20 YEARS ON

178

Drug Delivery

OCTOBER 15TH 2025

PREFILLED SYRINGES & INJECTION DEVICES

DCA

reddot design winner

GOOD DESIGN

Helping our clients achieve success through great product design

Two-step autoinjector platform

www.dca-design.com

RNS safetyPlus™

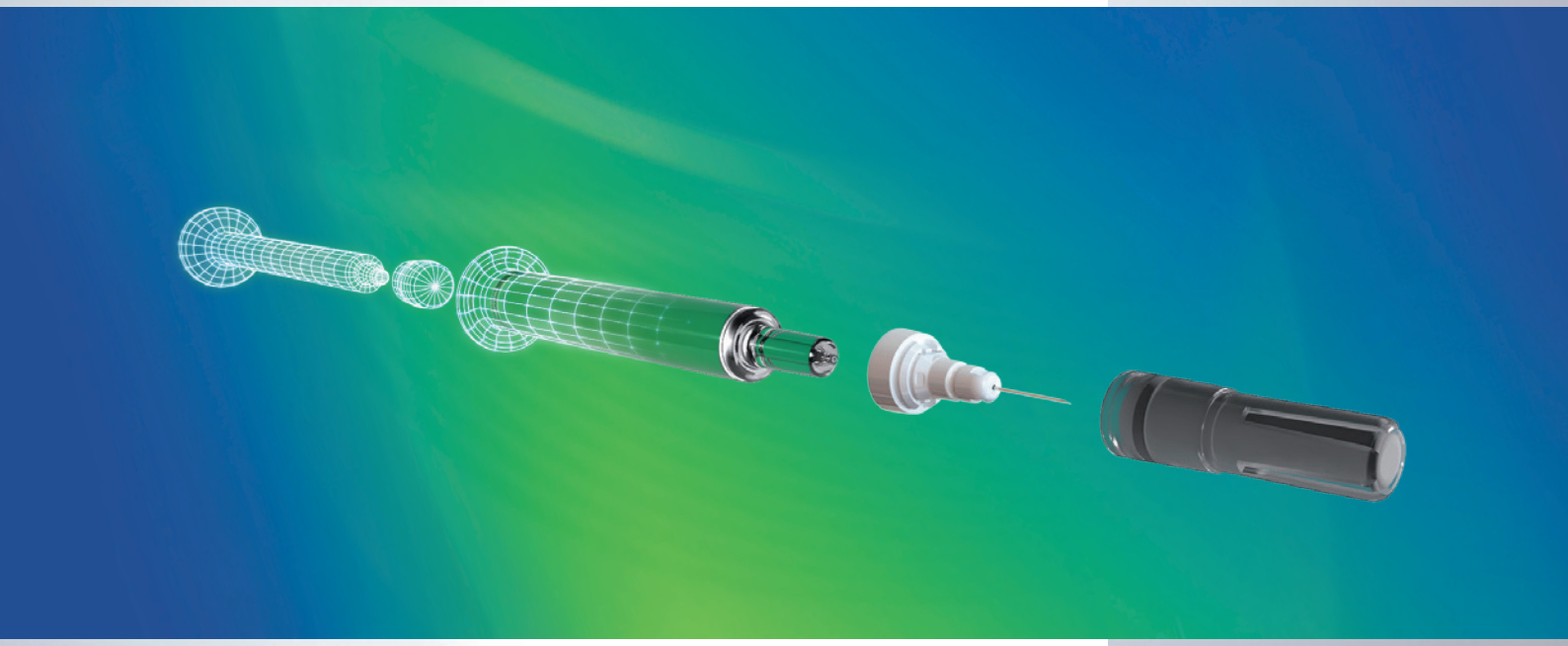
Provides integrated needlestick protection
for prefillable syringes supplied in Nest & Tub formats.

Pharmapack Paris 2026 Booth 4J118

tip-top.com

FROM CONCEPT TO COMMERCIALIZATION

CUSTOMIZATION IS PART OF OUR DNA



If you think the Credence Dual Chamber System sets the bar, wait until you see what we can build together. From solving unique drug delivery challenges to tailoring engineering solutions that fit your product, process, and patients, customization is in our DNA.

Our flexible platforms, proven engineering expertise, and efficient development process deliver measurable value, accelerate time to market, and ensure regulatory compliance. Credence will create customized solutions to address your drug delivery challenges, and guide the program from prototyping to commercial supply.

WHY PARTNER WITH CREDENCE?

- Broad Expertise – From Dual Chamber systems to ophthalmic, aesthetics, and other specialty platforms.
- Built for Evolving Demands – Enhance usability and adherence for both at-home and HCP use.
- Ready for Complex Formulations – Handle high viscosities, microliter dosing, and separation of sensitive components.

Connect with Credence to start addressing your custom drug delivery challenges today!

Credence MedSystems, Inc. | +1 844-236-3797
credencemed.com | info@credencemed.com

CREDENCE MEDSYSTEMS

WHAT CLIENTS ARE SAYING:

"Credence is a trusted and valuable partner. Their ability to understand our commercial needs, translate that into detailed plans and then modify their core drug delivery technology to meet the challenging requirements for our unique Ophthalmic Ointment has been outstanding. They continue to demonstrate expertise in delivery device development while fostering a collaborative spirit with Azura and our other supply chain partners."

Marc Gleeson, CEO,
Azura Ophthalmics

Unsure your filling needs will be fulfilled?

Bring it.

- U.S.-based
- Annex 1 compliant
- 40+ year track record
- Isolator filling

Lifecore®
INJECTABLES CDMO

Contents

PREFILLED SYRINGES & INJECTION DEVICES

ONdrugDelivery Issue N° 178, October 15th, 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.

SHL MEDICAL

Reconstitution made simple

Introducing Reunite™

Reunite is an **easy-to-use dual-chamber cartridge autoinjector** featuring SHL Medical's **Needle Isolation Technology (NIT®)**, designed to support the **automated reconstitution** and **delivery of lyophilized formulations.**

Automated reconstitution

Easy-to-use autoinjector

Pre-attached and hidden needle (NIT®)

Discover

REUNITE™

shl-medical.com/products/autoinjectors/**reunite**

Curious to learn more about the device?
Catch our experts at this year's PDA Universe, CPHI Frankfurt, and PODD® Conference.

A Staple of Drug Delivery:
A Wide-Angle Look at Prefilled Syringes

In this issue, we return to one of our core topics – prefilled syringes. The very first issue of the magazine focused entirely on this topic and now, 20 years later, we are proud to bring you the biggest ONdrugDelivery ever! This edition comprises a spread of articles – covering novel devices, design, manufacturing, fill-finish, primary container materials and more – that together provide industry professionals with a comprehensive briefing document, all the very latest from this dynamic and growing sector.

To begin, we hear from **Stevanato Group** (Page 10) and **Ypsomed** (Page 18). In partnership with **SHL Medical, Stevanato Group** elucidate recent progress on the integration of the Molly® autoinjector with Alba® and Nexa® syringes. Ypsomed, meanwhile, details how its expert regulatory affairs team is integrated throughout the product lifecycle. Next, **Teva Pharmaceuticals** puts forward a more streamlined, human factors centred approach to device substitutability (Page 28).

Following that, we have a trio of articles on novel devices. **Owen Mumford** discusses its 1 mL safety syringe platform and companion reusable autoinjector (Page 36). **SMC** explores how its configurable Bios platform meets the challenges of today's drug formulations (Page 42). Lastly, **Terumo** presents its Immucise™ intradermal injection system as a modern approach to this difficult delivery method (Page 50).

Continuing the issue, we move the focus to design principles. Beginning this run of articles, **West Pharmaceutical Services** digs into a shift in thinking towards designing systems as a single whole, rather than as a group of different components (Page 56). **Sanner Group** then discusses software it has developed in partnership with **Pfizer** to model injection times and forecast the impact of ageing on device performance (Page 60). **Gerresheimer**, in collaboration with **SHL** and **Aptar Pharma**, contributes to the discussion with an article illustrating the value of collaboration between suppliers (Page 65).

A key aspect of any combination product is its component parts, which is the subject of the next run of articles. Kicking this section off, **RPK** discusses its approach to stamped metal parts for injection devices (Page 72), followed by **Wirthwein Medical** making the case for cyclo-olefin copolymer syringes as an alternative to glass (Page 78). **BAUMANN Medical** then considers how quality assurance needs to be embedded as a key part of company culture (Page 84). Lastly, **SCHOTT Pharma** presents its new syriQ BioPure® 5.5 mL glass syringes for large-volume subcutaneous delivery (page 91).

Once a device is designed, it must then be manufactured. Beginning our coverage of this topic, **IGS GeboJagema** talks about the integration of track-and-trace throughout its production process (Page 96). **Contexo** discusses high-speed manufacturing for assembling rigid needle shields (Page 102). Following this, **Grand River Aseptic Manufacturing** shifts the focus to the nuances of the fill-finish process (Page 108). Concluding the section, **Nolato** details its virtual factory approach (Page 114) and **BBS Automation** provides an overview of overall equipment effectiveness to (Page 118).

Rounding out this issue, **Springboard** presents a consideration of the current state and potential future of large-volume drug delivery (Page 124) and we hear from **Portal Instruments** in an exclusive interview with Steven Kaufmann (Page 130). Concluding the issue, **Mitsubishi Gas Chemical** provides an update on the latest studies done with its OXYCAPT™ multilayer vials at ultra-low temperatures (Page 134).

James Arnold
Production Editor

EDITORIAL:
James Arnold, Production Editor
james.arnold@ondrugdelivery.com
Subeditors:
Sarah Tomblin, Zoe Billyard

CREATIVE DESIGN:
Simon Smith, Head of Creative
simon.smith@ondrugdelivery.com

SUBSCRIPTIONS:
Print + Digital subscription:
£99/year + postage.
Digital Only subscription: free.
subscriptions@ondrugdelivery.com

ADVERTISING & SPONSORSHIP:
Guy Furness, Founder and Publisher
+44 1273 47 28 28
guy.furness@ondrugdelivery.com

ONdrugDelivery is published by
FURNESS PUBLISHING
The Candlemakers, West Street, Lewes,
East Sussex, BN7 2NZ, United Kingdom
Board Directors: **Guy Furness**, **Audrey Furness**
Registered in England: Company No 8348388
ISSN 2049-145X print / ISSN 2049-1468 pdf

The ONdrugDelivery logo is a registered trademark of Furness Publishing Ltd.

www.ondrugdelivery.com

RECYCLED
Paper made from recycled material
FSC® C022819
www.fsc.org

WORLD LAND TRUST™
www.carbonbalancedpaper.com

GOGREEN PLUS

ONdrugDelivery Magazine is printed sustainably by Newman Thomson Ltd, West Sussex, UK, using Forest Stewardship Council® certified recycled paper, vegetable-based inks, biodegradable laminates and carbon balanced materials offset via the World Land Trust™ following ISO140001 processes. ONdrugDelivery in print is sustainably shipped to events by DHL using GoGreen Plus whereby carbon insetting of at least 30% is achieved through the use of Sustainable Aviation Fuel (SAF), a biofuel substitute for traditional jet fuel, produced from renewable sources such as vegetable oils, animal fats, waste products, and agricultural crops. The magazine is mailed to individual readers outside the UK by DHL using GoGreen, which offsets 100% of CO_2 emissions.

Needle inner diameter increases reducing wall thickness

Our Special Thin-Wall (sTW) needle features an enlarged internal channel diameter, specifically designed to optimize the delivery of highly concentrated drugs without the need for larger needles.
Available in 25G, 27G, and 29G, it ensures compatibility with autoinjector device requirements while significantly enhancing the patient experience.

Visit us at CPHI Frankfurt
October 28 - 30, 2025
Booth 8.0H48 to learn more!

Stevanato Group

MANAGING COMPLEXITY, DELIVERING VALUE

stevanatogroup.com

PROVING THE DESIGN SPACE: ADVANCING THE DEVELOPMENT OF SYRINGE-DEVICE COMBINATIONS

Enrico Barichello of **Stevanato Group** and **Courtney Nicholas Sutton** of **SHL Medical** describe the innovative combination of the Molly® autoinjector with Alba® and Nexa® prefilled syringes, which addresses the need to streamline device approval by establishing comprehensive compatibility testing, collaboration between suppliers and validated solutions for drug delivery.

The increased use of biologic medicines and other therapeutic innovations for treating chronic and serious diseases has been accompanied by growing demand for at-home administration. Drug-device combination products, such as prefilled syringes (PFSs), autoinjectors and other drug delivery systems, have evolved to meet this demand. Although these products have been used for over two decades by patients and caregivers with great success, drug developers still seek to improve the patient experience. Reducing injection frequency is one such path to improvement. A key challenge to less frequent dosing is balancing drug characteristics – such as viscosity, which depends on drug concentration and the required dosage – with the performance capability of devices. In autoinjectors, for instance, achieving this balance can affect the injection time, which significantly contributes to the usability of the final drug delivery system.

Historically, the task of successfully integrating drug and device has fallen to the pharmaceutical companies developing these drugs. However, container closure system (CCS) and delivery device manufacturers play a critical role in supporting the development of these products. As such, there is an opportunity for manufacturers to collaborate and thus de-risk the pathway from investigational drug to approved product.

One approach is to determine the design space in advance with a thorough test strategy. Drug developers can then assess

Figure 1: Main steps in combination product development.

system compatibility with their drugs using robust data, giving them greater confidence during their formal primary container and autoinjector selection processes. The adoption of platform technologies via such a pathway can shorten time to clinic and, ultimately, time-to-market when applied across a pharmaceutical company's pipeline.

This article outlines market trends in patient-centric, self-administered injectable drugs and discusses how primary container and device technology developers can work together to de-risk the task of bringing such products to market.

MARKET TRENDS AND INNOVATION

As new therapies emerge, drug delivery methods evolve to improve patient outcomes. The current focus is on more effective, intuitive and convenient injectable drugs, including biologics and other high-value treatments that patients can self-administer at home, improving adherence and the overall treatment experience. Biologic therapies in particular are reshaping treatment landscapes due to advances in molecular biology and the rising prevalence of diseases in several dimensions, including chronic, immune-mediated, rare and oncological conditions. Other injectable drugs similarly benefit from innovations in patient-centric delivery systems.

"BIOLOGIC THERAPIES IN PARTICULAR ARE RESHAPING TREATMENT LANDSCAPES DUE TO ADVANCES IN MOLECULAR BIOLOGY AND THE RISING PREVALENCE OF DISEASES IN SEVERAL DIMENSIONS."

CHALLENGES OF DEVELOPING DRUG DELIVERY SYSTEMS

Drug delivery systems that integrate drugs, CCSs and delivery devices can be challenging to develop quickly and efficiently. These challenges arise because the usual development pathway has not yet been streamlined to meet the growing need for home-administered therapies (Figure 1). Pharmaceutical developers increasingly look beyond traditional vials and manual PFS injections in favour of autoinjector presentations, which are recognised as easier and safer for at-home use.

When developing systems such as PFSs and autoinjectors, it is essential to identify the critical parameters that could affect both product quality and patient safety. Some of the key factors manufacturers must address include:

Dimensional and Mechanical Compatibility

- Ensuring that PFSs fit reliably in the delivery device
- Reducing high reject rates during final assembly
- Preventing issues such as the rigid needle shield (RNS) not being removed or cap removal forces being too high
- Minimising variability in injection depth
- Maintaining favourable force and stress profiles to prevent device or syringe breakage.

Functionality and Usability

- Reducing the injection time of viscous formulations
- Avoiding incomplete injections, stalls or failures to start
- Reducing the risk of premature removal due to slow injection and confusion over whether the injection is complete.

Drug Stability

- Preventing protein aggregation caused by silicone oil
- Limiting interactions from multiple contact materials to control extractables and leachables
- Ensuring container closure integrity (e.g. avoiding plunger movement that could impact sterility or headspace conditions).

