for enhanced security and traceability (Figure 1).

Figure 1: Vytal's snap-fit closure.

Operational Efficiency and Risk Reduction

Vytal enhances efficiency, it streamlines the closure process, reduces the likelihood of human error and seamlessly integrates into existing workflows. Its compatibility with both glass and cyclo-olefin polymer (COP) containers helps to minimise contamination risks.

Comparison with Traditional Systems

Vytal's snap-fit technology reduces particle generation and material degradation, enhancing container integrity even at low temperatures (-80°C) compared with traditional systems. Vytal is compatible with standard closed-system transfer devices (CSTDs), setting a new benchmark in aseptic pharmaceutical processes.

CCI AND COMPATIBILITY WITH GLASS AND COP VIALS

Manufacturers of complex and biologic pharmaceuticals encounter significant challenges regarding container-closure integrity (CCI) during the vial filling process. Maintaining CCI is crucial for safeguarding against contaminants and preserving the product's sterility throughout storage and distribution. Any breach in CCI can jeopardise the drug's safety and effectiveness, posing health risks to patients and potentially subjecting the manufacturer to legal liabilities.

CCI is especially critical for biologics because they are sensitive to environmental factors such as light, temperature and oxidation, which can lead to the degradation of proteins and complex molecules (Figure 2).

Common problems with CCI arise from failures in vial sealing, which can be caused by defects in rubber stoppers,

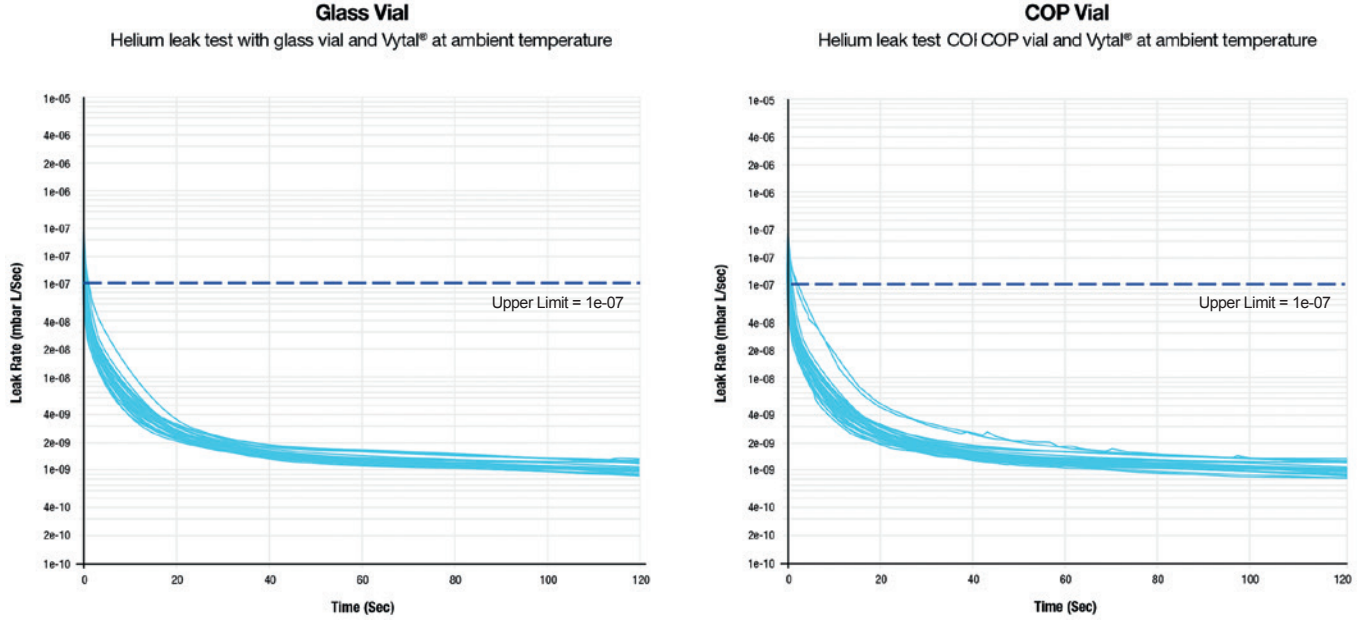


Figure 2: CCI with Vytal and glass vial (left) and Vytal and COP vial (right) at ambient temperature.

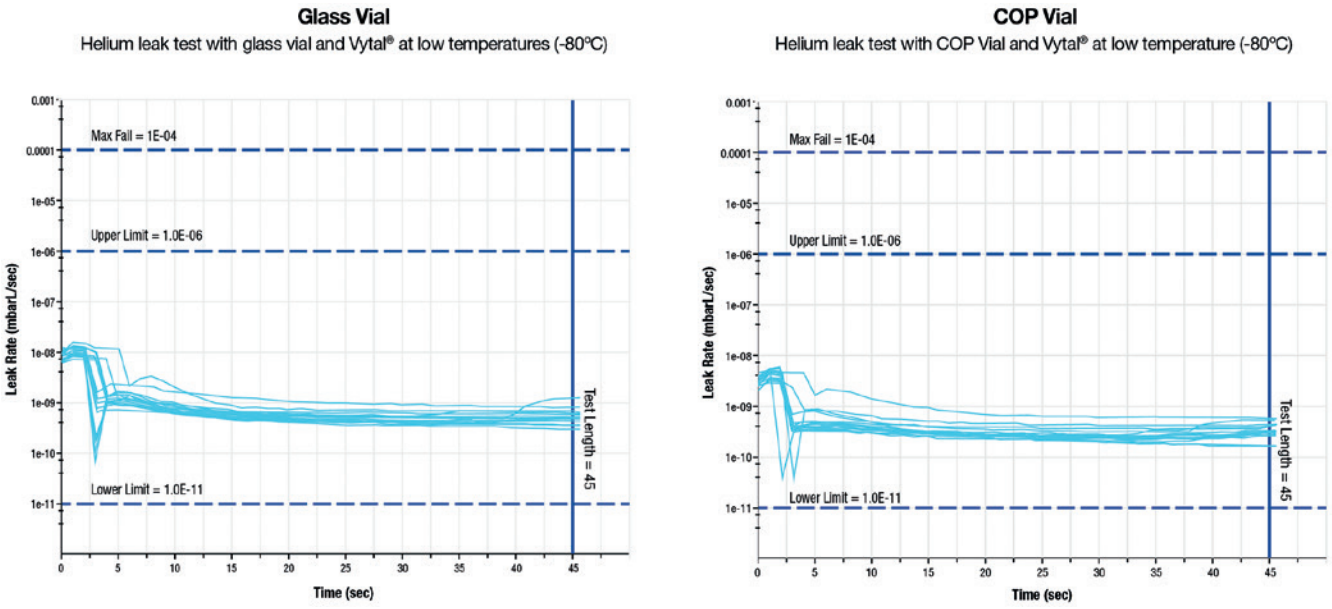


Figure 3: CCI with Vytal and glass and Vytal and COP at low temperature.

imperfections in glass vials or errors during the sealing process. Innovations in aseptic filling technologies, along with the development of snap-fit closures, are addressing these challenges. These advancements enhance automation and precision, reducing contamination risk and improving CCI.

Snap-fit closures provide a more efficient and secure sealing method by eliminating the need for traditional crimping, thus simplifying the process and minimising errors.

Vytal is pioneering advancements in CCI assurance at ultra-low temperatures (up to -80° C), which are crucial for preserving temperature-sensitive biologics. Such technological advancements substantially enhance the safety, efficacy and integrity of complex biologic pharmaceuticals (Figure 3).

H&T Presspart's Vytal performs exceptionally well with both borosilicate glass and COP containers. Its adaptive sealing mechanism effectively accommodates dimensional variations, ensuring consistent CCI. Stress analysis confirms that there are no localised tension points that could compromise CCI, highlighting the system's reliability in diverse pharmaceutical packaging applications.

COMPATIBILITY WITH CSTDs

In handling hazardous drugs, CSTDs are crucial for protecting healthcare professionals from toxic exposure. Vytal has been tested successfully with standard marketed CSTDs, as the integration of these devices with snap-fit container closures is of paramount importance for several fundamental reasons:

- **Safety:** CSTDs, when combined with snap-fit closures, form a robust barrier against hazardous drug aerosols and vapours, protecting healthcare professionals in hospitals and labs .
- **Product Integrity:** CSTDs maintain drug stability by providing a hermetic seal that protects against contamination, ensuring medications remain safe and effective until use.
- **Regulatory Compliance:** Compatibility with snap-fit systems helps healthcare facilities meet international CSTD regulations, preventing legal issues and ensuring compliance.
- **Operational Efficiency:** Snap-fit systems compatible with CSTDs streamline medication handling, reduce errors and optimise workflow, allowing more time for patient care.

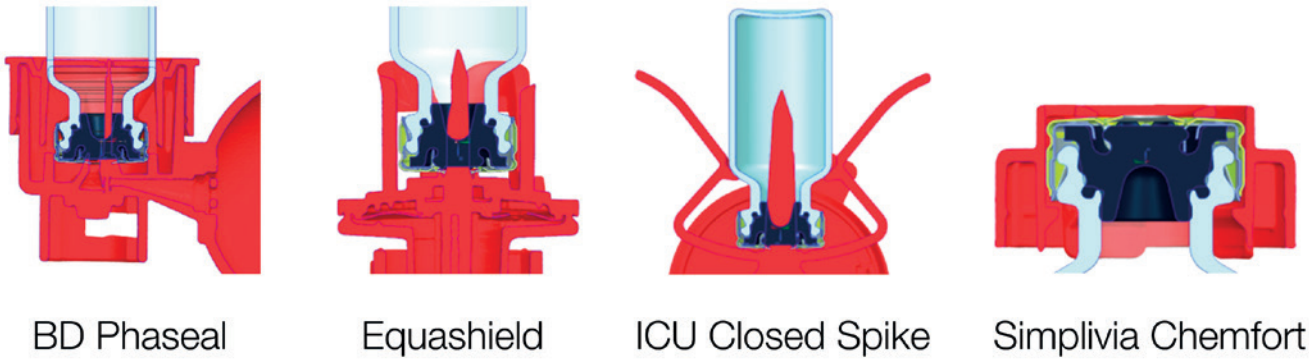
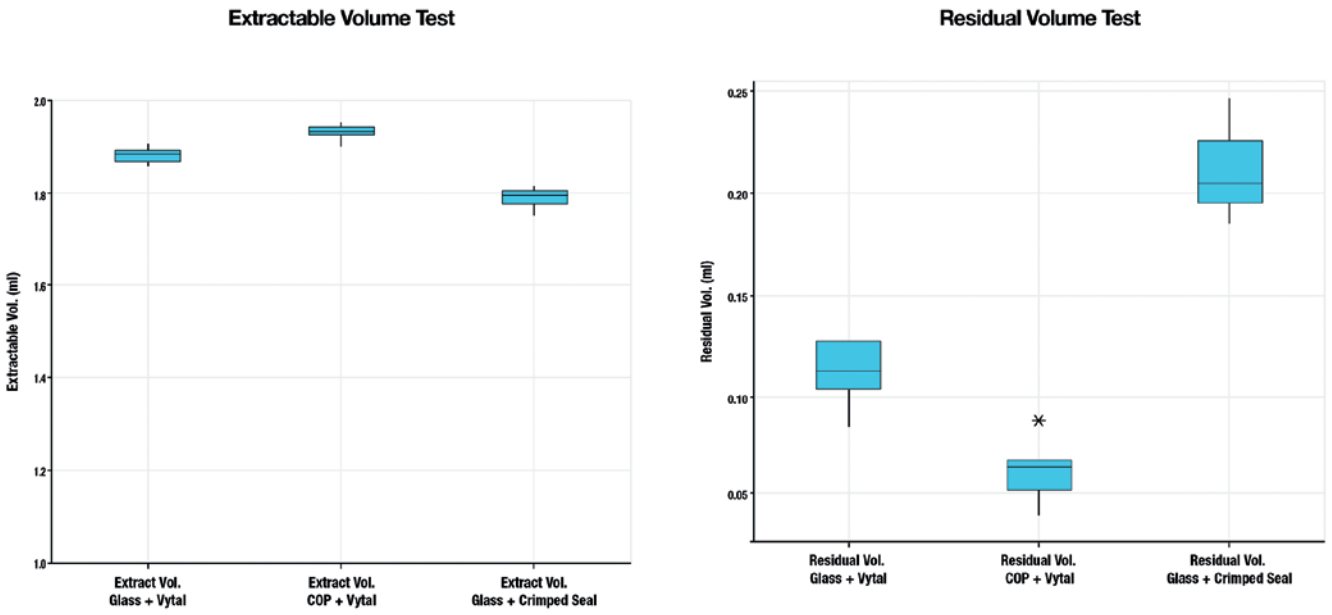


Figure 4: Compatibility with standard marketed CSTDs.



Extractable and residual volume tests were undertaken with WFI and 21G/1" (0.8 x 25 mm) needle BD in three different configurations:
(1) Glass vial + Vytal with coated stopper
(2) COP vial + Vytal with coated stopper
(3) Glass vial + coated stopper + crimped Seal.

The test results were positive, showing that Vytal® was superior compared to crimped closures.

Figure 5: Extractable and residual volume with Vytal.

Vytal's compatibility with CSTDs is essential for ensuring safety, integrity, compliance and efficiency. Drug manufacturers adopting these technologies prioritise the protection of healthcare personnel and patients while meeting regulatory standards – all while simplifying processes and ensuring drug safety (Figure 4).

RESIDUAL VOLUME OPTIMISATION

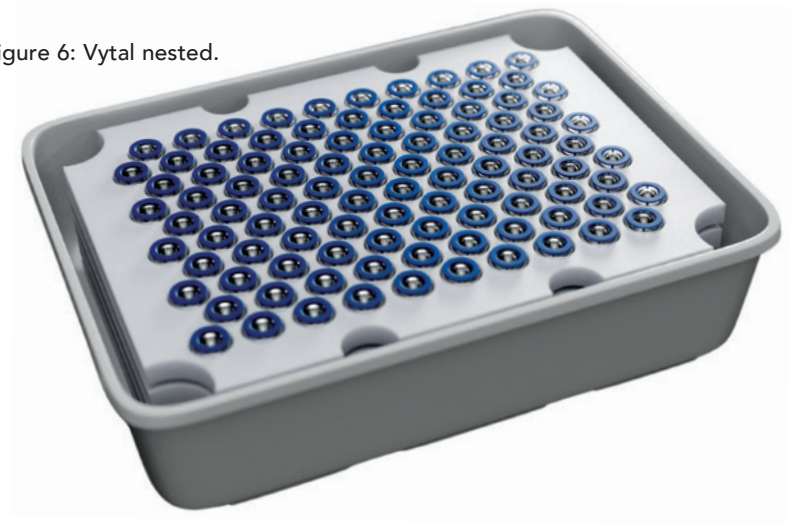
When dosing drugs from vials, optimising residual volume is vital, especially for highly sensitive medications. These drugs often involve complex production and filling processes, leading to high costs.

Vytal is designed as a snap-fit concept for container-closure systems, preserving the traditional look by maintaining a complete view of the vial's neck. This design strategy addresses several key areas:

- **Economic Impact:** Reducing residual volume helps to minimise medication waste, leading to substantial cost savings for healthcare providers and pharmaceutical companies, particularly with costly drugs.
- **Technical Solutions:** Vytal's closure system enhances syringe access and improves the efficiency of drug extraction by providing a clear view of the vial neck, thereby effectively reducing residual volume.
- **Benefits for Patients and Healthcare Providers:** By ensuring complete dosing, patients receive all of their prescribed treatment, thereby enhancing therapeutic outcomes. Healthcare providers also benefit from cost reductions and increased efficiency in resource allocation.
- **Comparative Efficiency:** Vytal, with its unobstructed vial neck visibility, outperforms traditional systems by minimising waste and enhancing the efficiency of drug retrieval (Figure 5).