These challenges underscore the importance of robust performance and compatibility testing. Demonstrating that the drug, container and device function together reliably is critical for pharmaceutical companies to streamline regulatory approvals, reduce development risk and gain a competitive edge. Pharmaceutical companies require this evidence before selecting a solution for an individual drug, and it can be especially useful when choosing a platform solution to support their pipeline of products.

DE-RISKING THROUGH PLATFORM INTEGRATION

The collaboration between SHL Medical and Stevanato Group demonstrates a platform approach to de-risking. By combining the Molly® autoinjector with Alba® and Nexa® PFSs, the partners provide performance data across critical attributes – cap removal force, activation force, injection time, needle extension and dose accuracy.

This approach demonstrates robust compatibility across multiple formulations, reduces stock-keeping unit complexity and simplifies container-device integration. By using a platform-based solution with multiple options with regards to product performance, pharmaceutical partners can accommodate variability in pipeline products, reduce development and registration complexity, and accelerate time-to-market for high-value, home-administered injectable drugs.

BUILDING FROM A STRONG PLATFORM

For an autoinjector to function safely and effectively in patients' hands, multiple critical design factors must be considered during development. Among these, compatibility between the drug container and delivery device is paramount.

> "SHL MEDICAL AND STEVANATO GROUP BRING A LONG TRACK RECORD OF JOINTLY DEVELOPING COMMERCIALLY AVAILABLE DRUG DELIVERY SYSTEMS, WITH NINE PRODUCTS SUCCESSFULLY COMMERCIALISED IN A STEVANATO GROUP SYRINGE WITH THE MOLLY® AUTOINJECTOR TO DATE."

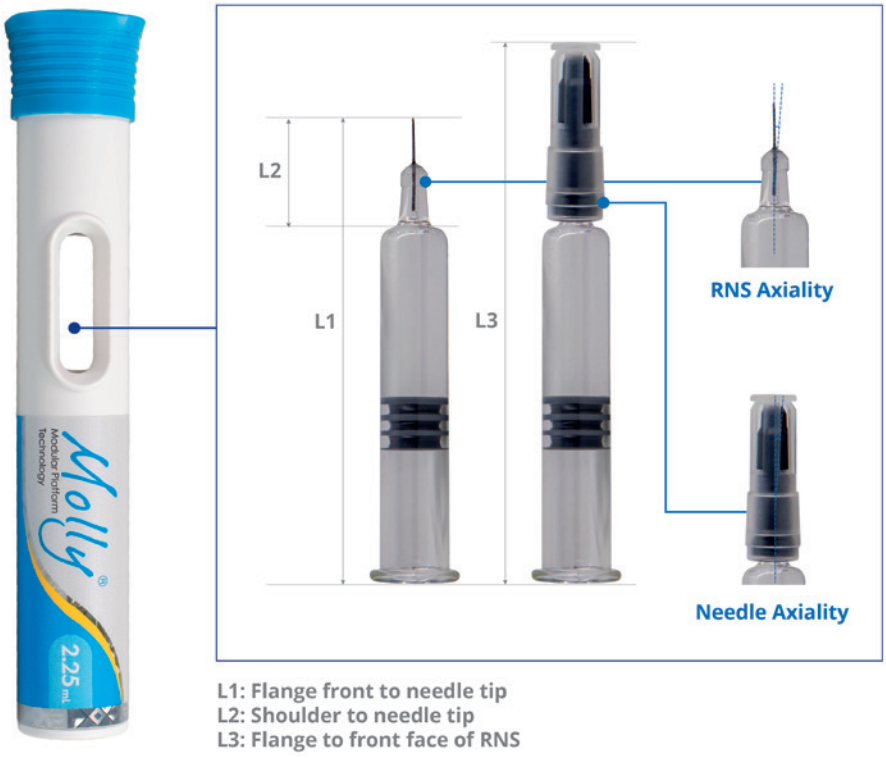


Figure 2: PFS critical interface dimensions for autoinjector compatibility.

SHL Medical and Stevanato Group bring a long track record of jointly developing commercially available drug delivery systems, with nine products successfully commercialised in a Stevanato Group syringe with the Molly® autoinjector to date. This experience allows them to apply pre-existing knowledge of container-device compatibility to new projects. This foundation provides a proven platform that mitigates risk and supports consistent performance across a range of formulations.

DIMENSIONAL FIT

Alba® and Nexa® PFSs can be reliably integrated into autoinjector platforms, including SHL Medical devices (Figure 2). Key design features include:

- Tightly controlled dimensional tolerances and optimised barrel geometries for consistent fit and secure assembly
- Carefully defined critical dimensional parameters – overall syringe length without closure (L1), length above the shoulder (L2) and total length including the RNS (L3) – to support accurate injection depth and proper engagement during device assembly
- Controlled axial alignment between the RNS and syringe barrel, ensuring repeatable performance across automated assembly processes.

These design elements collectively minimise mechanical risk, enhance assembly reliability and ensure that the syringe-device interface performs consistently – even under the stress of high-viscosity formulations.

FUNCTIONALITY

High-viscosity biologics present a significant challenge for self-injection devices. As viscosity increases, so does the force required to push the fluid through the needle, which can result in long injection times, incomplete injections, or delivery failures. Poorly designed devices may experience stalls, delayed injection start or premature removal, all of which can negatively impact patient experience, adherence and treatment outcomes.

The key challenge, therefore, is to demonstrate that the combination system can reliably deliver highly viscous biologics while maintaining acceptable injection forces and timing, ensuring accurate dose delivery and enabling easier self-administration.

Device	PFS	Needle	RNS	Plunger	Viscosities
2.25 mL Molly®	Alba® (Cross-Linked)	8 mm 27G sTW	RNS #1	PremiumCoat Plunger by Aptar Pharma (IL, US)	1, 15, 30, 50 cP
	Nexa® (Sprayed-On Silicone Oil)	8 mm 27G sTW	RNS #1		
		½" 27G sTW	RNS #2		
		½" 27G TW	RNS #2		
		½" 25G sTW	RNS #2		

Table 1: Study design configuration table.

To address this, Stevanato Group and SHL Medical conducted a rigorous compatibility study, illustrated in Table 1. The evaluation involved laboratory testing under simulated real-world conditions, including standard storage, clinical use and handling mishaps.

Study Design

Syringes were filled with placebo formulations spanning viscosities from 1 cP (water-like) to 50 cP (representing highly viscous biologics). These syringes were then incorporated into SHL Medical's Molly® autoinjector devices. Performance tests were conducted at room temperature (RT), after cold storage (2–8°C), and following a one-metre free-fall drop in compliance with ISO 11608-1.

Outcomes

The integrated system successfully administered formulations up to 50 cP viscosity with injection times increasing linearly and predictably in correlation with viscosity. As shown in Figure 3, the injection times in the optimised category Alba® and Nexa® 8 mm 27G sTW (special thin-wall), as well as Nexa 25G sTW ½" (12.7 mm), were recorded at under 20 seconds with high-viscosity solutions up to 50 cP. These results highlight the system's ability to maintain efficient delivery across a range of formulation viscosities while using sTW needle technology.

Alba® 27G sTW 8 mm demonstrated slightly higher injection time compared with Nexa® 27G sTW 8 mm, which can be attributed to the structure of its cross-linked silicone layer.

Figure 4 illustrates how injection times are reduced when using optimised needle gauges and lengths compared with the standard ½" 27G thin-wall configuration. The 8 mm 27G sTW configuration consistently delivered shorter injection times relative to the ½" 27G TW reference.

At low viscosity (1 cP), this reduction in injection time was modest, around 25% (data not shown). For higher viscosity formulations (15–50 cP), the 8 mm 27G sTW needle achieved greater reductions, approximately 45–55%. The 25G sTW,

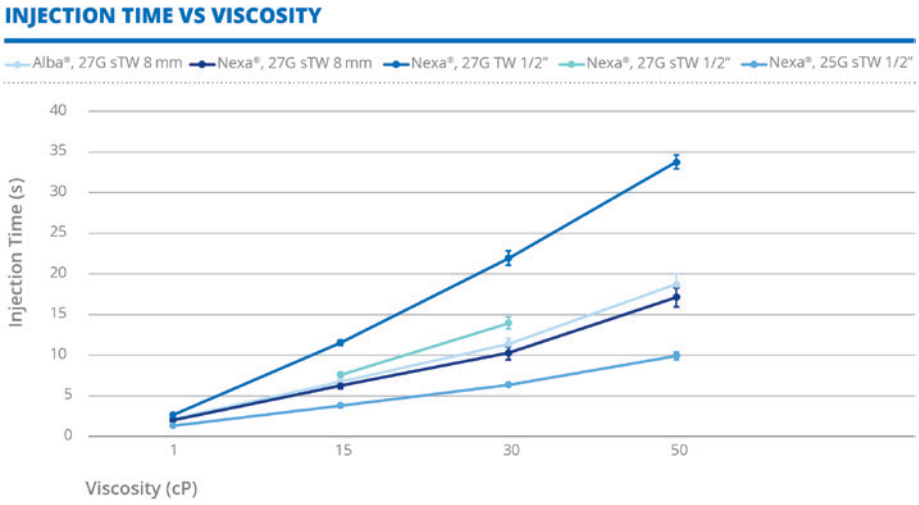


Figure 3: Injection time versus viscosity.

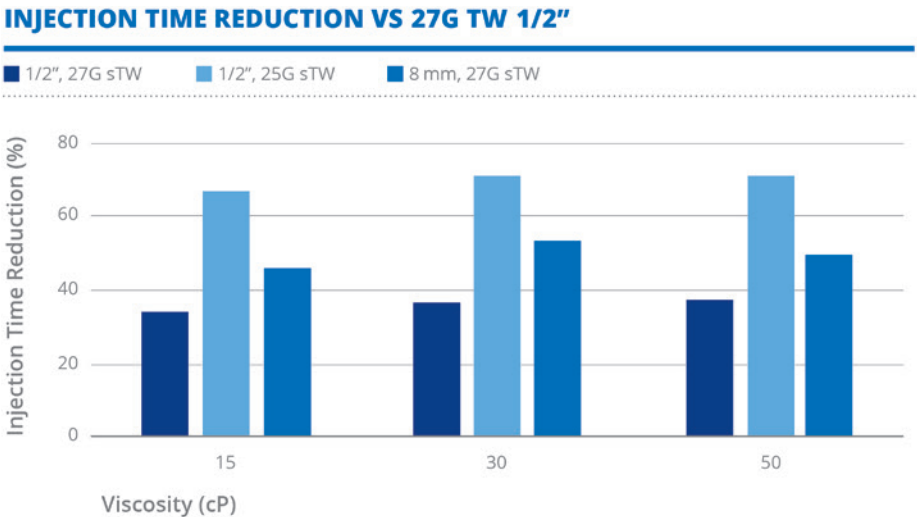


Figure 4: Injection time reduction relative to 27G TW ½". Note: For the 27G sTW categories at 50 cP, the values were derived from empirical measurements obtained in previous experimental studies.

with its larger inner diameter, allowed for more pronounced optimisation, with a reduction of 65–70%. The 27G sTW also demonstrated improvement, with injection time reductions of approximately 35%, attributable to the optimised inner diameter while maintaining the same external diameter. Collectively, these findings highlight the advantages of shorter, optimised needle designs in enhancing injection efficiency, particularly for viscous biologic formulations.

When uncapping an autoinjector, high removal forces may make it difficult for the user to remove the cap. If the removal force is too low, the cap may fall off prematurely during shipping or handling and cause problems for the end user.

The study measured autoinjector cap removal for two commercial RNSs with needle gauges of 27G and 25G (Figure 5):

- All values were below the industry-accepted upper specification limit (35 N)
- RNS #2 displayed lower values reflecting the different composition of the elastomer
- Variability was in a comparable range, irrespective of the RNS and needle gauge.

All tested performance attributes were within predefined specifications, confirming the robustness of the Molly® platform and Stevanato Group syringe.

Activation forces were syringe-independent and demonstrated stability

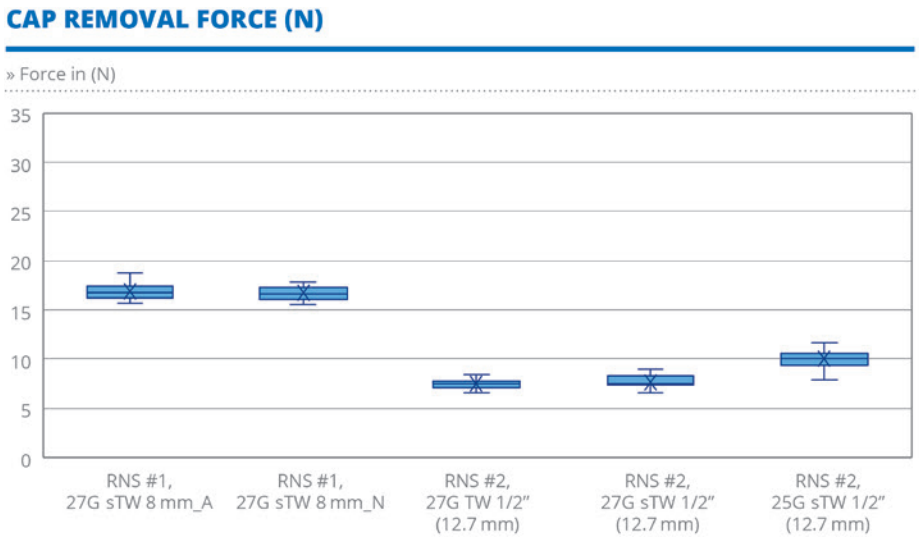


Figure 5: Cap removal force (N).

across the tested temperature conditions, confirming the robustness of device firing performance under varying environmental scenarios. Needle extension was reliable and met specifications across different needle types.

DRUG STABILITY

Maintaining drug stability within the primary container is a critical consideration in the development of drug delivery systems for biologics and other sensitive injectables. Conventional PFSs typically rely on silicone oil as a lubricant. However, silicone oil can interact with protein-based formulations, promoting aggregation or denaturation. These instabilities may adversely affect drug safety, efficacy and shelf life.

To mitigate these risks, Stevanato Group has developed the Alba® syringe platform, which incorporates an internal cross-linked silicone coating (Figure 6). This design substantially reduces the amount of free silicone oil in contact with the drug product, thereby lowering the risk of protein aggregation and particle formation. At the same time, the coating maintains the functional performance required for injection, including stable glide forces and consistent break-loose behaviour.

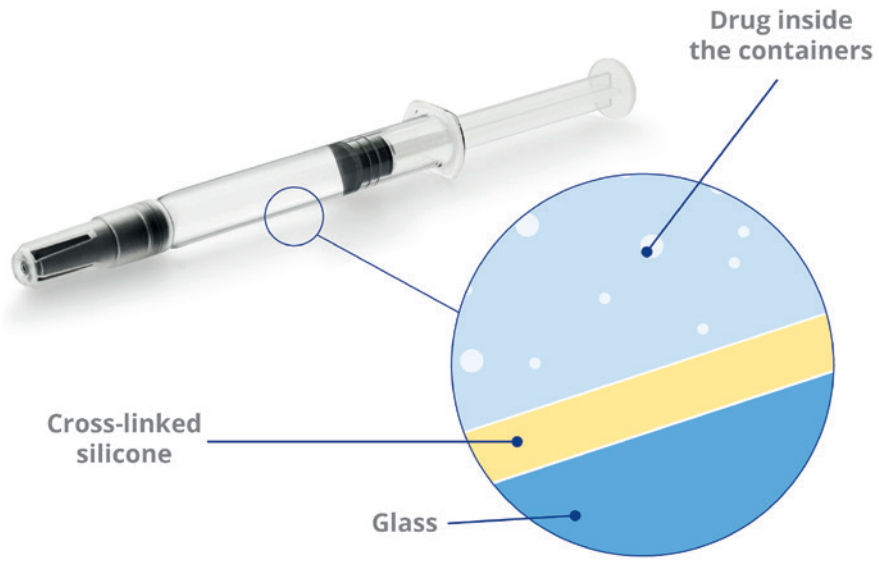


Figure 6: Alba® glass syringes: advanced coating for enhanced stability of sensitive drugs.