Overall, Vytal's innovation underscores its value by ensuring economic efficiency, enhancing medication administration efficacy and reinforcing patient safety within healthcare settings.

Figure 6: Vytal nested.



"SNAP-FIT SYSTEMS SUBSTANTIALLY REDUCE PARTICLE GENERATION – ENHANCING PRODUCT QUALITY AND COMPLIANCE – WHILE SUPPORTING CLEANER ENVIRONMENTS ESSENTIAL FOR PHARMACEUTICAL MANUFACTURING."

NESTED AND BULK FORMATS

Vytal offers flexibility with both nested and bulk formats. The nested option allows for the efficient closure of 100 vials simultaneously using current technologies, thereby enhancing operational efficiency. Meanwhile, the bulk format, available in ported bags, is designed for compatibility with automatic filling machines in controlled environments, such as isolators. This versatility ensures that Vytal meets varied processing needs while optimising throughput and maintaining high-quality standards in pharmaceutical applications (Figure 6).

PARTICLE CONTROL AND QUALITY

Snap-fit container-closure systems offer significant advantages over classical crimping systems, particularly in reducing particle generation, which is crucial in pharmaceutical manufacturing and safety.

Reduced Mechanical Action

Snap-fit systems use a straightforward snapping mechanism, minimising mechanical stress and reducing particle generation compared with the substantial force required in crimping (Figure 7).

Minimisation of Material Wear

Unlike crimping, which can cause abrasion and generate metallic particles, snap-fit systems interlock smoothly without intensive material contact, reducing wear and particle contamination.

Enhanced Cleanliness

With fewer steps and less equipment, snap-fit systems again limit particle formation, reducing contamination risks compared with complex crimping equipment.

Compliance With Stringent Regulations

Snap-fit systems naturally meet stringent regulatory requirements, like those from the US FDA and EMA, by offering a cleaner sealing method.

In summary, snap-fit systems substantially reduce particle generation – enhancing product quality and compliance – while supporting cleaner environments essential for pharmaceutical manufacturing.

ANTI-COUNTERFEITING

Vytal's container-closure system incorporates advanced anti-counterfeiting features to combat pharmaceutical counterfeiting. The aluminium cover seal supports laser coding, enabling serialised 2D matrix codes for unit-level traceability and integration with global track-and-trace systems (Figure 8).

Figure 7: Vytal snap-fit closure.

Figure 8: Anti-counterfeiting laser marking.

A patented transparent window in Vytal's plastic button provides instant tamper detection. Users can see any breach in closure integrity, as broken aluminium bridges are visible through the window (Figure 9).

These features comply with WHO guidelines and regulatory standards, such as the FDA's Unique Device Identification system and the EU's Falsified Medicines Directive, enhancing authenticity and integrity in the pharmaceutical supply chain.

REDUCING TIME TO MARKET

Vytal is designed to seamlessly integrate with both well-established, high-speed filling machines and emerging modular filling machine concepts. Modular options are becoming more prominent due to their suitability for producing biological drugs, which often require small batch sizes of multiple drug variants.

Figure 9: Anti-counterfeiting – tamper evidence.

These machines provide a significant advantage by reducing time to market, thanks to their availability and faster manufacturing and qualification processes when compared with traditional high-speed lines – a crucial factor for achieving competitiveness in the pharmaceutical industry.

Moreover, these machines offer remarkable flexibility, allowing for rapid transitions between different drugs, vial sizes and even other formats without the downtimes typically associated with conventional equipment modifications.

This adaptability is essential for accommodating a wide range of products efficiently and cost effectively. Consequently, Vytal offers the flexibility to choose either traditional lines or the most advanced options for producing small to medium batches.

CONCLUSION

Vytal is establishing itself as the new benchmark in aseptic fill-finish processes for biologics and complex pharmaceuticals. The snap-fit closure adheres to rigorous containment and safety standards, rendering it particularly suitable for advanced therapeutic products. Developed in compliance with ISO13485 and GMP Annex I, Vytal is versatile in its sterilisation compatibility, accommodating ethylene oxide, X-ray, gamma and steam post-capping methodologies.

The system features three sealing areas to ensure superior CCI and includes a visible withdrawing area designed to minimise residual volume, thus addressing contemporary requirements for efficiency. Its tamper-evident capabilities and laser marking potential enhance security and traceability, which are crucial amid increasingly stringent regulatory frameworks.

With compatibility across D13 closures and 2R vials in both glass and COP formats, Vytal offers significant operational flexibility while maintaining a conventional appearance, ensuring seamless integration with ISO standards and existing CSTDs.

In conclusion, Vytal is optimally positioned to serve as the standard in aseptic processing, meeting both current and forthcoming industry imperatives for quality and operational efficiency.

"VYTAL OFFERS THE FLEXIBILITY TO CHOOSE EITHER TRADITIONAL LINES OR THE MOST ADVANCED OPTIONS FOR PRODUCING SMALL TO MEDIUM BATCHES."

Ana Isabel Gutierrez

Ana Isabel Gutierrez joined H&T Presspart in 2023 as Global Business Development Manager, driving the company's parenteral applications programme. Before joining H&T Presspart, Ms Gutierrez spent over 12 years at West Pharmaceutical Services, where she held a prominent sales leadership position, specialising in the generics, pharma, biotech and veterinary sectors across Southern Europe. Ms Gutierrez holds a degree in chemical engineering and a postgraduate specialisation in polymers.

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Vytal® is an innovative RTU snap-fit closure for small molecules and biologics, manufactured in small-medium batches under the highest containment requirements.

Vytal® meets the demand of new filling technologies and reduces time-to-market, whilst maintaining the highest quality standards.

- Snap-fit system
- Ready-to-use (RTU)
- ISO dimensions
- Glass & COP vial compatibility
- Nested & Bulk
- Anti-counterfeiting: Tamper evidence
- CCI assured even at low temperature (-80 °C)
- Compatibility to standard marketed CSTDs
- Low particle generation
- Low residual volume
- Full visibility
- Anti-counterfeiting: Laser marking

vytal

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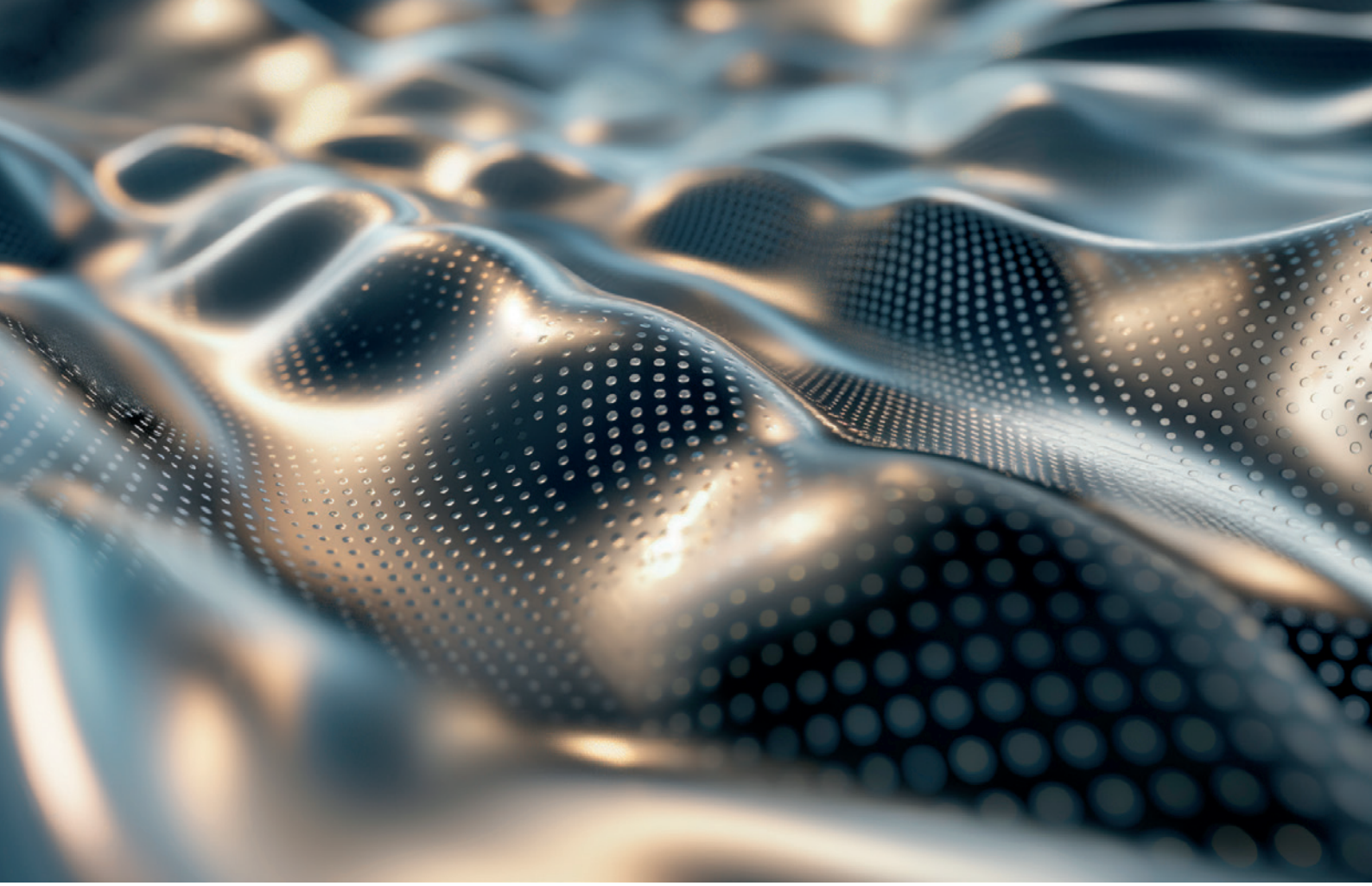