"STEVANATO GROUP AND SHL MEDICAL PROVIDE A COMPATIBLE CONTAINER-DEVICE PLATFORM THAT MAINTAINS CAP AND NEEDLE-SHIELD REMOVAL FORCES WITHIN A RANGE THAT ENSURES CLOSURE INTEGRITY BUT REMAINS OPERABLE WITHOUT EXCESSIVE PATIENT EFFORT."

The Alba® and Nexa® Syringe Platforms

The combination of Alba® and Nexa® syringes with SHL Medical's autoinjector technology provides a robust solution for sensitive biologics. The reduction in silicone-drug interactions contributes to consistent injection times and reliable dose delivery, supporting device performance across a wide range of formulations.

THE PATIENT PERSPECTIVE

For patients managing chronic conditions such as rheumatoid arthritis, multiple sclerosis or diabetes, ease of use and comfort are paramount if we are to expect them to remain adherent. Reduced dexterity complicates device operation, underscoring the importance of predictable actuation forces and manageable preparation steps.

Stevanato Group and SHL Medical provide a compatible container-device platform that maintains cap and needle-shield removal forces within a range that ensures closure integrity but remains operable without excessive patient effort. Activation force consistency assures dependable autoinjector function, reducing frustration and the risk of partial dosing. Injection times remain in a range that can be injected tolerably and simultaneously enable comfortable holding of the device against the skin to ensure a complete injection.

CONCLUSION

Compatibility tests on the Nexa® and Alba® 2.25 mL PFSs with the Molly® 2.25 mL autoinjector confirm full compatibility between these components. In combination, they reliably deliver high-viscosity biologics with predictable injection times, consistent mechanical performance and accurate dosing.

By using pre-verified solutions such as this, drug developers can simplify container and device selection, reduce development timelines and lower integration risks – accelerating time-to-market (Figure 7). The combined expertise of Stevanato Group and SHL Medical supports complex drug delivery projects, offering a practical, de-risked approach for pharmaceutical partners. Together, these platform-based solutions illustrate how co-development and integrated expertise can streamline the path to patient-centric biologic therapies.

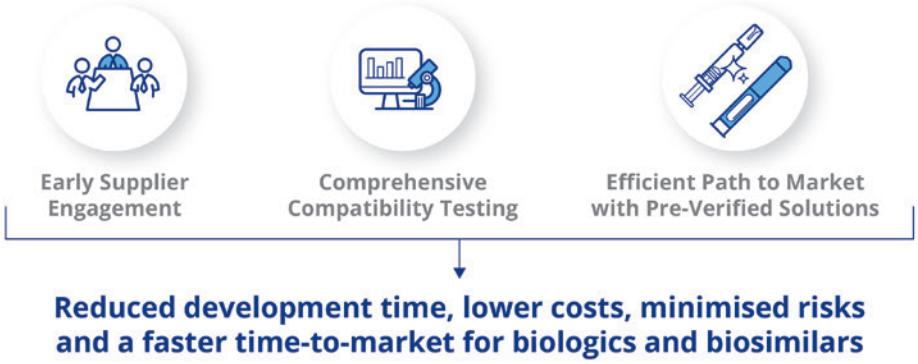


Figure 7: Risk mitigation strategies.

Enrico Barichello

Enrico Barichello, Product Manager, Syringe Platform, Stevanato Group, holds a master's degree in Industrial Engineering from the University of Padua (Italy). Since joining Stevanato Group in 2017, Mr Barichello has worked closely with cross-functional teams to define and execute the roadmap for new products, including the Alba® platform. Since 2023, he has overseen the glass syringe platform, and as of January 2025, he also manages the polymer syringe platform, driving innovation and growth across Stevanato Group's syringe portfolio.

E: enrico.barichello@stevanatogroup.com

Stevanato Group

Via Molinella 17, 35017 Piombino Dese, Padova, Italy

www.stevanatogroup.com

Courtney Nicholas Sutton

Courtney Nicholas Sutton is the Head of Portfolio Strategy at SHL Medical where she leads the strategy for current and future drug delivery systems. She previously worked for AstraZeneca and Regeneron, where she led device development teams, new technology evaluation, primary container development and drove the device strategy for early-stage molecules. Ms Sutton holds a Bachelor of Science in Biomedical Engineering from Rensselaer Polytechnic Institute (NY, US).

E: courtney.sutton@shl-medical.com

SHL Medical AG

Gubelstrasse 22, 6302 Zug, Switzerland

www.shl-medical.com

Figure 2, featuring 2.25 mL syringes with PremiumCoat® plungers, provided courtesy of Aptar Pharma.

D2F™
Direct To Fill

GLASS VIALS[1]

ready-to-use vials for aseptic pharmaceutical processing

Improved Total Cost of Ownership

costs for development, equipment, validation/audit, labor, energy/WFI, and storage are saved due to outsourcing of non-core activities (washing, depyrogenation, sterilization)

Fast Time to Market

tub and nest formats are compatible with main filling lines and implantation is support by an experienced cross-functional team

Tub and Nest Formats Prevent Glass-to-glass Contact

vials will keep their original strength, mechanical durability, and high cosmetic quality during transportation and handling operations

1. Powered by Stevanato Group EZ-fill® technology

NIPRO

pharmapackaging@nipro-group.com
www.nipro-group.com

THE COMPASS FOR INNOVATION: REGULATORY AFFAIRS AT YPSOMED

YPSOMED
SELFCARE SOLUTIONS

Stefanie Stark and **Sandra Schaerer-Lickova** of **Ypsomed** highlight how regulatory strategy enables ideas to become solutions, supports development through the product lifecycle and helps ensure that patients worldwide obtain safe and timely access.

If you pick up an Ypsomed injection pen or autoinjector, the first things you notice are likely the technology, design or ease of use. These are the tangible outcomes of Ypsomed's purpose – making self-care simpler and easier. What is less apparent, but equally essential, is the framework that allows such innovations to become reality. Every new idea must navigate a complex landscape of global regulatory requirements before it can safely reach patients. As such, regulatory affairs plays an indispensable role in enabling and supporting innovation.

Regulatory affairs is the part of drug delivery device development that rarely makes headlines. However, it is critical for ensuring that promising concepts don't remain sketches but develop into trusted solutions that meet the highest standards of safety and performance. If innovation is the visible face of delivery device development, regulatory affairs is the compass that keeps it on course.

YPSOMED'S CORE VALUES AND THEIR REGULATORY RELEVANCE

In today's drug delivery environment, the pace and complexity of development are ever increasing. The growth of innovative biologics, fast-emerging biosimilars and the rapid penetration of glucagon-like peptide-1 agonists (GLP-1s) into new treatments are just a few examples of how therapeutic areas, molecules and patient needs are all evolving.

"THE GROWTH OF INNOVATIVE BIOLOGICS, FAST-EMERGING BIOSIMILARS AND THE RAPID PENETRATION OF GLP-1S INTO NEW TREATMENTS ARE JUST A FEW EXAMPLES OF HOW THERAPEUTIC AREAS, MOLECULES AND PATIENT NEEDS ARE ALL EVOLVING."

There is a rising demand for devices that enable outpatient and, in particular, at-home care. This is partly driven by more engaged patients who expect user-friendly, sometimes connected solutions and a seamless user experience with their medication. Simultaneously, regulatory priorities are evolving in step with geopolitical shifts, creating a growing trend toward mandatory localisation, more rigorous documentation and enhanced supply chain visibility across different markets. In this rapidly evolving environment, Ypsomed's four strategic pillars serve as guiding principles (Figure 1):

- Commitment to innovation
- Standardised yet highly adaptable device platforms
- Operational excellence
- A deep sense of responsibility.

Figure 1: Ypsomed's core values and their regulatory relevance.

Over the past decades, these values have enabled Ypsomed to establish a mature and proactive approach to regulatory partnership. Rather than simply reacting to new health authority requirements or waiting for the new guidelines to emerge, Ypsomed integrates regulatory expertise as one of several guiding factors throughout development, from innovation to early platform design and throughout the product lifecycle.

This philosophy ensures that innovation is consistently aligned with both regulatory expectations and the evolving needs of patients and pharma partners. Innovation often starts with a new idea – as part of this, Ypsomed considers regulatory feasibility early on, alongside user needs and technical design, asking "Can this idea survive the scrutiny of global regulators?"

PLATFORMS SUPPORTED BY REGULATORY INSIGHT

Ypsomed's platform portfolio – ranging from injection pens to autoinjectors and patch injectors (Figure 2) – embodies both technical innovation and regulatory strength, enabling pharma partners to advance new therapies with greater speed and reduced risk. To stay ahead in a rapidly evolving healthcare environment, Ypsomed invests dedicated resources into

Figure 2: Ypsomed's comprehensive portfolio including pens, autoinjectors, patch injectors and digital health.

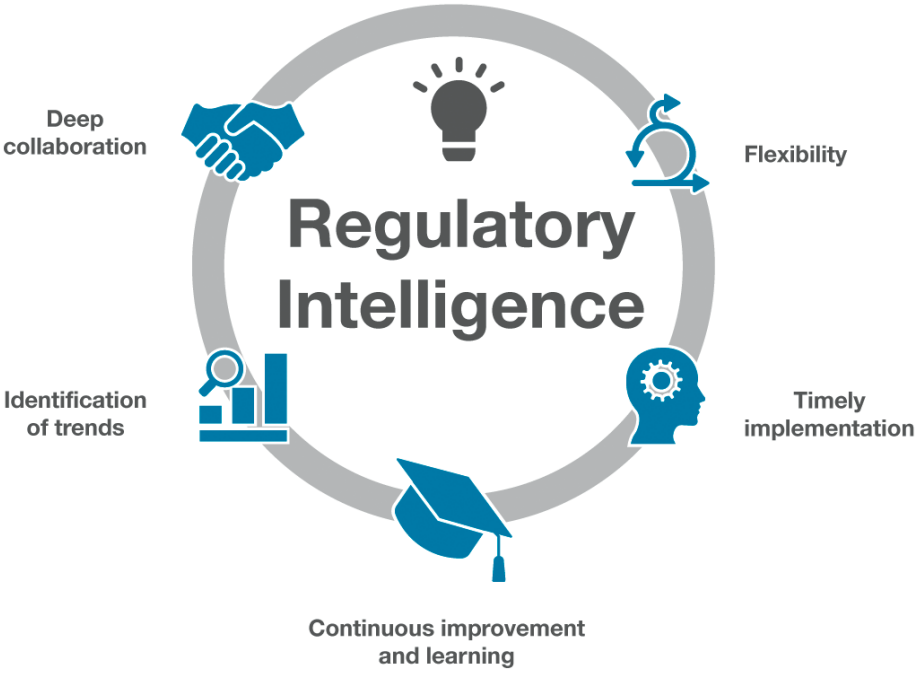


Figure 3: Regulatory intelligence as a differentiator.

regulatory intelligence (Figure 3). This "regulatory radar" enables the company to continuously monitor global frameworks, anticipate upcoming changes and assess their impact on its product portfolio.

To remain aligned with evolving regulatory expectations, Ypsomed follows a structured, cross-functional process focused on the following practices:

- **Proactive Engagement:** Ypsomed continuously monitors international regulatory trends, with contributions made to public consultations on draft laws and standards when opportunities arise.
- **Cross-Industry Insights:** Beyond medical devices, Ypsomed observes regulations in related sectors, such as pharmaceuticals and chemicals, to identify relevant best practices.
- **Early Requirement Analysis:** Ypsomed's teams provide timely insights into new and emerging regulations, ensuring that potential impacts are considered early in product development.
- **Continuous Adaptation of Processes:** Ypsomed's internal procedures are regularly updated to reflect the latest guidelines and regulatory requirements.

"THIS "REGULATORY RADAR" ENABLES THE COMPANY TO CONTINUOUSLY MONITOR GLOBAL FRAMEWORKS, ANTICIPATE UPCOMING CHANGES AND ASSESS THEIR IMPACT ON ITS PRODUCT PORTFOLIO."

A key strength of Ypsomed's strategy is the active participation of subject matter experts in international standardisation committees and industry associations. This involvement enables the company not only to contribute its expertise, such as in the enhancement of the ISO 11608 series of regulations for needle-based injection systems, but also to anticipate emerging priorities, such as user-centric design and sustainability, well before they become formal requirements.

For example, when health authorities began placing greater emphasis on human factors data, Ypsomed was able to respond proactively. Its regulatory affairs and usability engineering teams co-developed study protocols that directly addressed both US FDA and EMA expectations. This ability to adapt drug delivery platforms in real time demonstrates how regulatory intelligence can support compliance while fostering innovation and market readiness.

INNOVATION BEHIND TECHNOLOGY: PLATFORMS THAT EVOLVE

At Ypsomed, innovation is not just about developing new devices or technologies. It is defined by how drug delivery solutions integrate with evolving therapies, regulatory frameworks and the reality of real-world applications. The shift from hospitals to the home illustrates this perfectly. Patients now expect devices that are simple, easy to use, reliable and increasingly connected – a demand that is reshaping both technical and regulatory pathways.

Ypsomed's innovation strategy is closely tied to its configurable, standardised platform technologies for injection pens, autoinjectors and patch injectors. Each new project builds on a foundation of proven expertise, transferring learnings and regulatory insights from previous projects. This platform approach ensures that when therapeutic requirement changes, such as high viscosities or large volumes, devices can be adapted without unnecessary compliance or development risk. Ypsomed engineers platform modularity from the outset with flexibility in mind, supported by regulatory insight, making subsequent adaptation and scaling far more straightforward.

THE POWER OF PLATFORM MODULARITY

As platform components are already characterised and validated in manufacturing, new projects can focus on therapy-specific adaptations rather than re-proving fundamentals, accelerating the development process. A combination of proven platforms and robust technical documentation enables regulatory affairs, together with the project team and quality colleagues, to support or manage multiple submissions for drug-device combination products and medical devices in parallel. Ypsomed's platform documentation is maintained as "living regulatory

"A COMBINATION OF PROVEN PLATFORMS AND ROBUST TECHNICAL DOCUMENTATION ENABLES REGULATORY AFFAIRS, TOGETHER WITH THE PROJECT TEAM AND QUALITY COLLEAGUES, TO SUPPORT OR MANAGE MULTIPLE SUBMISSIONS FOR DRUG-DEVICE COMBINATION PRODUCTS AND MEDICAL DEVICES IN PARALLEL."

files", being continuously updated with authority feedback and systematic voice-of-customer input.

Overall, Ypsomed's innovation process combines collaboration, multidisciplinary expertise and transparency. With regulatory professionals embedded from the earliest concept stage, new developments are de-risked, regulatory strategies are strengthened and submissions become more predictable and timely worldwide.

FROM INNOVATION AND DEVELOPMENT TO GLOBAL REGULATORY READINESS

Ypsomed manages the transition from innovation to product development with precision, guided by its certified quality management system and global regulatory frameworks. Aside from regulatory affairs specialists embedded across the organisation, several functions contribute to a compliant and efficient pathway from concept to market:

- **R&D and Engineering:** Align device concepts with regulatory pathways from the earliest stages.
- **Human Factors & Usability:** Design and conduct formative and summative studies that meet the expectations of regulatory authorities.
- **Risk Management:** Define and integrate risk mitigation measures into documentation and processes from the very beginning.
- **Manufacturing and Supply Chain:** Anticipate requirements for scale-up, localisation and traceability.
- **Marketing and Communications:** Align labelling, claims and global launch strategies.
- **Business Development:** Translate regulatory insights into value propositions, partner strategies and market-entry opportunities.

Throughout the development process, comprehensive documentation is prepared to ensure that all safety and performance requirements are consistently fulfilled. These records provide clear traceability to supporting test data and risk analyses, while also taking regional regulatory expectations into account.

Anticipating Authority Expectations

With decades of experience across drug-device combination products and medical devices, Ypsomed applies its deep regulatory expertise to anticipate authority expectations, identify trends and resolve contradictions before they impact partner projects. In this way, Ypsomed ensures that development is not only innovative and efficient, but also submission-ready and highly standardised, enabling timely approvals and reliable market access.

Lifecycle Confidence Through Regulatory Continuity

Regulatory responsibilities do not end with approval; they extend throughout the entire product lifecycle (Figure 4).

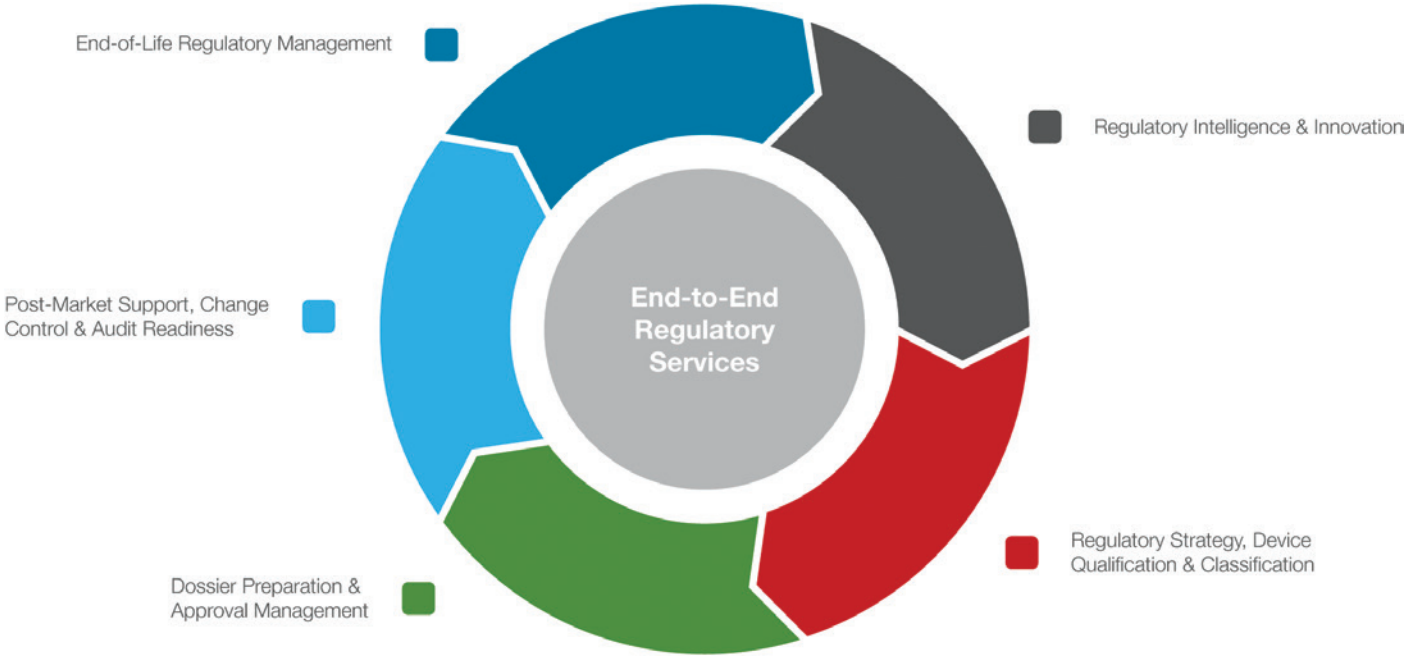


Figure 4: From innovation to end-of-life – regulatory leadership at every step.

Ypsomed's lifecycle management approach is driven by robust and agile change-control processes, rigorous updates and surveillance programmes, and a commitment to continuous improvement. By taking responsibility for ongoing file maintenance, implementing technical updates in line with evolving requirements and managing interactions with health authorities, Ypsomed reduces the regulatory workload for its partners and helps to ensure smooth, compliant market continuity.

One of Ypsomed's strengths is its ability to co-ordinate multi-regional launches, either in parallel or in sequence, in the US, EU, China, India, Japan and other markets (Figure 5). Local regulatory teams, complemented by manufacturing and supply chain hubs, such as the company's strategic presence in China, ensure region-specific requirements are met and that local market expectations are addressed.

To further strengthen this global footprint, Ypsomed is also preparing to establish a physical presence in the US. This step carries strategic importance by:

- Placing Ypsomed closer to its customers
- Enabling faster response to market expectations
- Mitigating the impact of regional factors, such as pricing pressures and tax frameworks.

Together with its European and Asian sites, a US hub will complete Ypsomed's global network – ensuring agile, compliant and cost-efficient access to all major healthcare markets.

Embedding Evolving Requirements

Ypsomed seamlessly embeds changes to regulations and requirements into its platform portfolio, from revised technical standards to growing sustainability demands. In parallel, a continuous stream of global submissions is supported by an ongoing and structured dialogue with health authorities, enabling the company to remain aligned with current expectations and to anticipate forthcoming regulatory developments.

Managing End-of-Life Responsibility

The end of a product's lifecycle is not just discontinuation. Regulatory compliance and partner obligations must remain aligned until final market withdrawal. Ypsomed's regulatory affairs experts ensure that documentation, labelling and authority requirements are maintained, providing predictability and transparency. In this way, Ypsomed's regulatory involvement spans the entire journey of a product, from innovation and development through global submissions and market access to end of life, ensuring consistent regulatory excellence at every stage.

"YPSOMED REDUCES THE REGULATORY WORKLOAD FOR ITS PARTNERS AND HELPS TO ENSURE SMOOTH, COMPLIANT MARKET CONTINUITY."

WHAT SETS YPSOMED APART

Ypsomed's strengths in regulatory expertise stem not from a single process or capability, but from a unique combination of enduring factors:

- Deep collaboration with pharma partners
- High submission volume support, giving nuanced insight into how regulatory trends are enforced in practice
- Timely implementation of new requirements
- Organisational agility based on continuous improvement and learning.

This readiness, built on core values of innovation, platform flexibility, operational rigor and a genuine sense of responsibility, enables Ypsomed to anticipate the needs of both regulatory authorities and partners, providing a strong foundation for building long-term trust and value.

Figure 5: Ypsomed's global footprint.

TURNING COMPLEXITY INTO OPPORTUNITY

In a world where drug delivery technology, regulatory expectations and patient needs are all in continuous motion, success is not guaranteed by simple compliance. It requires anticipation, adaptation and leadership. For Ypsomed, this means embedding regulatory excellence at every stage, from the very first brainstorm of a new idea through project development and market launch to end of life.

With its regulatory compass, Ypsomed transforms difficulty into opportunity. With decades of expertise, trusted services and a platform-based approach, the company steers through complex issues to ensure that products are market-ready, compliant and aligned with future trends on the horizon. By embedding regulatory excellence at every stage, Ypsomed supports improved patient outcomes and delivers long-term value for partners.

Stefanie Stark

Stefanie Stark is Head of Regulatory Affairs for Pen and Autoinjectors at Ypsomed. Since joining the company in 2021, she has led a team of regulatory professionals responsible for guiding drug device combination products and medical devices from early innovation through to regulatory strategy, global submissions and lifecycle management in close collaboration with pharmaceutical partners. With more than 16 years of experience in regulatory affairs, she has held senior roles focused on international registrations as well as project and portfolio management. Ms Stark holds a diploma in Business Administration, is a certified medical documentalist and a trained nurse.

E: stefanie.stark@ypsomed.com

Sandra Schaerer-Lickova

Sandra Schaerer-Lickova is Regulatory Affairs Manager at Ypsomed, where she supports strategic regulatory projects for pen injectors and drug-device combination products. She started her regulatory career in the pharmaceutical sector, preparing common technical documents and managing medicinal product submissions, before expanding into medical technology. Her expertise spans EU MDR CE marking, Article 117 assessments and US FDA CFR regulations for medical devices and combination products, alongside registrations in global markets, including the US, China, Korea, Brazil and Russia. With a background in chemistry and bioprocess engineering, she now focuses on lifecycle management, technical documentation and guiding cross-functional teams to ensure regulatory compliance and successful market access.

E: sandra.schaerer@ypsomed.com

Ypsomed Delivery Systems
Brunnmattstrasse 6, 3401 Burgdorf, Switzerland
www.ypsomed.com

15TH Annual PODD®

PARTNERSHIP OPPORTUNITIES IN DRUG DELIVERY

October 27-28, 2025 • Westin Copley Place, Boston, MA

Covering Cutting-Edge Scientific and Business Trends

Keynotes and Co-Chairs

GLP-1 Keynote

Dr Lotte Bjerre Knudsen
Novo Nordisk

Endogenous Delivery Zeitgeist

Dr Mansoor Amiji
Northeastern University

Annual Keynote

Dr Robert Langer
MIT

Patient Keynote

Jimi Olaghere
Patient Advocate,
Lived-Experience Expert

Co-Chair

Dr Sherri Biondi
AstraZeneca

Co-Chair

Dr Clare Beddoes
Cambridge Design Partnership

Co-Chair

Dr Beate Bittner
Roche

Program Features

- 1000+ Attendees from Pharma, Biotech, Drug Delivery, Academia, Investors and More
- 10 Tracks Covering a Wide Range of Drug Delivery Technologies
- Partnering Opportunities including One-on-One Scheduled Meetings
- And Much More!

PODDConference.com
20% Off with Code ONDD20

Count on performance.

Over 40 years of expertise dedicated to making selfcare simpler and easier.

- More than 70 combination products in 15 therapeutic areas, covering both originators and biosimilars.
- Improving the quality of life of over 8 million people around the globe.
- Over 130 large, medium and small biopharma and biotech customers worldwide.
- Scalable business models for clinical trials and full-scale production.
- 100% electricity from renewable sources since 2021.

For more information visit www.ypsomed.com or scan the QR code

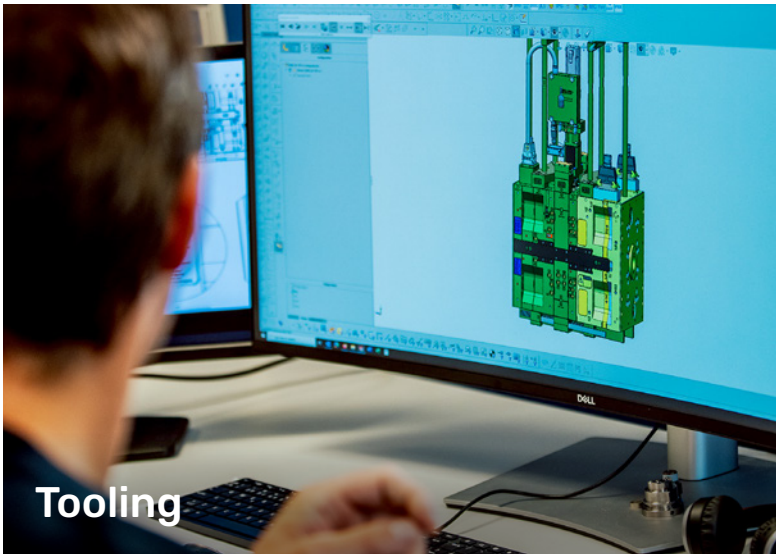
Ypsomed AG // Brunnmattstrasse 6 // 3401 Burgdorf // Switzerland //
info@ypsomed.com // www.ypsomed.com // +41 34 424 41 11

YPSOMED SELFCARE SOLUTIONS

10427753-MSTR-en/V04

MGS Healthcare Manufacturing

Bridging the Gap Between Imagination and Realization

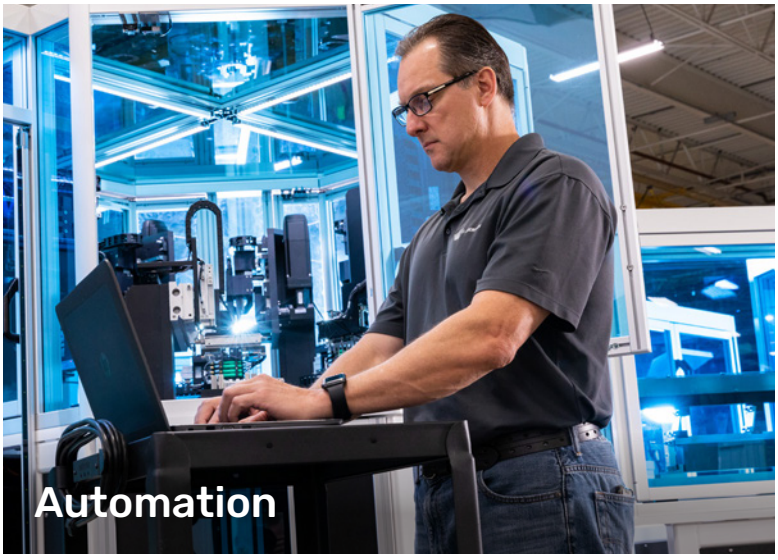


Driving Speed-to-Market from Ideation to Delivery

Global pharmaceutical companies turn to MGS to transform their most pressing challenges into innovations that improve lives. From first sketch to final solution, our passionate people collaborate to deliver with speed, precision and confidence. We help Pharma innovators seamlessly navigate the increasing demands of regulatory compliance and transform concepts into market-ready, complex drug delivery devices.

We’re more than consultants. More than manufacturers.

We’re end-to-end partners driven by technology leadership and vertically integrated expertise.



Global Healthcare CDMO

Discover Your Competitive Advantage at mgsmfg.com

ALTERNATIVE APPROACH FOR DEVICE SUBSTITUTABILITY: HUMAN FACTORS STUDIES FOR GENERIC AND BIOSIMILAR PRODUCTS

Carrie O'Donel, **Henri Akouka** and **Mark DeStefano** of **Teva Pharmaceuticals**, along with **Leslie Sanchez-Torres**, discuss the shortcomings of current comparative use approaches to determining substitutability of devices for generics and biosimilars and propose an alternative approach to human factors studies based on long-standing methodologies that has the potential to unlock innovation and improve the user experience for patients.

"IT SEEMS COUNTERPRODUCTIVE TO REPLICATE A DESIGN THAT DOES NOT REFLECT CURRENT BEST PRACTICES, ESPECIALLY WHEN THERE ARE OPPORTUNITIES TO IMPROVE THE USER EXPERIENCE AND REDUCE RISKS WITHOUT CREATING AN INCREASE IN USE ERRORS."

As developers of generic and biosimilar combination products, Teva frequently encounters questions around device substitutability – specifically, whether to replicate the reference device exactly or take the opportunity to improve upon it. These discussions often centre on the trade-offs between strict replication and thoughtful innovation, especially when the original device may not be optimal for patient use.

Simply copying a reference device – regardless of its complexity or usability – can result in products that are more difficult to manufacture, less reliable and prone to the same user errors already identified in the original design. This approach can unintentionally carry forward known issues, rather than address them.

It seems counterproductive to replicate a design that does not reflect current best practices, especially when there are opportunities to improve the user experience and reduce risks without creating an increase in use errors. The idea that patients cannot adapt to improved device interfaces is outdated. In fact, this assumption can slow down the delivery of more affordable medicines to patients who need them.

That is why exploring a shift away from the current comparative use human factors (CUHF) model is warranted. Instead, this article proposes using more traditional human factors methods, such as early usability testing and summative validation principles, to demonstrate substitutability. To that end, the authors embarked on a device usability study designed using ANSI/AAMI HE75, Faulkner and US FDA guidance principles to show that device substitutability across various device types was possible without an increase in user errors. This approach better supports innovation, patient safety and faster access to high-quality, cost-effective therapies.

STREAMLINING HUMAN FACTORS FOR DEVICE SUBSTITUTABILITY

The FDA's recommended CUHF study methodology guidance for demonstrating device substitutability in generic and biosimilar combination products brings notable challenges to device development efforts. The study method complexity, inconsistencies and time-intensive nature often overshadow the benefits it aims to deliver. Considering current human factors practices, this approach may not be the optimal path for proving therapeutic equivalence.

The fundamental goal of substitutability is clear – to enable patients to use alternative devices for generic medications without an unacceptable increase in use errors, thereby expanding access to affordable treatments. However, duplicating device design and functionality features – a strategy often chosen for ease of FDA approval – can delay patient access and stifle innovation and improved standards of care.