NEXT-GENERATION SURFACE TECHNOLOGIES FOR MEDICAL INJECTION MOULDING

Rob Doorakkers of **IGS GeboJagema** and **Dr Stephan Plassmann** of **Gloss & Coating** discuss their new Translatio-Coating technology for treating the surfaces of steel parts to achieve microscopic levels of optimisation and open new possibilities for efficiency and quality in drug delivery device manufacturing.

In high-precision injection moulding, every aspect is crucial for efficiency and product quality, from steel parts manufactured with micron-level precision to thermal management, material flow dynamics and optimised process settings. Yet, as injection-moulding technology for drug delivery devices has evolved, one crucial element has remained unchanged – the interaction between molten plastic and steel surfaces. Until now.

THREE LEVELS OF MOULD SURFACE STRUCTURE

Understanding mould surfaces requires distinguishing between three distinct levels of detail. At the highest level, there is the primary structure: the fundamental shape and dimensions defined by computer-aided design data. The secondary structure encompasses the visible manufacturing marks: the patterns left by milling and electrical discharge machining processes, as well as manual finishing processes, such as polishing and bead blasting. But there is a third level that plays a crucial role in the moulding process: the nanostructure.

This nanostructure, typically less than one micron deep, is the actual surface that molten plastic comes into contact with when it fills the mould cavity. For years, it was not possible to adjust this tertiary structure without altering the secondary structure. However, advances in technology now allow us to deliberately modify these nanoscale surface characteristics.

"THE ABILITY TO CONTROL THE NANOSTRUCTURE HAS PROVEN POWERFUL IN OPTIMISING THE DEMOULDING PROCESS."

WHY ALTER THE NANOSTRUCTURE?

The ability to control the nanostructure has proven powerful in optimising the demoulding process. Most moulded products tend to stick to the mould. By fine-tuning these surface characteristics, mould manufacturers can significantly alter how much a product adheres to the mould surface during release. This delivers two key results.

Firstly, it reduces the forces required to overcome sticking during product ejection. This is crucial because when a product is ejected, its core is still relatively soft and susceptible to deformation. Lower demoulding forces mean less stress on the product, preventing unwanted geometrical changes that can affect product quality.

Second, this smoother ejection process allows for reduced cooling times. As the product can be safely removed from the mould earlier in its cooling cycle, overall cycle time decreases, leading to improved production efficiency.

Furthermore, this technology offers several advantages that make it an excellent choice for high-precision moulding of drug delivery devices:

- The technology performs mechanical surface modification and does not introduce chemical changes to the mould
- The dimensional integrity of the moulded product remains completely unchanged and there is no effect on tool parting lines
- The substantial reduction in demoulding forces is uniform across the product, ensuring even product removal and appearance
- The technology allows for precise control of the optical effect on the moulded product, ranging from no effect at all to distinctly visible changes in appearance.

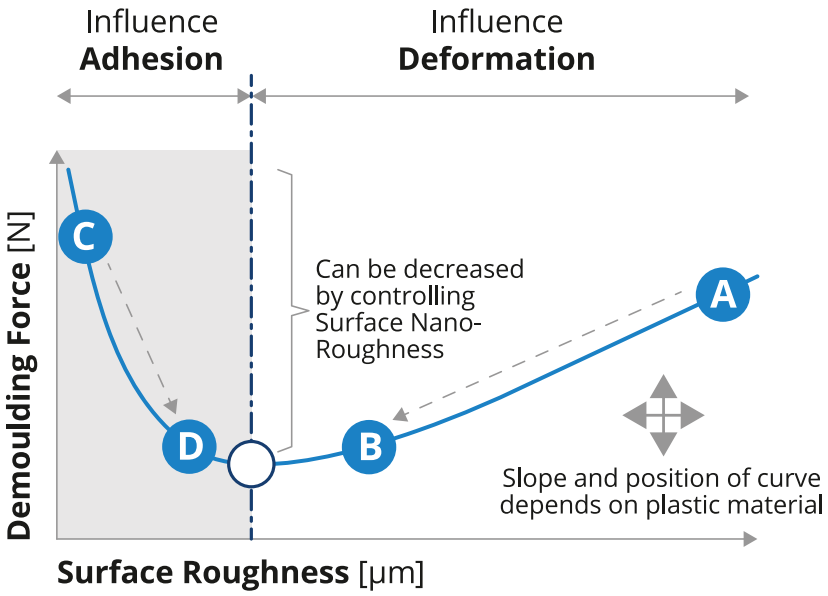

Figure 1: The relationship between surface roughness and demoulding force shows an optimal point where forces are minimised through precise nanostructure control. A – the roughness of a VDI3400 ERO 24 structure. B – the ERO 24 structure nanostructured and thus reduced roughness. C – typical ASPI2 high-gloss finish. D – a nanostructured finish of C. In A–B the roughness is reduced and in C–D the roughness is increased, moving to the sweet spot without compromising the appearance of the plastic parts.

UNDERSTANDING THE IMPACT OF SURFACE ROUGHNESS

As stated, nanostructure modification can make surfaces either rougher or smoother to minimise demoulding forces. However, the relationship between surface roughness and demoulding force is more complex than one might assume. As illustrated in Figure 1, this relationship can be divided into two distinct regions: adhesion and deformation. The graph shows how demoulding force changes with surface roughness, revealing an optimal point where these forces are minimised.

In the adhesion region, extremely smooth surfaces can actually lead to higher demoulding forces due to increased surface contact area. As roughness increases, these forces initially decrease until reaching an optimal point. However, if the surface becomes too rough, it enters the deformation-dominated region, where demoulding forces begin to rise again due to more aggressive interactions between the plastic material and the surface texture.

The key to optimal demoulding lies in finding the sweet spot between these two extremes, indicated by the white circle on the graph. Through precise control of surface nano-roughness, it is possible to engineer this optimal condition, where demoulding forces are minimised while maintaining product quality.

A CASE STUDY ON NANOSTRUCTURE EFFECTIVENESS

Several of IGS GeboJagema's clients are already using this surface modification technology to gain a significant competitive edge in pharmaceutical manufacturing. While these specific applications are confidential, testing data clearly demonstrate the technology's transformative impact.

"THROUGH PRECISE CONTROL OF SURFACE NANO-ROUGHNESS, IT IS POSSIBLE TO ENGINEER THIS OPTIMAL CONDITION, WHERE DEMOULDING FORCES ARE MINIMISED WHILE MAINTAINING PRODUCT QUALITY."

To quantify these benefits, a specialised test tool was used to measure the force required to remove plastic parts from the mould. This tool measures the torque (twisting force) required during ejection to reveal how strongly the plastic sticks to the mould surface. In a comparison of demoulding forces for parts with standard high-gloss polished surfaces (SPI-A2) and those with nanostructure-treated surfaces, the peak torque demoulding force for the treated parts was approximately 40% less than for the parts with polished surfaces. This striking reduction in demoulding force translates directly to less stress on moulded components, faster cycle times and improved product consistency. These results illustrate why leading manufacturers are increasingly adopting this innovation to stay ahead in the demanding drug delivery device market (Figure 2).

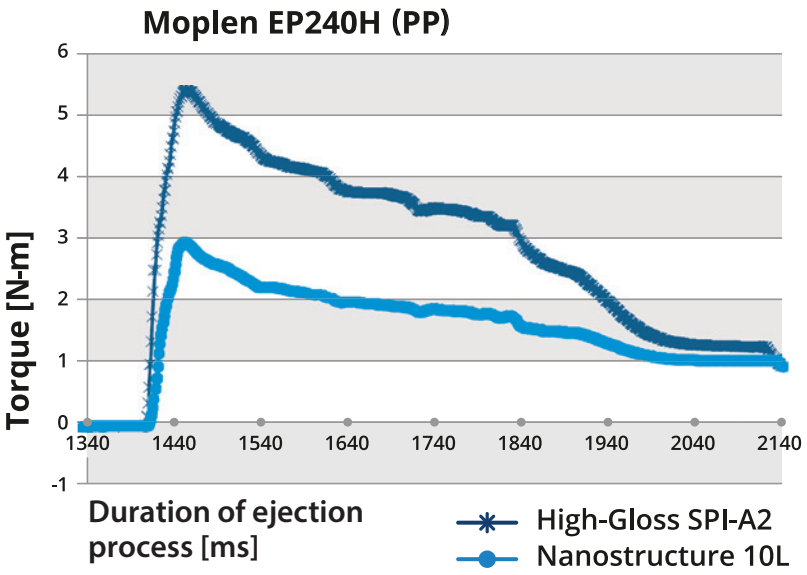

Figure 2: Nanostructure-treated surfaces require 40% less force during ejection than standard high-gloss surfaces.

OPTIMISING SURFACE CHEMISTRY

In addition to modifying the nanostructure, a second innovation can help to further reduce demoulding forces as well as residue formation: the Translatio-Coating. Coatings have been used in the industry for many years, and the challenges are well known. Traditional coatings typically add around 2 µm of thickness to tool surfaces – a factor that must be accounted for during the initial engineering phase. This becomes particularly problematic when demoulding issues arise during validation or throughout the tool's operational lifetime. Applying additional coating to a mould that is already operational is extremely challenging, if not impossible, without compromising the tool's critical dimensions and tolerances.

Temperature limitations present another significant barrier. Many coating processes require high-temperature application, which might exceed what the tool can endure without having a detrimental effect on the quality of the steel.

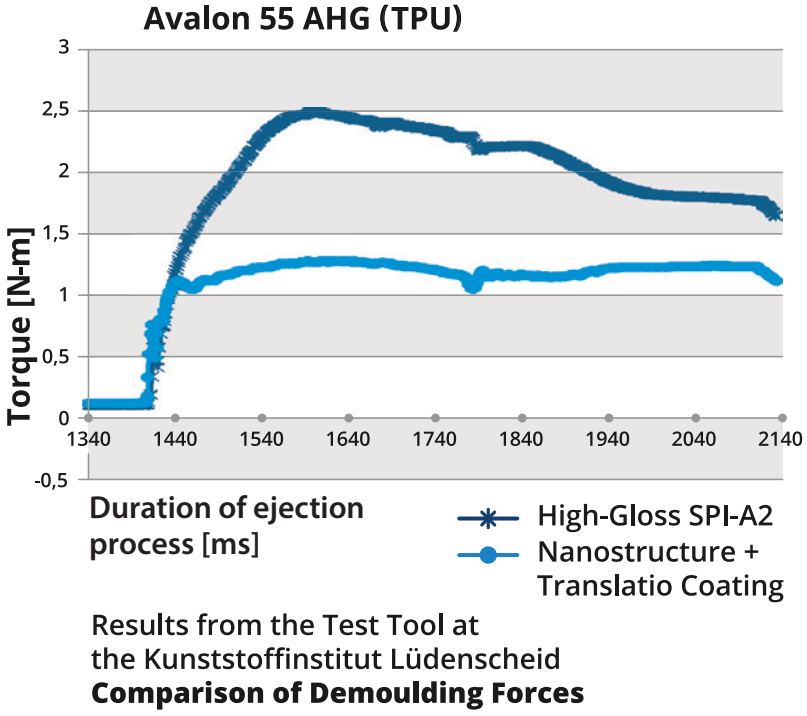

Figure 3: Nanostructure modification combined with Translatio-Coating significantly reduces demoulding forces compared with standard high-gloss surfaces.

THE NOVEL TRANSLATIO-COATING

The development of the Translatio-Coating started from the observation that new moulds typically require a 'run-in' period of several hours to days before reaching optimal production conditions. During this time, a nanometre-thin layer of plastic gradually builds up on the tool surface until reaching a steady state where deposition and removal rates balance. This observation raised the question, what if it were possible to deliberately create this optimised surface layer from the start, using the same plastic material that forms the final product? In other words, what if a specialised coating could be applied?

The Translatio-Coating is the answer to this question. This technology deliberately applies an ultra-thin layer (140–150 nanometres) of the product's plastic material onto the mould surface. During testing, this "native" coating proved to significantly reduce demoulding forces, as can be seen in Figure 3.

"TRANSLATIO-COATING ELIMINATES THE BIGGEST CHALLENGES OF COATINGS. BECAUSE IT IS ULTRA-THIN, IT DOES NOT AFFECT TOLERANCES, AND IT CAN BE APPLIED WITHOUT SIGNIFICANT HEAT. THIS ALLOWS THE TRANSLATIO-COATING TO BE RETROFITTED ONTO ANY MOULD AT ANY POINT."

Critically, this new technology eliminates the biggest challenges of coatings. Because it is ultra-thin, it does not affect tolerances and it can be applied without significant heat. This allows the Translatio-Coating to be retrofitted onto any mould at any point. It provides advantages to both existing and new moulds:

- **Immediate Production Readiness:** Tools achieve full production capacity from the first shot, eliminating run-in time.
- **Enhanced Product Quality:** The system improves both demoulding characteristics and geometric conformity.
- **Reduced Maintenance:** Significant decrease in plastic residue formation on tool surfaces, which lengthens the mould maintenance cycle.
- **Regulatory Compliance:** Unlike any other coating, the Translatio-Coating is automatically US FDA and EMA approved because it is made from the same resin as the moulded product itself (as confirmed by Fourier transform infrared spectroscopy measurements), which eliminates additional certification requirements for medical injection moulding processes.

Rob Doorakkers

Rob Doorakkers is Chief Innovation Officer at IGS GeboJagema, where he focuses on optimising production processes, continuously improving product quality and finding innovative solutions to solve the most demanding technical challenges. Mr Doorakkers has over 30 years of experience in the injection moulding and manufacturing industry.

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Dr Stephan Plassmann

Stephan Plassmann, PhD, is CEO of Gloss & Coating GmbH, specialising in innovative surface modification technologies. With over 25 years of experience in surface engineering, from plasma polymerisation to thin-film technologies, Dr Plassmann has pioneered several breakthrough technologies in injection-moulding surface treatment. Previously, he developed the Caveo diffusion process at Hotec GmbH, and held leadership positions in surface technology at Bekaert.