CUHF studies rely on "clinical non-inferiority" methods to demonstrate sameness, but it is worth asking – can more traditional human factors methodologies deliver the same results with less complexity, faster timelines and more opportunities to optimise usability and safety? The study outlined here dives deeper into this question, presenting real-world insights from actual device testing, under real-world conditions, using alternative yet well-established methodologies.

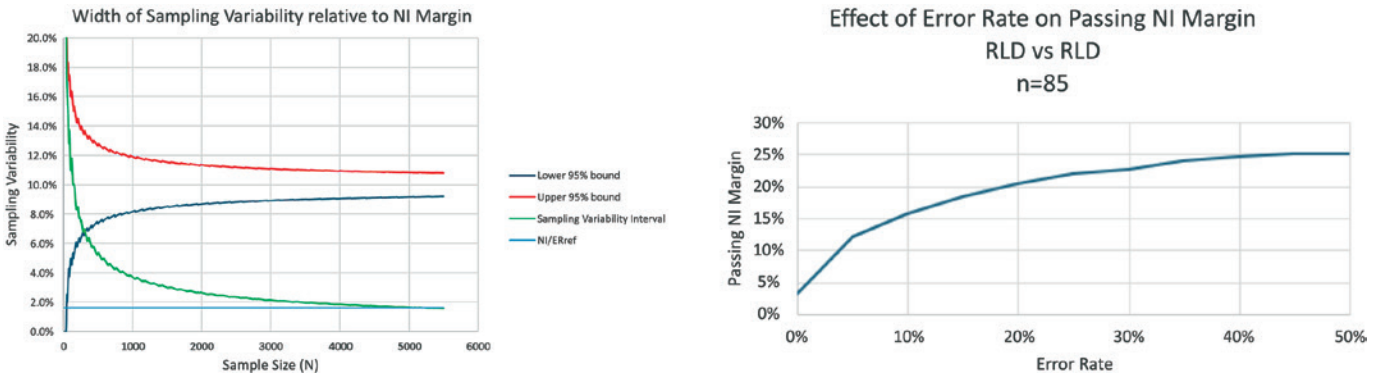


Figure 1: Contribution of sample size to sampling variability.

Developers of 505(j) generics and 351(k) biosimilars have a shared mission – to provide patients with affordable treatments quickly. To achieve this, human factors assessments are essential – not just for compliance, but for minimising use errors, reducing user risk and improving the overall user experience where possible, while aligning with established standards, such as IEC 62366-1:2015/AMD1:2020.

Abbreviated approval pathways created under the Hatch-Waxman amendments prioritise therapeutic equivalence, requiring generic drugs to match the clinical effect and safety profile of their reference-listed drug (RLD). Similarly, biosimilars seeking interchangeability must demonstrate that they are "highly similar" to their reference drug product without compromising safety or usability. Human factors play a critical role in ensuring that the substitution of these products does not lead to unacceptable use errors or additional training or intervention requirements – a pivotal concern for both regulators and developers.

RETHINKING COMPARATIVE USE GUIDANCE

The goal of developing a substitutable drug-device combination product (DDCP) – and the FDA's evaluation of such – is not "sameness" of user interface, rather, it is safe and effective use without healthcare provider intervention or patient/user training. While the comparative use guidance emphasises user interface "sameness" to minimise critical risks, this approach can pose barriers to innovation, propagate antiquated and problematic device designs and limit usability enhancements that are beneficial to patients.

CUHF study designs employ a clinical non-inferiority model, which is better suited for objective measures and placebo controls. In contrast, human factors and the sources of use errors involve subjective complexities that are difficult to address through statistical comparisons alone. For example, negative transfer – where prior mental models interfere with understanding new devices – can introduce use errors that are not detectable through traditional objective methods.

By applying rigid clinical frameworks to human factors validation, there is a risk of complicating approval processes for safe, effective products and delaying patient access to affordable treatments. For example, a human factors study requires 85 users to pass a non-inferiority (NI) margin of 16% at 95% power – a large sample size. Sampling variability often dominates the NI margin, leading to a high false negative rate. Adapting continuous data methods to small sample sizes requires a larger NI margin or more participants, as shown in Figure 1, which illustrates the relationship of sampling variability to the NI margin, as well as the ratio of the NI margin to the reference error rate (NI/ERref).

> "HUMAN FACTORS AND THE SOURCES OF USE ERRORS INVOLVE SUBJECTIVE COMPLEXITIES THAT ARE DIFFICULT TO ADDRESS THROUGH STATISTICAL COMPARISONS ALONE."

Alternative methodologies, such as the human factors validation study presented here, offer a promising solution. Grounded in human factors best practices such as IEC 62366-1 and ISO 14971, this approach emphasises use specifications for devices targeting users familiar with reference product interfaces. It includes use-related risk assessments (URRAs) to identify tasks prone to negative transfer and evaluates resulting use errors without relying on placebo-controlled statistical analyses. This streamlined design aligns with FDA human factors expertise while addressing mental model challenges in users experienced with the reference product (RP).

This alternative study design also considers how use errors evolve over time. Errors not caused by negative transfer are often resolved through repeated use, though the tolerance for learning curves depends on the treatment's safety profile. Emergency-use products demand greater scrutiny and lower tolerance for learning through experience, while chronic treatment products may allow for some user adaptation. By leveraging expanded risk mitigation strategies that go beyond minimising design differences, this innovative human factors validation framework paves the way for safer, more accessible combination products, empowering developers, regulators and patients alike.

INNOVATIVE STUDY DESIGN FOR SUBSTITUTABLE DDCPs

The proposed human factors study design for substitutable DDCPs aligns with the framework outlined in the FDA's Complete Submission Guidance. This study focused on participants experienced

with four-step autoinjectors, three-step autoinjectors or prefilled syringes (PFSs) for various conditions, assessing their ability to complete a dose using a two-step autoinjector, as shown in Table 1, without prior training or intervention during first-time use and simulated realistic user scenarios to validate DDCP usability.

A key feature of the study scenario involved representing the real-world situation where a pharmacist would substitute the RP for the DDCP without the knowledge of the user. Unlike the CUHF study model, which primarily compares the RP and DDCP in controlled settings, this study design emphasises patient-centric usability. Study recruitment criteria mirrored the intended RP product use specification, ensuring that participants had established prior experience with the RP interface. To replicate home-use environments, the study setting was designed for familiarity and comfort, reflecting standard human factors assessment practices.

PROACTIVE RISK ASSESSMENT AND TASK ANALYSIS

A risk evaluation was conducted on the device using use failure mode and effects analysis (uFMEA) and threshold analysis (TA) methodologies. TA identified "other design differences" in task analysis and physical comparison, underscoring the practical application of human factors validation as per comparative use guidance. A labelling comparison was not conducted since the focus of these analyses was on the functional usability aspects of the device user interface.

The URRA pinpointed critical tasks prone to errors stemming from design differences. The URRA should consider all conceivable use errors and mitigate them as much as possible. However, this is also accomplished through improving the user interface of the substitutable DDCP, such as by reducing the number of critical tasks, as was done in this study. The critical tasks were defined for this study in Table 2, each representing actions essential to dose completion.

These tasks were evaluated for potential use errors caused by negative transfer. Additionally, all user challenges observed

Description	Physical Presentation*	Example
3-step Autoinjector	Rounded body, button on back	
4-Step Autoinjector 1	Rounded body, button on back, locking mechanism, twist-off cap	
4-Step Autoinjector 2	Rounded body, two caps to remove prior to activation, button on back	
PFS with NSS	1 mL long syringe, passive NSS	
2-step Autoinjector (proposed substitutable DDCP)	Rounded body with squared edges, single cap	

Table 1: Physical attributes of study reference products (*attributes that would typically be considered as other differences).

Step	Evaluation Type	Success Criteria
Prepare/visually inspect the autoinjector for physical damages, medication colour/quality	Observation of performance	Inspects the device contents for quality
Inject/uncap the autoinjector	Observation of performance	Pulls the cap off the device
Inject/place the autoinjector against the skin	Observation of performance	Places the device against the skin at a 90° angle
Inject/press and hold down the autoinjector against the skin until a click is heard	Observation of performance	Firmly presses the device down against the skin
	Root cause investigation/ post-test interview	Reports: Hearing a click, feeling device actuation, seeing the plunger start movement, indication that the injection has begun
Inject/continue to hold down the autoinjector until a second click is heard and a blue indicator is seen in the fill window	Observation of performance	Delivers a full dose
	Root cause investigation/ post-test interview	Reports: Hearing a second click, feeling end of injection, seeing the blue indicator in the viewing window. Or waiting 15 sec after start of injection, indication that the injection is complete.

Table 2: Two-step autoinjector critical tasks with success criteria.

$$\textit{(Design Verification)}\ n = \frac{\ln(1-C)}{\ln(R)} = \frac{\ln(1-0.95)}{\ln(0.95)} = 59$$

$$\textit{(Human Factors Validation)}\ n = \frac{\ln(1-C)}{\ln(R)} = \frac{\ln(1-0.95)}{\ln(0.86)} = 20$$

Figure 2: Attribute design verification equations.

during the simulated use scenario were analysed to identify root causes, regardless of their classification as critical tasks.

Determining an appropriate sample size is critical to ensure robust human factors validation. Attribute design verification equations and methodologies, such as those outlined by Faulkner, guided the sample size selection (Figure 2). The sample size for this study was selected to optimise for observation of use errors based on the risk profile of the product under evaluation. For example, a sample size of 59 with zero observed failures ensures 95% reliability with 95% confidence. Alternative reliability targets were recommended based on each product's benefit-risk profile, with examples provided in Table 3.

	Design Verification		Design Validation	
Primary Endpoint	Confidence/ Reliability	Attribute Sample Size	Error rate sensitivity	HF Sample Size for primary endpoint
Complete Dose (maintenance/ preventive use)	95%/95%	59	14-18%	15-20
Needle Safety Activation and Override	95%/99%	299	6-14%	20-50

Table 3: Sample size examples for objective and subjective measures.

For maintenance treatments, a success rate of 82–86% can meet benefit-risk thresholds even with an observed error rate of 14–18% (95% confidence level) using 15–20 subjects successfully completing the dose. Here, understanding whether primary endpoint failures are attributable to negative transfer is essential, and the subjective nature of use errors and varied root causes underline the importance of targeted risk mitigation.

This study used a sample size of 20 users per group, aligning with industry standards, to scale human factors validation proportional to the product's safety profile. The goal was to evaluate use errors until an increased sample size yielded diminishing returns, ensuring validation remained practical and efficient.

STUDY RESULTS ON DEVICE SUBSTITUTABILITY

The findings from this four-part study revealed promising insights into device substitutability. Experienced users of all RP devices demonstrated a successful transition to alternative devices incorporating "other design differences" with minimal use errors and no need for prior training or intervention, when the user's RP was substituted with an alternate device by the pharmacist. These results highlight the feasibility of designing devices that

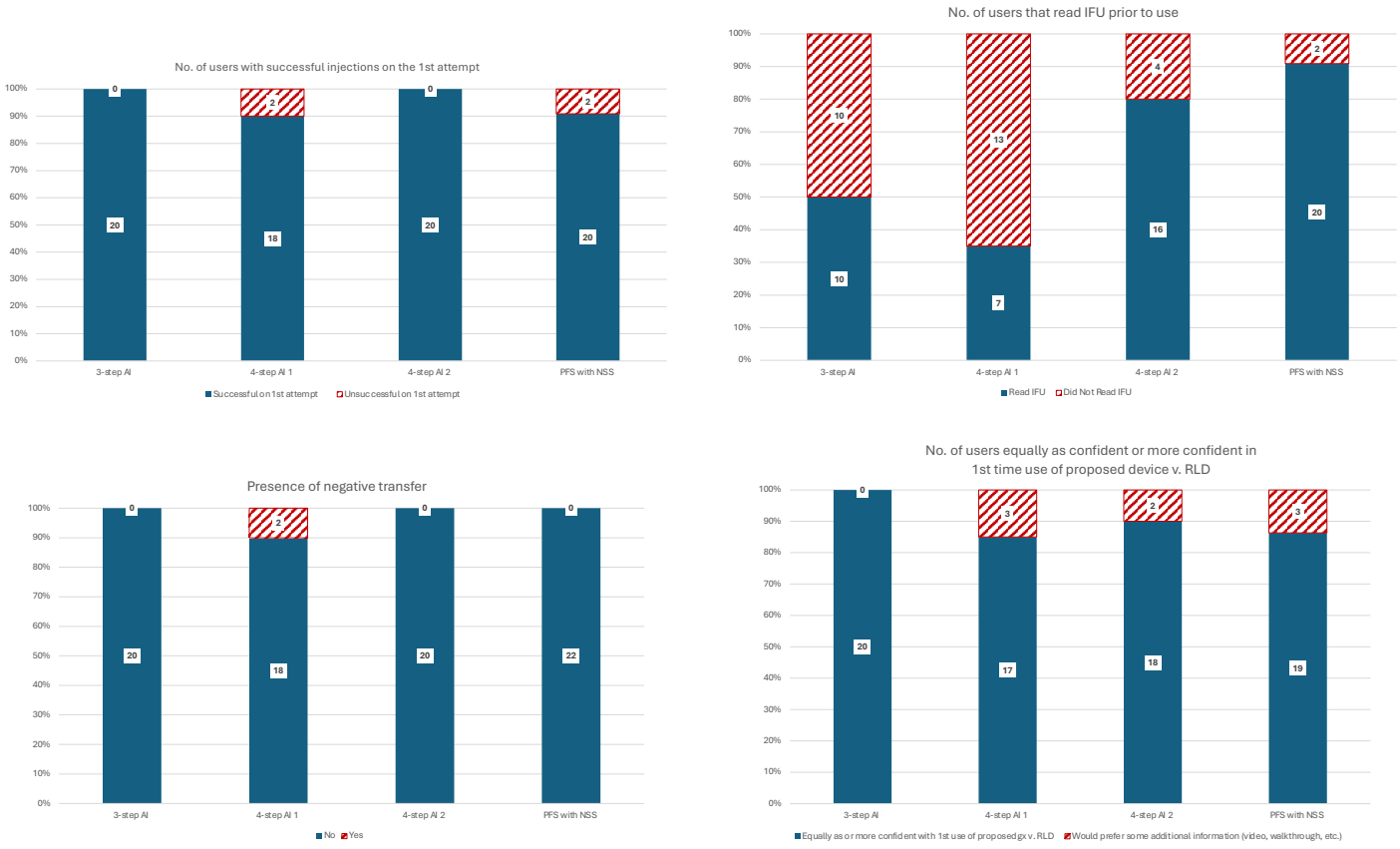


Figure 3: Summary results.

maintain usability while offering design flexibility. The data summary is illustrated in Figure 3, emphasising key metrics that validate this methodology as a practical alternative to CUHF studies.

The results are quite clear. Unlike the CUHF study model, which emphasises error rate comparisons and often struggles with statistical complexities surrounding subjective outcomes, this study took a more pragmatic approach. By shifting the focus to identify sources of negative transfer and defining acceptable error rates tailored to the product's safety profile, it provides a more targeted and efficient framework for human factors evaluations.

Of note, the two observed failures with the four-step autoinjector were attributed to mismatched injection times during sample preparation, with the injection time of the substitute device being two times longer than that of the RP. Both users lifted the two-step autoinjector from their skin too early, assuming that the injection duration would match that of their RP or be faster due to expectations tied to new technology. One user achieved success on a third attempt during follow-up. Crucially, these injection time discrepancies are an artefact of the study setup and sample device creation and would not exist in a generic or biosimilar product application, as injection times are standardised across DDCP devices relative to the RP.

For PFSs with needle-safety systems, unsuccessful dose completions were linked to accidental early activation and confusion regarding the instructions for use, specifically about maintaining pressure during injection. These issues underscore the value of improved labelling to enhance usability and ensure treatment consistency without necessitating a clinical investigation.

ENSURING SAFETY, EFFICACY AND BIOEQUIVALENCE FOR SUBSTITUTABLE DDCPs

For substitutable DDCPs, the primary objective is clear – to deliver the same clinical effect and safety profile as the RP. Achieving this requires bioequivalence, which hinges on administering the full therapeutic dose without error. This four-part study highlighted that RP-experienced users can successfully transition to an alternative device featuring "other design differences," achieving the primary endpoint without the need for additional training. The results demonstrate that substitutable devices can maintain safety, efficacy and bioequivalence even when alternative designs are introduced. Importantly, root cause analysis and URRAs confirmed that design differences did not contribute to primary endpoint failures or negative transfer.

This study supports the viability of standard human factors validation methodologies for substitution and bioequivalence evaluations. By leveraging best practices from IEC 62366, ISO 14971 and FDA draft guidance, the proposed approach focuses on usability improvements and error mitigation specific to pharmacy substitution scenarios. Rather than mirroring reference designs exactly, it emphasises innovation and user-centric design to enhance safety and usability beyond the RP.

"AS INJECTION TECHNOLOGIES CONTINUE TO EVOLVE, PRIORITISING THE USER EXPERIENCE IS NOT JUST BENEFICIAL – IT IS ESSENTIAL."

As injection technologies continue to evolve, prioritising the user experience is not just beneficial – it is essential. Generic and biosimilar DDCP developers can innovate, striving for "state of the art" devices, while adhering to regulatory frameworks, such as the EU MDR. By assessing risk based on negative transfer and its impact on primary endpoints, developers can uphold high standards of care while streamlining market introduction. This flexible strategy accelerates access to affordable, substitutable DDCPs, meeting patient needs efficiently and effectively.

ABOUT THE COMPANY

Teva Pharmaceuticals is an innovative biopharmaceutical company, enabled by a generics business. From in-house innovation to strategic partnerships, Teva is persistent in the creation of innovative medications, generic medicines and biologics to increase the accessibility and affordability of existing medicines. The Teva Combination Product and Device R&D group is the internal Teva entity responsible for all device development for Teva's combination product portfolio.

BIBLIOGRAPHY

1. *"ANSI/AAMI HE75:2009/(R)2018; Human factors engineering – Design of medical devices". AAMI, 2021.*
2. *Brunet-Manquat L et al, "Pre-ANDA strategy and Human Factors activities to de-risk pharmaceutical companies ANDA submission of drug-device combination products: case study of a formative Comparative Use Human Factors study". Expert Opin Drug Deliv, 2024, Vol 21(5), pp 767–778.*
3. *"IEC 62366-1:2015/AMD1:2020 Amendment 1 - Medical devices - Part 1: Application of usability engineering to medical devices". IEC, 2020.*
4. *"ISO 14971:2019 Medical devices — Application of risk management to medical devices". ISO, 2019.*
5. *Faulkner L, "Beyond the five-user assumption: Benefits of increased sample sizes in usability testing". Behav Res Methods, 2003, Vol 35, pp 379–383.*
6. *"How People Learn". National Research Council, 2000.*

Carrie O'Donel

Carrie O'Donel is Associate Director, MS&T, External Manufacturing at Teva Pharmaceuticals. She obtained her Bachelor of Arts in Physics from State University of New York, Buffalo State University (NY, US) in 2013, and her Master of Science in Mechanical Engineering from Villanova University (PA, US) in 2017.

T: +1 484 319 8798
E: carrie.odonel@tevapharm.com

Henri Akouka

Henri Akouka is Director of Biopharmaceutical Combination Products at Teva Branded Pharmaceutical Products R&D. He received his Bachelor of Science in Mechanical Engineering from Norwich University (Northfield, VT, US) in 1999 and has been developing combination products since 2007.

T: +1 732 647 6028
E: henri.akouka@tevapharm.com

Mark DeStefano

Mark DeStefano is Director, Global Technology Innovation, Combination Products and Device Research & Development at Teva Pharmaceuticals. He obtained his Bachelor of Science in Mechanical Engineering from Drexel University (Philadelphia, PA, US) in 1985 and has been developing medical devices since 1990.

T: +1 267 472 6984
E: mark.destefano@tevapharm.com

Teva Branded Pharmaceuticals R&D
145 Brandywine Parkway, West Chester, PA 19380, United States
www.tevapharm.com

Leslie Sanchez-Torres

Leslie Sanchez-Torres is a former employee of Combination Products and Device Research & Development at Teva Pharmaceuticals. She obtained her Bachelor of Science in Biomedical Engineering degree from Purdue University, West Lafayette (IN, US) in 2018.

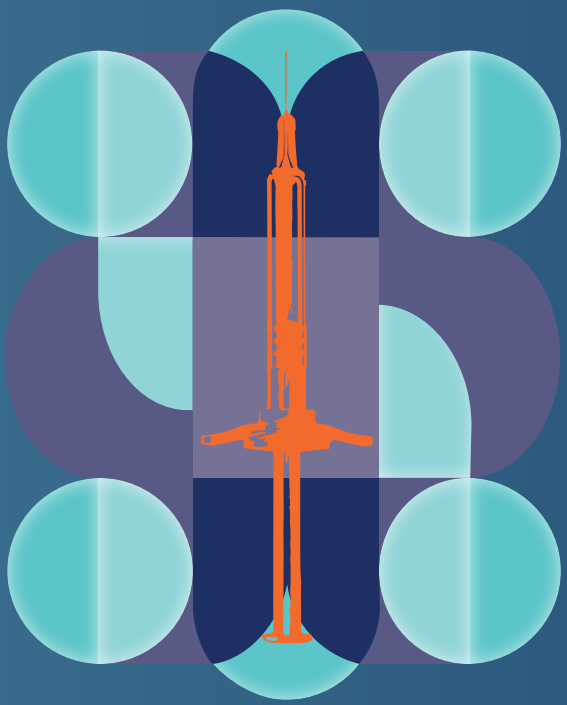
UNIVERSE OF PRE-FILLED SYRINGES AND INJECTION DEVICES CONFERENCE 2025

PDA Parenteral Drug Association

BRANDING, NETWORKING,
AND LEAD GENERATION OPPORTUNITIES

REGISTER NOW!

21 – 22 OCTOBER 2025
VIENNA, AUSTRIA



pda.org/ups2025

Connecting People, Science and Regulation®

H&T PRESSPART

Impacting Tomorrow. Together.

Innovative snap-fit closure

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

presspart.com/vytal

SMARTER FOR BUDGETS & KINDER TO THE PLANET: ECOSAFE® SAFETY SYRINGE PLATFORM

OWEN MUMFORD
Pharmaceutical Services

Tim Holden describes the key objectives behind **Owen Mumford**'s 1 mL safety syringe injection platform and how the company sought to provide a single platform for all patients (able, less dexterous and needle-phobic) while minimising cost, waste and carbon footprint impact.

All healthcare providers (HCPs) want as many patients with chronic conditions as possible to adhere to, tolerate and successfully self-administer their injection. To meet this need, Owen Mumford designed its EcoSafe® safety syringe to be easy to use, safe (passive needle shielding), cost effective and low waste (5 g disposable weight). For around four in every five patients, safety syringes enable safe, independent self-administration. But what about those who are needle-phobic or who do not have the manual dexterity to self-administer?

Sensitive Patient Populations

Many studies show that needle-phobia prevents some patients from successfully self-administering.[1] Sheer physical, emotional and/or cognitive ability to self-administer is also the subject of multiple studies.[2] Most analysts regard the dexterity issue as a particularly important one, affecting a significant proportion of patients and escalating with age, once again making it imperative for a drug delivery device (in the form of an autoinjector) to make the administration process as simple and easy as possible.

This was the challenge faced by the Owen Mumford development team. How could the EcoSafe safety syringe be extended to cover the needs of all patients – the able, the phobic and the less dexterous? And how could that be achieved without pushing up costs or generating unsustainable plastic waste and carbon emissions? The challenge was on for EcoSafe.

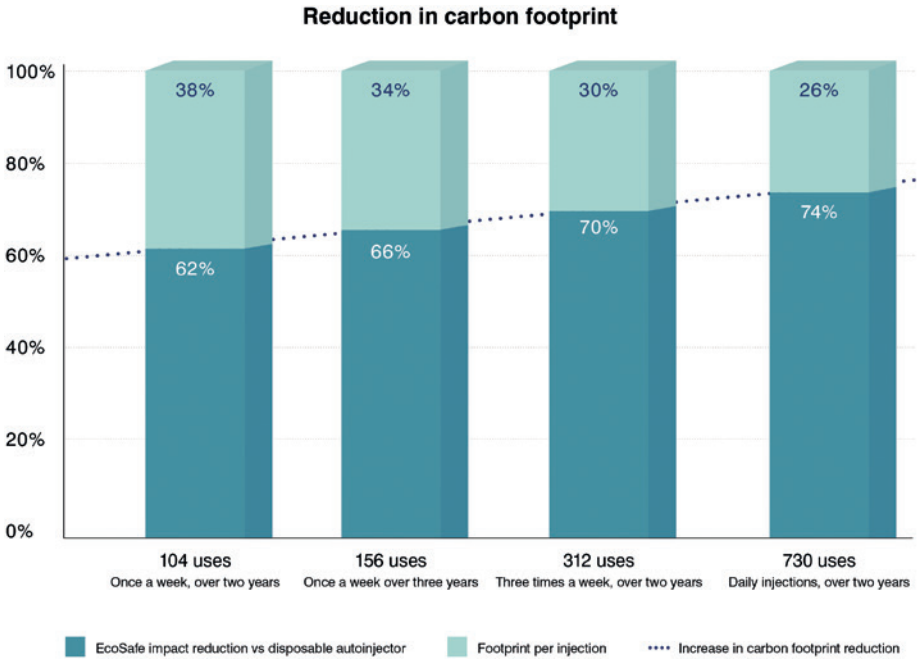


Figure 1: Carbon footprint reduction per injection – reusable EcoSafe autoinjector versus a disposable autoinjector.

WHY IS SUCCESSFUL SELF-ADMINISTRATION FOR ALL PATIENTS SO IMPORTANT?

Drug delivery systems that enable successful self-administration for all patients form the ideal solution for HCPs. Why? Well, there are three reasons:

1. **Successful Self-Administration Typically Delivers Substantial Healthcare Cost Savings:** All round the world, healthcare payers are urgently seeking ways of minimising spiralling costs (resulting from ageing populations and new therapies). Patient self-administration helps healthcare systems cope better with staff shortages. Staff time spent administering drugs to patients unnecessarily – where this can be avoided through self-administration – is hugely wasteful and expensive.

2. **A Single Drug Delivery Platform Covering All Patient Needs Has Multiple Patient and Procurement Benefits:** HCPs are looking to simplify procurement. This reduces administrative time and cost, simplifies drug administration for HCPs and provides a single consistent platform for patient training, comfort and experience.

3. **Successful Self-Administration at Home Has a Hugely Positive Impact on Waste and Carbon Footprint:** If self-administration fails – because the patient is insufficiently dexterous to handle a standard drug delivery device (e.g. a safety syringe), or they are needle-phobic or have cognitive (mental) issues – then they either have to be visited by a district nurse or they need to go (or be taken) into hospital. The carbon footprint of this unnecessary activity – for instance, road transport – is so great that it makes CO_2 emission comparisons between drug delivery devices pale into relative insignificance (Figure 1).

A review of injectable therapies concluded that home injection was associated with economic savings compared with healthcare-setting administration.[3] Studies consistently show that when patients with multiple sclerosis can self-inject subcutaneous biologics, the total annual cost per patient drops significantly (>40%) compared with hospital-based administration.[4] A clinical paper on asthma biologic administration found that home administration was typically significantly more cost effective.[5] An Australian study found that home-based self-administration of immunoglobulin delivered savings of over 80% over hospital administration.[6]

CONCEPTUAL BREAKTHROUGH – A "COMPANION" REUSABLE AUTOINJECTOR

With the EcoSafe platform, Owen Mumford aimed to create an optimal solution for *all* parties – patients, pharma companies and healthcare professionals and systems.

The conceptual breakthrough was to regard the EcoSafe 1 mL safety syringe as the "cartridge" component of the EcoSafe reusable autoinjector. The optional "companion" – a reusable autoinjector – becomes a wrap-around solution when combined with the safety syringe for those sensitive patient groups.

For the pharma company, engineering, product development and combination product assembly/filling is made far more efficient through a single product family concept. Prefilled safety syringes also act as the autoinjector's cartridge – one single, simple filling line with no variations for sensitive patients. No longer needing to offer different drug delivery products across a single therapy. Production economies of scale come into play. And the commercial proposition for healthcare customers is simple, integrated and unified – no gaps, no complications.

THE ECOSAFE STORY

Owen Mumford's development team set out to achieve three key goals that would offer benefits to patients, HCPs and their pharmaceutical suppliers

"WITH THE ECOSAFE PLATFORM, OWEN MUMFORD AIMED TO CREATE AN OPTIMAL SOLUTION FOR ALL PARTIES – PATIENTS, PHARMA COMPANIES AND HEALTHCARE PROFESSIONALS AND SYSTEMS."

alike, designing a single 1 mL safety syringe platform that:

- Encourages adherence through inclusive design – serving the able, the non-dexterous and the phobic alike
- Delivers significantly lower cost-per-dose for sensitive patients by removing HCP costs associated with dose administration
- Minimises carbon footprint across the range of dosage scenarios (validated through an independent lifecycle analysis (LCA).

The inclusivity solution has already been described – extending the safety syringe platform with an optional companion autoinjector. But how did the team also manage to deliver minimised cost-per-dose, along with reduction in plastic waste and carbon footprint?

HCPs are looking for reliable solutions that improve patients' lives while minimising cost and footprint. As such, there is a growing trend towards devices with a reusable element – but the savings achieved will depend on frequency of use.

It is considerably harder to develop a reusable platform device that is optimised for both cost and sustainability than a single-use device with a specific purpose.[7] Ultimately, the success of reusable platforms depends on whether they deliver a safe, convenient and trustworthy experience for patients while reducing waste.

As well as covering the full gamut of patient self-administration needs, including the less dexterous and the needle-phobic, the EcoSafe safety syringe plus companion reusable autoinjector was also designed to minimise environmental footprint by offering a sustainable solution.

Sustainability Imperatives

Reducing carbon footprint is now a constant expectation – from patients, from HCPs and from pharma companies. In the US, the Decarbonisation and Resilience Initiative of the Centers for Medicare & Medicaid Services is currently sparking intense debate.[8] In Europe, mandatory environmental standards are being developed.[9] And across Asia, various sustainability initiatives are already in progress.[10]

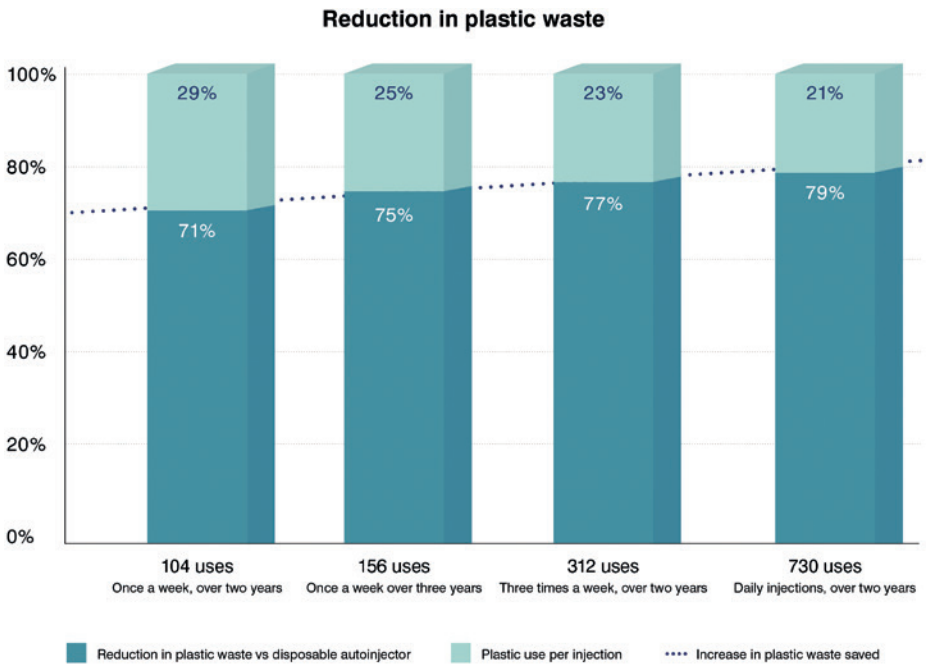


Figure 2: Plastic reduction with EcoSafe.