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- **Reduced Cycle Time:** Shorter production cycles increase overall manufacturing efficiency.
- **Improved Mould Filling:** The coating enhances material flow by 20–30%, resulting in more consistent part quality and reduced defects.

CONCLUSION

The convergence of nanostructure modification and Translatio-Coating technology marks a milestone in injection-moulding capabilities. These innovations address long-standing challenges in medical device manufacturing, offering manufacturers increased control over product quality while improving operational efficiency.

What makes these developments particularly significant is their practical implementation. Both technologies can be applied to existing tools, allowing manufacturers to enhance their current production capabilities. As the medical industry continues to evolve, IGS GeboJagema's surface optimisation technologies not only solve current manufacturing challenges but also set the bar for future injection moulds for medical devices.

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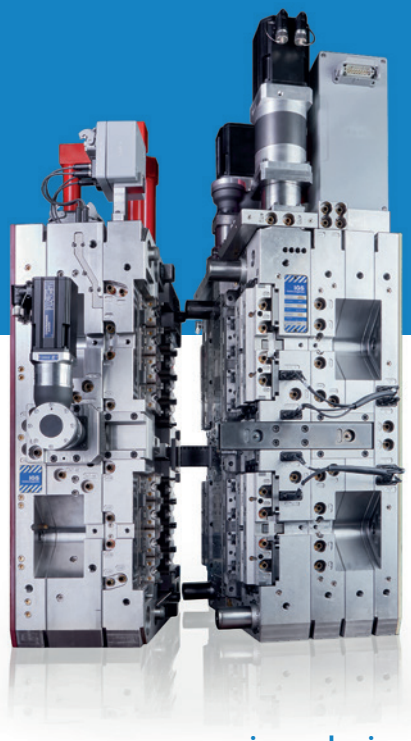

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PROTECTION AND PRODUCTION: OPTIMISING PRIMARY PACKAGING SOLUTIONS FOR mRNA THERAPIES

Enrico Barichello and **Riccardo Prete** of **Stevanato Group** discuss the impact that messenger RNA-based therapies are having on the modern pharmaceutical market and how these delicate therapies require careful handling, with a particular focus on how the company's portfolio of primary packaging products can be highly beneficial when bringing these critical medicines to market.

Over the past five years, significant advances have been made across the pharmaceutical sector, particularly with the rise of messenger RNA (mRNA) therapies. This development was propelled by the successful creation of the world's first mRNA-based vaccine, which demonstrated the potential of this technology. This was a milestone achievement that underlined the promise of mRNA technologies and fuelled further advances in their use to tackle a wider range of diseases, including cancer and rare genetic conditions, beyond their continued development as a potent platform for vaccines.

In mRNA therapies, molecules that are inherently prone to degradation are transported into cells within the protective wrapper of a carrier or vector, such as a lipid nanoparticle (LNP).[1] Safely at its target site, the mRNA delivers its "message", instructing the body to produce protective proteins that bolster immunity and safeguard against the effect of disease. Boosted by the catalyst of covid-19, mRNA vaccines are expected to register a

"THERE ARE MORE THAN 450 mRNA DRUGS AT THE PRECLINICAL AND CLINICAL TRIAL STAGE, WITH mRNA PROVING TO BE THE PREFERRED RNA MODALITY IN THE RESEARCH PIPELINE."

compound annual growth rate (CAGR) of 18% in the years leading up to 2030, significantly outstripping the 4% growth expected for traditional vaccines over the same period, according to IQVIA data. More widely, it is estimated that there are more than 450 mRNA drugs at the preclinical and clinical trial stage, with mRNA proving to be the preferred RNA modality in the research pipeline.[2]

PRIMARY PACKAGING FOR mRNA THERAPIES

For the innovators behind these developments, the challenge of bringing an effective mRNA therapy to market is not limited to the complexities of formulation science. Indeed, the choice of primary packaging is also a crucial concern, and there are various important considerations to incorporate into this decision-making process.

Arguably, the primary question is how to ensure that the stability of the mRNA therapy is supported over the product lifecycle, as this has critical bearing on its potency and efficacy when a patient is injected. Various influences are known to have a negative impact on stability, including ribonuclease enzymes, excipients and pH levels.[3] The presence of particulates in the container closure system also introduces potential for degradation. Moreover, it is essential to safeguard sterility and container closure integrity (CCI), as well as to ensure that there is no interaction with contact surfaces that might compromise the drug product quality. These characteristics underline the importance of containing mRNA therapies within primary packaging components that can accommodate their physicochemical fragility.

Another factor that has a major bearing on stability in mRNA therapies is temperature. Indeed, the first mRNA covid-19 vaccines placed significant demands on logistics through their ultra-cold storage requirements. While advances in formulation science continue to address the difficulties associated with maintaining low-temperature conditions throughout manufacture, distribution and storage, the need to maintain CCI within deep-cold storage conditions remains a priority for mRNA therapies.[4]

"ARGUABLY, THE PRIMARY QUESTION IS HOW TO ENSURE THAT THE STABILITY OF THE mRNA THERAPY IS SUPPORTED OVER THE PRODUCT LIFECYCLE, AS THIS HAS CRITICAL BEARING ON ITS POTENCY AND EFFICACY WHEN A PATIENT IS INJECTED."

All of this highlights the importance of addressing the physical, chemical and thermal risks associated with primary packaging. Particularly in mRNA applications, it is also important to note some of the pragmatic considerations in relation to manufacture and fill-finish. With high value and small batch sizes, close control must be maintained over all stages of production. Enforcing the highest levels of quality and being able to rely on the highest quality primary packaging components ensures that the risk of drug wastage is minimised and production efficiency is optimised.

This is particularly the case for vaccines, where the rapid evolution of a virus can precipitate equally rapid development of updated versions in order to keep populations protected. These new iterations must, of course, be packaged appropriately, whether in vials or prefilled syringes (PFS), placing a higher burden on production facilities to be flexible while limiting impact on time and cost. In this context, the benefit of accessing the right containment solution is significantly augmented by the flexibility to quickly and easily adapt fill-finish environments, keeping any production changes down to an absolute minimum.

THE EZ-FILL® PLATFORM

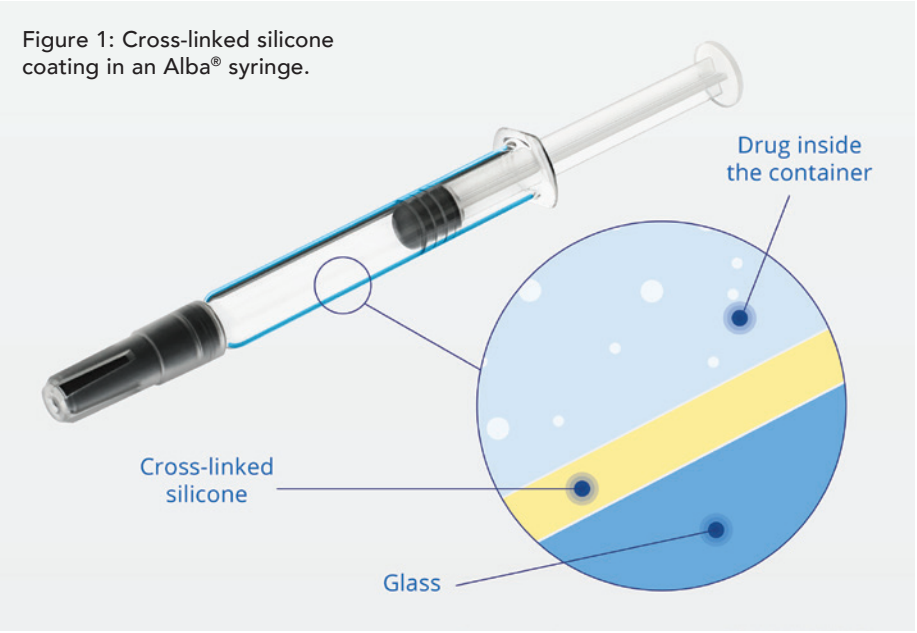
Working with Stevanato Group, companies developing mRNA therapies have access to a comprehensive portfolio of containment solutions that integrates a robust supply of high-quality products with extensive manufacturing expertise to simplify the complex issues that must be considered for the packaging of mRNA therapies. Stevanato Group's EZ-fill® customisable containment solution, for example, presents vials, syringes and cartridges in a ready-to-use (RTU) format to streamline aseptic fill-finish processing, reducing both time-to-market and total cost of ownership. Available in nest-and-tub and tray configurations, EZ-fill containers are separated in the secondary packaging to prevent the risk of contact and damage during transportation, and at buffering or in-feeding points in production. This limits glass-to-glass interaction – a key source of breakages, cosmetic issues and particle creation – to maintain container integrity and limit rejects.