To support the new EcoSafe reusable autoinjector with robust data, Owen Mumford commissioned an independent LCA to examine:

1. What is the carbon footprint per injection of the combined EcoSafe® safety syringe and reusable EcoSafe® autoinjector?
2. How does frequency of use affect the impact of the reusable autoinjector?

Firstly, the carbon footprint per injection is under 0.1 kg CO_2e. This is the case even for just 100 uses, and it marks a new milestone in absolute carbon footprint reduction.

This carbon emissions value is the reusable autoinjector's contribution plus the impact of the disposable EcoSafe safety syringe. This level of associated emissions appears to be far less than published emissions data on other reusable autoinjectors on the market. Moreover, other reusable autoinjectors do not incorporate a safety syringe to play the part of a standard "cartridge".

Reducing Plastic Waste

Other than substituting materials that are truly less harmful than fossil fuel-derived plastics,[11] one strategy to reduce materials impact is to minimise the amount of plastic used. Coupled with a simple design and a minimal number of parts (think of the EcoSafe syringe's springless design), this strategy aids end-of-life recycling and disposal.

A disposable autoinjector typically weighs around 25 g. One hundred uses produces over 2 kg of waste. A reusable solution, which incorporates the extremely light EcoSafe safety syringe (just 5 g), can considerably reduce those waste levels.

Pharma companies and healthcare users therefore have a vested interest in exploring reusable companion autoinjector solutions for their phobic or less dexterous patients. The graph in Figure 2 illustrates just how substantial the waste reduction can be versus using disposable autoinjector options. This is becoming increasingly important as healthcare organisations embed mandatory waste-reduction programmes in their ongoing operational policies.[12]

Why Assess Carbon Footprint Per Injection?

The functional unit for this LCA study was: "The injecting of a single dose of pharmaceutical using a 1 mL EcoSafe safety syringe with minimum and maximum fill volumes of 0.1 mL, with an EcoSafe reusable autoinjector."

Assessing the impact of a drug delivery device across its lifecycle must consider the number of uses – but these vary. Determining footprint per injection offers a starting point for a number of calculations – whether a device is used once or hundreds of times.

CONCLUSIONS

Clearly, a sustainability assessment is not a once-and-done activity. Owen Mumford has developed its own internal, bespoke lifecycle-based eco-design tool in collaboration with a world-leading LCA consultancy, PRé Sustainability (Amersfoort, the Netherlands). The tool allows the user to autonomously build various scenarios, assess different product concepts and configurations – including material choices, component weights, packaging, efficiency, transportation, material supply and manufacturing location and various end-of-life scenarios.

"THE SAFETY SYRINGE AND COMPANION AUTOINJECTOR ARE REGARDED AS PART OF THE SAME PRODUCT FAMILY, WITH THE 1 ML SAFETY SYRINGE ACTING AS THE "CARTRIDGE" FOR THE AUTOINJECTOR. THE RESULT IS ONE PRODUCT PLATFORM COVERING ALL PATIENT GROUPS – ABLE AND SENSITIVE."

In the meantime, the Owen Mumford approach has managed to reconcile apparently competing factors. The safety syringe and companion autoinjector are regarded as part of the same product family, with the 1 mL safety syringe acting as the "cartridge" for the autoinjector. The result is one product platform covering all patient groups – able and sensitive. This minimises expensive self-administration "fails" that result in an HCP call or a hospital visit.

Reusability is engineered for a product lifetime of over a thousand uses. The result is achieving cost-control by diluting across multiple uses, meaning better value and functionality for all patients without the escalation in cost associated with disposable options. Carbon emissions and plastic waste are also minimised, and are only marginally more than the use of a safety syringe on its own. This contributes positively to sustainability goals for HCPs and pharmaceuticals companies alike.

EcoSafe set out to fulfil all these objectives. The data shown in this article illustrate how this was achieved and the extent of that success (Box 1).

BOX 1: ECOSAFE® SAFETY SYRINGE PLATFORM – CONFIDENCE IN EVERY DOSE

EcoSafe Safety Syringe

An eco-friendly, spring-free safety syringe range. The only safety syringe that helps needle-phobic patients' confidence, offering a reusable autoinjector*:

- **Intuitive:** A familiar passive injection technique
- **User-Friendly:** Full visibility of syringe barrel for user assurance
- **Cost Effective:** Simplified assembly, lower manufacturing costs and extended shelf life of three years
- **Spring-Free:** Lack of spring prevents accidental activation during transit
- **Secure:** Integrated plunger rod stays sealed in packaging, minimising risks of drug spillage, contamination and container closure integrity issues

EcoSafe autoinjector

A reusable, mechanical companion autoinjector for the EcoSafe 1 mL safety syringe:

- **User-Friendly:** Designed to offer a calmer, more confident injection experience, making it ideal for improving adherence in sensitive patient populations
- **Cost Effective:** Lower cost per dose than single-use autoinjector and therefore highly economical for frequently dosed therapies
- **Sustainable:** EcoSafe safety syringe is the only disposable plastic part and weighs only 5 g – significantly less than cassette-based systems
- **Simplified Design:** Mechanical drug delivery is not dependent on battery function
- **Optional Connectivity:** Available with connectivity, if required; lifetime battery and internal memory with no charging required and no need for docking stations.

* 1 mL safety syringe version only

REFERENCES

1. *Wibisono AH et al, "Fear of injections among people with type 2 diabetes: Overview of the problem". J Diabetes Nurs, 2017, Vol 21(3), pp 91–95.*
2. *Toschi E, Munshi MN, "Benefits and challenges of diabetes technology use in older adults". Endocrin Metab Clin North Am, 2020, Vol 49(1), pp 57–67.*
3. *Boguszewski CL et al, "Evaluating home injection compared with healthcare-setting injection of somatostatin analogs: a systematic literature review". Endocrine, 2023, Vol 79(3), pp 527–536.*
4. *Shrestha S, Simonson D, Zagel A, "A Pilot Study of Ocrelizumab Infusion Reaction Rates Among Multiple Sclerosis Patients Treated in a Hospital and 2 Outpatient Sites of Care".*

Infusion Journal, 2022, Vol 1(3), pp 10–17.
5. *Shaker M et al, "Estimation of Health and Economic Benefits of Clinic Versus Home Administration of Omalizumab and Mepolizumab". J All Clin Immunol Pract, 2019, Vol 8(10).*
6. *Ritchie B et al, "Economic impact of self-administered subcutaneous versus clinic-administered intravenous immunoglobulin G therapy in Alberta, Canada: a population-based cohort study". Allergy, Asthma Clin Immunol, 2022, Vol 18(10).*
7. *Willoughby A, Tank P-S, "Reusable Versus Single-Use Devices: Trade-offs in Improving Sustainability". ONdrugDelivery, Issue 159 (Apr/May 2024), pp 24–27.*
8. *Southwick R, "Feds want hospitals, health providers to provide data on carbon emissions". Chief Healthcare Executive, Apr 2024.*
9. *Gerecke G, Tziambazis E, Hadfield M, "Decarbonising Healthcare: How a Competitive Medical Technology Industry Can Contribute". MedTech Europe, 2025.*
10. *Bhaskar HC, "Driving Net Zero Healthcare in Asia and beyond". BioSpectrum Asia Edition, Apr 2024.*
11. *Cho R, "The Truth About Bioplastics". Columbia Climate School, Dec 2017.*
12. *"NHS clinical waste strategy". UK NHS, Mar 2023.*

Tim Holden

Tim Holden has 35 years' experience in pharma and medical device commercial leadership with a pharma licensing background across multiple therapy areas. He is presently heading Pharma Services for Owen Mumford ensuring combination products in the company's drug delivery platforms are successfully partnered.

T: +44 1993 812021
E: pharmaservices@owenmumford.com

Owen Mumford Ltd
Brook Hill, Woodstock, Oxfordshire, OX20 1TU, United Kingdom
www.owenmumford.com

Owen Mumford
Pharmaceutical Services

EcoSafe®

Safety Syringe + reusable autoinjector*

Confidence in every dose

Smarter for budgets. Kinder to the planet

- ✓ Safety syringe: Safe, simple & spring-free design
- ✓ Reusable autoinjector: Confidence for needle phobic patients
- ✓ Less waste. More sustainability

Find out more and visit
ompharmaservices.com/ecosafe

*1mL only. EcoSafe® is a registered trademark of Owen Mumford Ltd, ©2025

A CONFIGURABLE PATIENT-CENTRIC DELIVERY PLATFORM FOR BIOLOGICS AND HIGH-CONCENTRATION FORMULATIONS

SMC® Ltd.

Asmita Khanolkar and **Marta Vilaplana**, both at **SMC**, explore key challenges in delivering complex biologics and formulations, as well as the importance of early device involvement in preclinical development. They go on to consider how configurable platform technologies can support delivery of biologics, suspensions and high-viscosity formulations.

The development of novel therapies and biologics increasingly depends on optimising both formulation and drug delivery to ensure therapeutic efficacy. Achieving consistent pharmacokinetics and a positive patient experience is critical for successful clinical outcomes. However, delivery poses significant challenges: biologics and other advanced formulations often require high concentrations, large doses, greater volumes and higher viscosities, while also being fragile and stability-sensitive throughout manufacturing, storage and administration.

The delivery device plays a central role – without the right enabling technology, drug optimisation remains incomplete. Beyond technical performance, considerations such as delivery time, patient comfort and tolerance are essential for patient-centric solutions.

CHALLENGES IN DELIVERING COMPLEX BIOLOGICS AND FORMULATIONS

Optimising drug delivery requires balancing multiple considerations across formulation, device integration and patient experience. From a pharmacology perspective, understanding pharmacokinetic and pharmacodynamic (PK/PD) performance is critical, while, on the patient side, factors such as tolerability, optimal dose, concentration and viscosity must be addressed. Achieving consistent pharmacokinetics relies heavily on understanding the formulation behaviour

and optimising delivery for dependable results. Complex formulations such as non-Newtonian fluids, high-viscosity biologics and suspensions demand thorough pre-characterisation to determine delivery feasibility and guide the selection of the most effective device pathway (Figure 1).[1]

The Role of an Enabling Delivery Device Platform

The shift from infusion-based therapies to rapid, subcutaneous (SC) delivery is reshaping patient care, enabling treatment to move from hospital to home. This transition offers clear benefits – greater convenience, reduced clinic time and improved quality of life – but it also requires careful adaptation of formulations from intravenous (IV) to SC use. Achieving therapeutic efficacy in this context demands reconfiguration of dose, concentration and viscosity, often resulting in more challenging formulations.

In this context, the delivery device platform becomes central. An enabling platform provides the flexibility to accommodate a range of variables: dose volumes, needle sizes, container formats, formulation stability and acceptable delivery times from a patient perspective. Integrating such a platform early in development allows iterative preclinical evaluation, reduces risk and accelerates the path to viable in-home therapies. In essence, device platforms are not just supporting technologies – they are key enablers of the transition towards patient-centric, advanced biologic delivery (Figure 2).

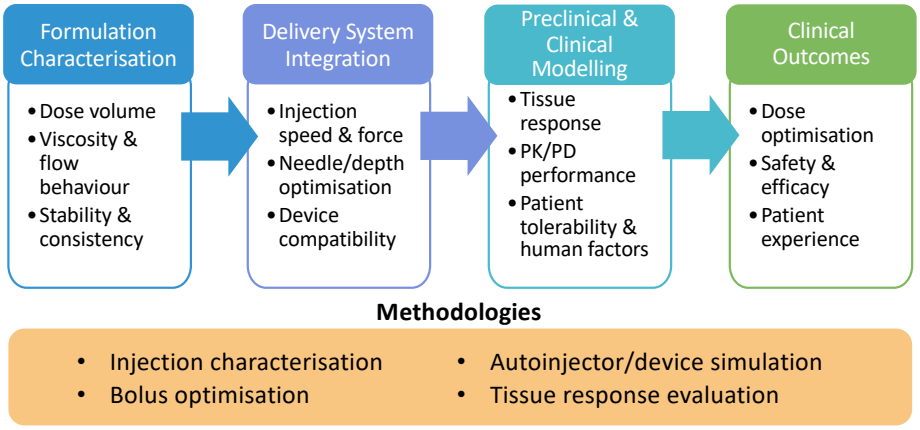


Figure 1: A continuum of optimisation – from formulation characterisation to clinical outcomes – showing how early device integration and systematic methodologies enable effective delivery of complex formulations.

The need is even more pronounced in biologics and immunotherapies, which push the limits on dose size and delivery volume. In line with high-viscosity requirements, developing high-pressure systems and container choices that withstand the mechanical stresses of delivering such formulations becomes a necessary challenge, with biosimilars adding further demand for scalable, adaptable solutions. Suspensions and non-Newtonian fluids amplify the complexity, requiring device platforms capable of consistent performance across a wide range of environments.

Additionally, the rise of precision medicine and orphan drugs highlights the importance of plausible and cost-effective solutions for smaller patient populations

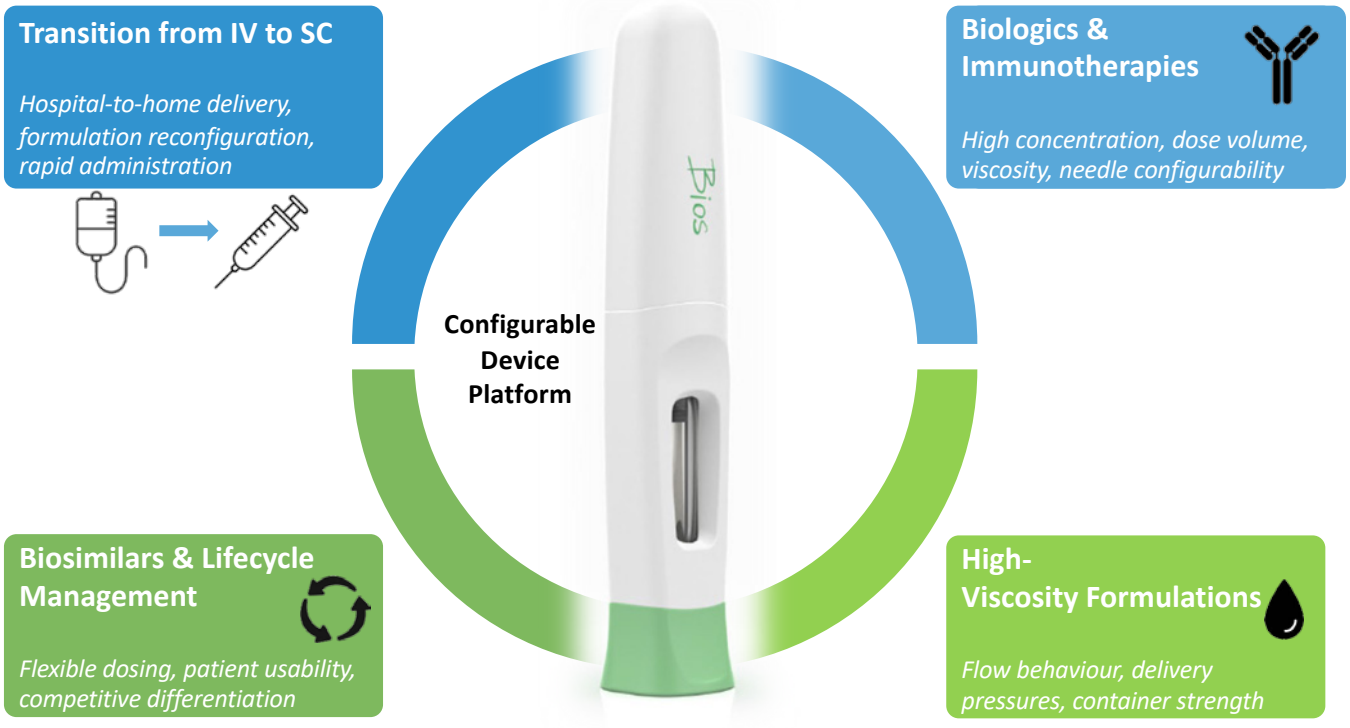


Figure 2: Device platforms act as a configurable foundation, addressing unique delivery challenges while ensuring patient usability and consistency.