EZ-fill has been further enhanced by Stevanato Group's EZ-fill Smart® platform. Here, for all components, manufacture and supply of the primary container has been optimised to increase regulatory acceptance and sustainability, further reducing total cost ownership. With no glass-to-glass and minimised glass-to-metal contact throughout a highly automated production process, as well as the option of low-temperature vaporised hydrogen peroxide sterilisation and the inclusion of secondary packaging with lower plastic content, EZ-fill Smart provides all the elements required to satisfy the demands of a rigorous particle-reduction strategy.

"FOR ALL COMPONENTS, MANUFACTURE AND SUPPLY OF THE PRIMARY CONTAINER HAS BEEN OPTIMISED TO INCREASE REGULATORY ACCEPTANCE AND SUSTAINABILITY, FURTHER REDUCING TOTAL COST OF OWNERSHIP."

As with all RTU containment solutions, because Stevanato Group manages all the preliminary stages of packaging, washing and sterilisation, the burden on pharmaceutical companies is reduced, with fewer operational processes required and less demand on cleanroom space. Furthermore, the company's comprehensive testing for processability with leading equipment suppliers ensures that containers can be seamlessly integrated into the fill-finish workflow. For applications where mRNA therapies are best suited to delivery via a PFS – with their advantages of dose containment, delivery convenience and waste reduction – Stevanato Group's containment portfolio offers the same level of support for CCI, drug stability and production flexibility as for vial-based solutions.

Figure 1: Cross-linked silicone coating in an Alba® syringe.



ALBA® GLASS SYRINGES

The Alba® range of glass-based syringes has been designed specifically for sensitive drug formulations where there is a heightened risk of interaction between the product and the container closure system. Rather than using a conventional coating, Alba features an innovative cross-linked silicone coating technology, providing enhanced protection against silicone oil particles, interactions between the drug and the container surface, extractables and pH shift, all without compromising the glide and break-loose performance (Figure 1).

The significant reduction in silicone particle migration with Alba syringes has been demonstrated through extensive in-house testing. These tests compared Alba against syringes featuring traditional silicone oil coating under storage conditions of -40°C to evaluate the levels of subvisible particles present in a placebo solution over time using light obscuration. The results clearly show the effectiveness of the cross-linked coating technology in keeping silicon particles to an absolute minimum (Figure 2).

Further tests reinforced that the storage conditions resulted in no noticeable impact on break-loose force and extrusion over time for Alba syringes. The same is true for CCI integrity, where Alba has been tested at -70 °C without reporting any failure among the samples tested (Figure 3).

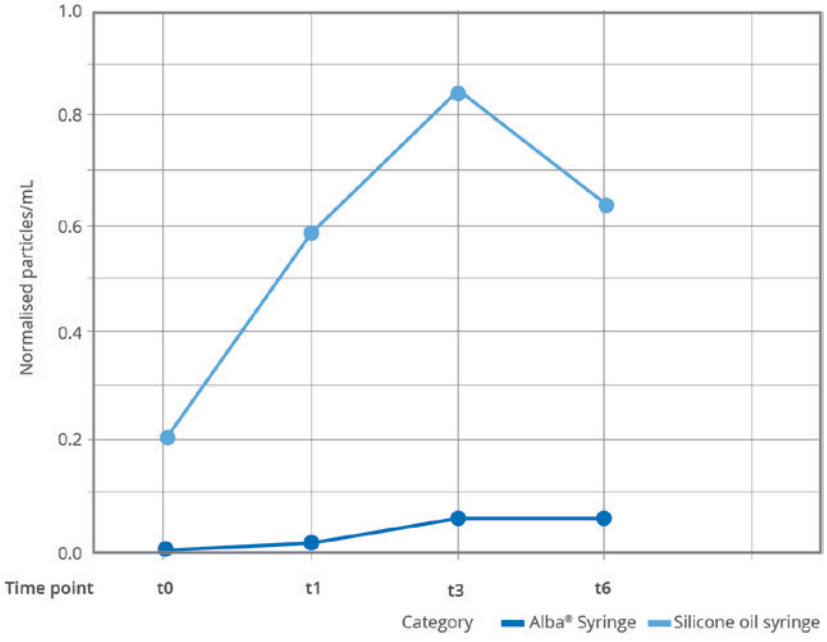


Figure 2: Results of subvisible particle (≥10 µm) testing at -40°C over six months. Alba's data at the 12-month time point are consistent with the findings from the preceding checkpoint.

NEXA FLEX™ POLYMER SYRINGES

In PFS applications where polymer is preferred over glass, Stevanato Group's diverse product range extends to the Nexa Flex™ pre-sterilised syringe, which also features a lower silicone particle profile (Figure 4). Available both in cyclic-olefin polymer (COP) and cyclic-olefin copolymer (COC), Nexa Flex containers are manufactured using a tungsten-free moulding process to limit interaction with sensitive drug products, such as mRNA therapies.

Nexa Flex syringes feature a similar coating to Alba syringes, with the polymerisation process incorporating silicone cross-linking to create an advanced protective barrier that reduces the risk of silicon particle creation. Stevanato Group's

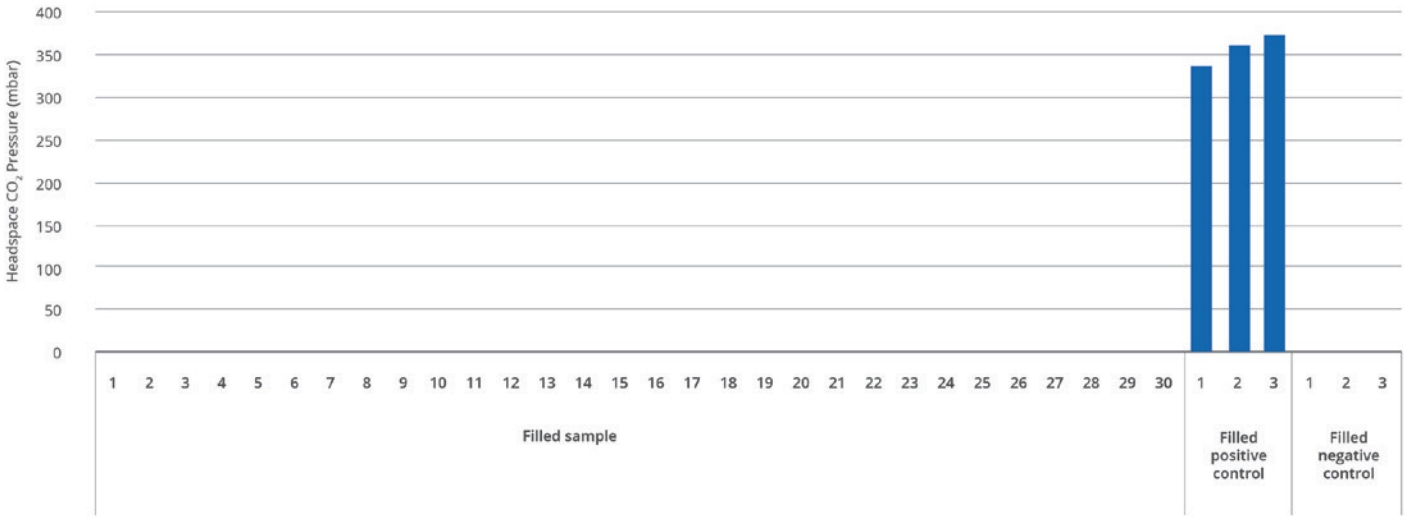


Figure 3: Alba syringe and CCI results for filled 1 mL long syringe at -70°C.

Figure 4: Stevanato Group's Nexa Flex™ polymer syringe.

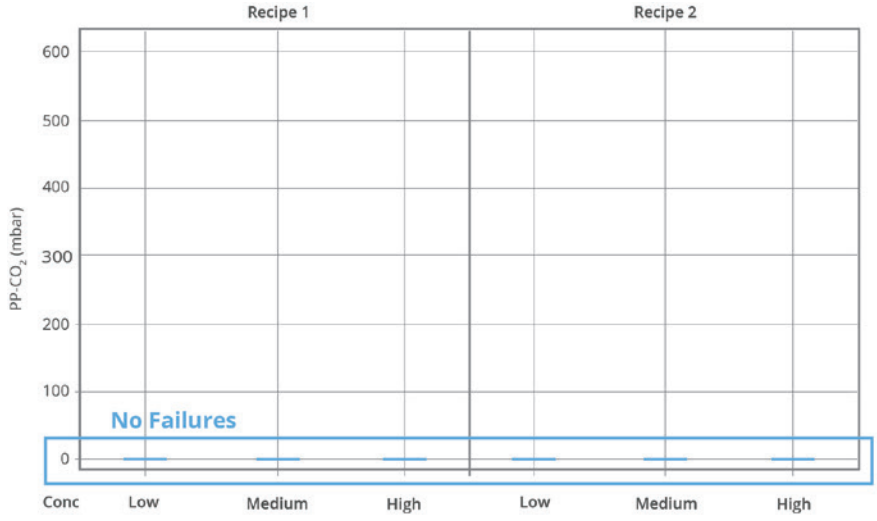


Figure 5: Evaluation of seal integrity during cold storage at -80°C using 1 mL Nexa Flex syringe with two silicone recipes and three test formulation concentrations (low/medium/high).

partnerships with leading elastomer manufacturers also ensure that CCI is maintained for the syringe in cold storage conditions, with testing demonstrating equivalent levels of shrinkage between the plunger and polymer container to provide assurance that the drug product remains protected (Figure 5).

AVOIDING DISRUPTIONS TO MANUFACTURING AND FILL-FINISH

While the characteristics demonstrated by Stevanato Group's primary packaging portfolio are critical for supporting the stability of sensitive mRNA therapies throughout their lifecycle and under potentially demanding conditions, the company has also designed its primary packaging options to provide benefits to manufacturers through the flexibility they offer in fill-finish environments. Here, there is potential for major disruption when adjusting production lines for relatively small batches of mRNA therapies based on the need to change an already validated infrastructure to align with the requirement of a different formulation and containment choice.

However, the flexibility of Alba, offered in the same formats as standard vaccine syringes, including secondary packaging, means that it is possible to introduce this syringe with little to no disruption to current manufacturing infrastructure, maintaining the same fill-finish platform. This minimal format

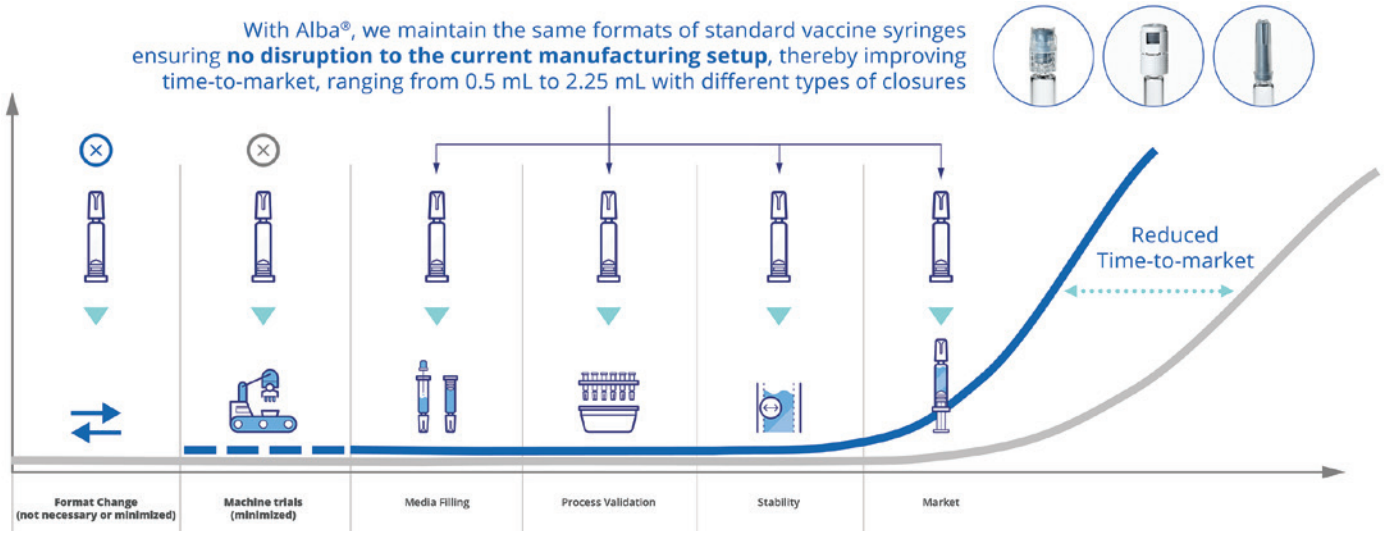


Figure 6: Alba improves time to market by minimising disruption.

change requirement results in swifter, simpler changeovers, which, in turn, delivers time- and cost-saving benefits, while crucially avoiding the higher capital investment associated with additional equipment purchases (Figure 6).

Another potential source of disruption to consider for mRNA therapies relates to changing containment needs over the course of a drug product's lifecycle. For example, vial-based containment solutions might be optimal for bringing a product to market, easing the transition from laboratory to commercial volume production by avoiding the need to validate a different type of container. However, once established, there might be a goal to deliver products in a

"ANOTHER POTENTIAL SOURCE OF DISRUPTION TO CONSIDER FOR mRNA THERAPIES RELATES TO CHANGING CONTAINMENT NEEDS OVER THE COURSE OF A DRUG PRODUCT'S LIFECYCLE."

PFS format ultimately, to support accuracy of dosing and avoid wastage.

CONCLUSION

As mRNA-based treatments and vaccines gain further traction in the market, there is likely to be an escalation in the need both to accommodate transitions in primary packaging and to adapt to changing formulations targeting new medical challenges. At the same time, there will be a constant need to protect the stability of these delicate drug products with high-performance containment solutions. It is a complex dynamic, but one that Stevanato Group's flexible product offering allows both manufacturing and pharmaceutical partners to resolve without compromise.

Don't miss the chance to attend the PDA Miniverse on June 25–26, 2025, which will include a tour of Stevanato Group's new, state-of-the-art US hub. Subscribe to the PDA Miniverse Conference, visit Stevanato Group at booth #218 and join us in Fishers (IN, US) on June 24. ***www.stevanatogroup.com/en/news-events/events/pda-miniverse-2025/***

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Stevanato Group is a global provider of drug containment, drug delivery and diagnostic solutions, with an integrated, end-to end portfolio of products, processes and services to address customer needs across the entire drug lifecycle. Stevanato Group's core capabilities in scientific research and development, its commitment to technical innovation and its engineering excellence are central to its ability to offer value-added solutions to clients.

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More Spotlights overleaf

The intrinsic nature of mRNA therapies poses specific challenges in maximizing product stability and ensuring effective drug delivery.

Stevanato Group addresses these challenges with **EZ-fill® Alba®** glass syringes and **EZ-fill® Nexa Flex™** polymer syringes, both featuring an internal cross-linked silicone oil coating that minimizes subvisible particle release and enhances stability for sensitive drugs.

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CCBio is a medical device designer and manufacturer with core competencies including tooling, moulding, assembly, validation, R&D, RA and pharmaceutical testing, all in-house. It offers combination products, medical devices and medical containers to pharma partners and, ultimately, patients.

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