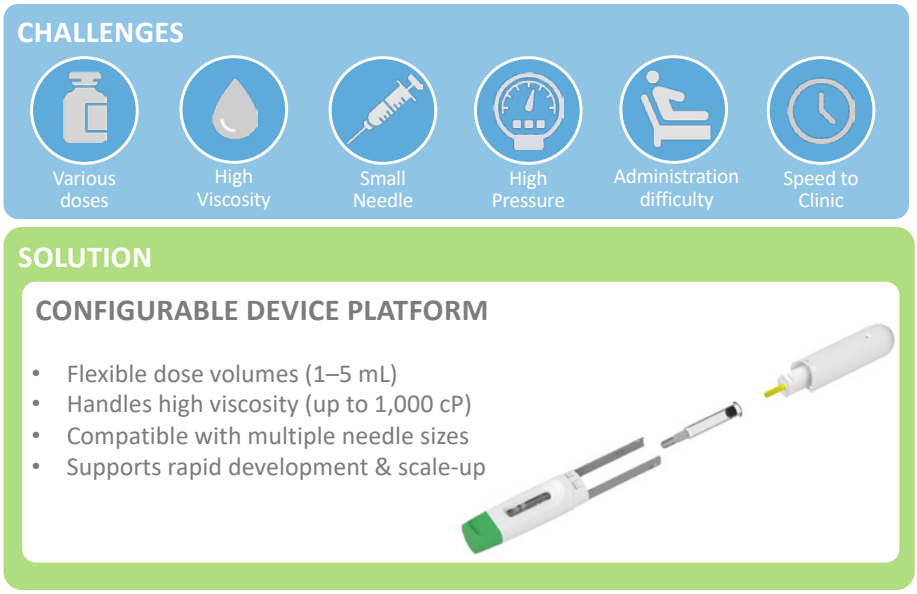


Figure 3: Configurable device platforms bridge the gap between delivery challenges and real-world solutions that accelerate development and enable patient-centric care.

with diverse dosing requirements. Success depends not only on technical delivery but also on patient adoption, which is driven by ease of use, comfort and trust in the device.

Ultimately, a configurable device platform – built on modular components such as powerpacks, containers and needles – provides the foundation for delivery optimisation from the preclinical stage through to real-world patient use. Far more than a support tool, such platforms are enablers of therapeutic success, bridging the gap between complex formulations and patient-centred outcomes (Figure 3).

EARLY DEVICE OPTIONS FOR DELIVERY OPTIMISATION

In the preclinical stage, formulators face the dual challenge of optimising drug formulations while anticipating the realities of delivery. Early involvement of device options provides critical insights into syringe suitability, formulation injectability, delivery consistency and achievable injection times. By integrating delivery considerations upstream, the path to a viable, patient-ready therapy becomes more predictable and efficient.

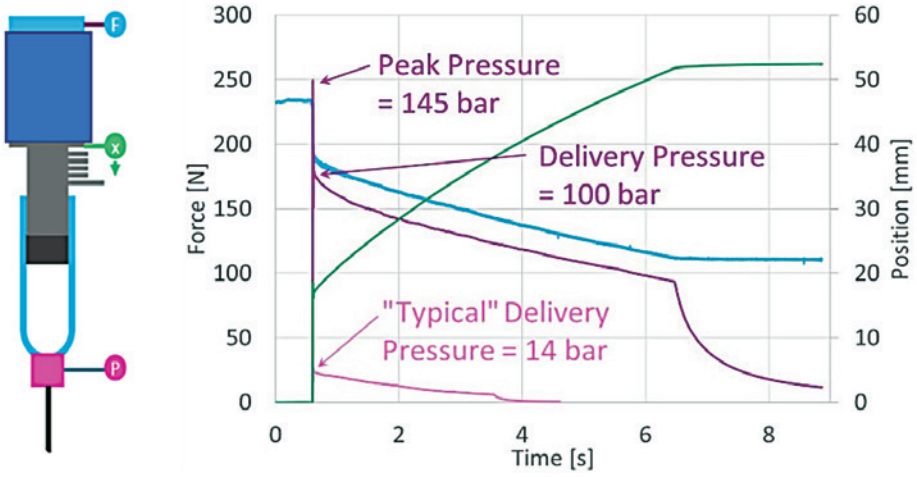


Figure 4: An injection characterisation system can map key delivery parameters e.g. force (F), pressure (P) and stroke (x) to inform predictions of injection times for non-Newtonian formulations.

"BY INTEGRATING DELIVERY CONSIDERATIONS UPSTREAM, THE PATH TO A VIABLE, PATIENT-READY THERAPY BECOMES MORE PREDICTABLE AND EFFICIENT."

Injection Characterisation of Complex Formulations

The first step in delivery optimisation is to characterise how a formulation behaves under actual injection conditions. An injection characterisation system enables empirical mapping of flow behaviour by measuring delivery pressure during injection. Because many biologics and suspensions exhibit non-Newtonian flow behaviour, multiple test iterations are required to assess viscosity stability under varying shear rates and temperatures. These tests generate large datasets (>10,000 points per run) across a range of needle sizes, forces and flow rates, making shear sensitivity more apparent. The resulting viscosity values can then be used to predict injection times and inform device requirements (Figure 4).

For non-Newtonian fluids, behaviour is further quantified using the power law model, where fluid mobility (K) and shear-thinning/thickening properties (n) define the relationship between shear stress and shear rate. These parameters establish a mathematical model that links formulation behaviour to delivery feasibility.

$$Shear\ Stress = K \times Shear\ Rate^{n}$$

Autoinjector Demonstration for Empirical Performance

Data from injection characterisation are translated into empirical device testing. A demonstrator system – mirroring the design and power source of the candidate autoinjector – validates whether predicted injection times align with real-world delivery performance. Using compressed

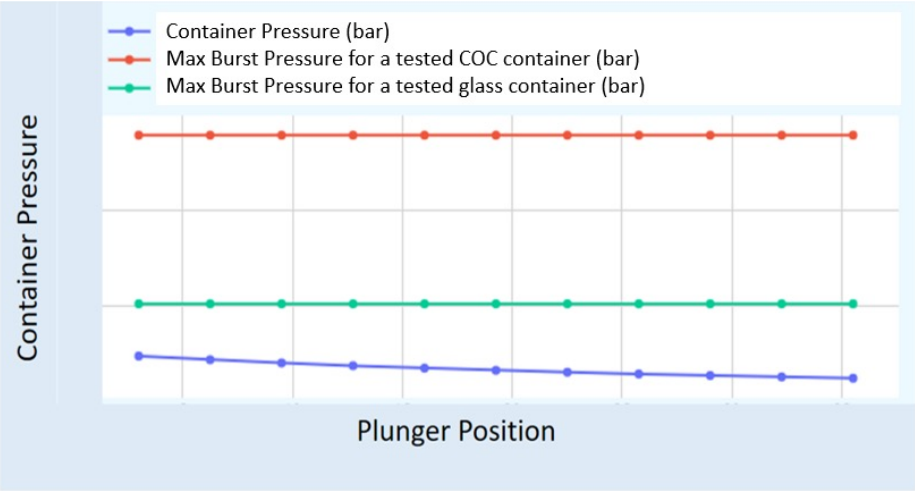


Figure 5: Syringe structural performance quantified in maximum burst pressure – tested to failure, relative to the required pressure within the syringe barrel for high-viscosity applications.

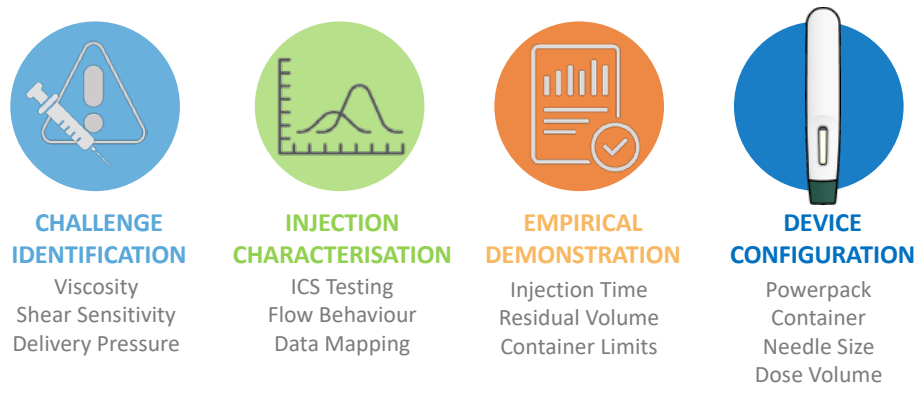


Figure 6: Path to device-formulation optimisation: iterative testing and device configurability enable robust delivery solutions aligned with formulation needs and patient experience.

gas to drive the plunger, the demonstrator system can accommodate a range of syringes, fill volumes and canister pressures. This allows comprehensive evaluation of delivery outcomes, including injection time ranges, residual volume and consistency across variables, demonstrating the capability of the device and providing an understanding of the expected data spread derived from the input variables. Such testing also highlights container limitations, particularly under high-viscosity conditions. The structural strength of the syringe (e.g. glass versus polymeric) may dictate safe operating pressures, requiring alignment between formulation, device power and container material to ensure reliable and safe injections.

Figure 5 shows results from a study comparing syringe structural performance depending on material. The insights gained from injection characterisation and empirical testing enable an informed path towards device configuration. By varying powerpack strength (gas pressure), container type, needle size and dose volume, a combination can be identified that delivers optimal performance for formulations of differing concentrations and viscosities. This iterative process underpins the role of a configurable device platform, ensuring that delivery challenges are addressed early and that the final result balances formulation requirements, technical feasibility and patient experience (Figure 6).

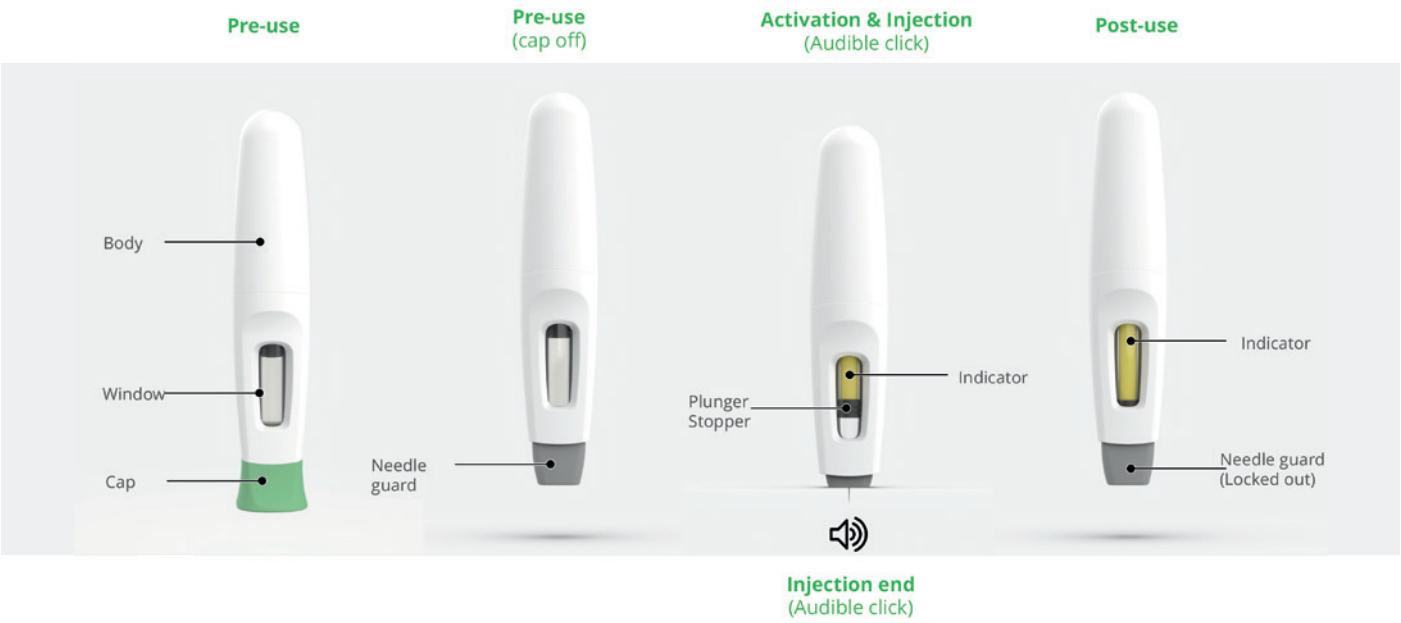


Figure 7: The Bios platform – an intuitive two-step solution, configurable and suited to patient requirements.

THE BIOS PLATFORM DESIGN: AN ENABLING PLATFORM SOLUTION

The Bios platform has been purposefully designed to address the full spectrum of challenges outlined above – from the shift of infusion therapies to rapid SC delivery, to the complexities of biologics, biosimilars and high-viscosity formulations.

As an adaptable, gas-powered autoinjector, it supports a wide range of volumes (0.5–5 mL) and viscosities (up to 1,000 cP) while remaining compatible with ISO 11040 staked-needle prefilled syringes. Its configurable architecture allows early integration into development and aligning of the device design with formulation properties from the outset.

Patient Centric by Design

The Bios device is built around the patient experience. With intuitive two-step operation, a large viewing window to track progress, hidden needle for comfort and audible start/end clicks, it is accessible even to patients with dexterous or visual limitations. These features not only improve usability and adherence but also support the hospital-to-home transition by making complex treatments simpler and safer in self-administration settings (Figure 7).

Accelerating Delivery Optimisation

By combining configurability with empirical validation of injection performance, the Bios platform creates a bridge between preclinical formulation development and clinical readiness. Its ability to accommodate a wide variety of container types, volumes, and flow behaviours makes it a versatile solution for biologics, biosimilars and orphan drugs alike. In doing so, it enables earlier, data-driven device integration, reduces risk in development and helps to accelerate speed-to-clinic.

REFERENCES

1. *Khanolkar A, White S, Margerison E, "A Novel Method to Optimize Drug Delivery for Parenteral Products Involving New Therapies and Unmet Needs". Pharm Res, 2023, Vol 40(10), pp 2303–2315.*

"THE BIOS PLATFORM HAS BEEN PURPOSEFULLY DESIGNED TO ADDRESS THE FULL SPECTRUM OF CHALLENGES OUTLINED ABOVE – FROM THE SHIFT OF INFUSION THERAPIES TO RAPID SC DELIVERY, TO THE COMPLEXITIES OF BIOLOGICS, BIOSIMILARS AND HIGH-VISCOSITY FORMULATIONS."

Asmita Khanolkar

Asmita Khanolkar has a master's degree in Materials Science & Engineering from Worcester Polytechnic Institute in Worcester (MA, US). With over two decades of manufacturing experience specialising in the medical device and pharmaceutical industry, she has managed various device projects from concept to commercial launch. Her product portfolio includes single-use, wearable and implantable devices, drug-device, device-biologic combination products for drug delivery, bio-therapeutics and pharmaceutical applications. Ms Khanolkar has held various engineering and management roles in new product development, manufacturing engineering, advanced quality planning, operations, supply chain and product lifecycle management. Her current responsibilities include a corporate leadership role supporting multiple sites in early technical engagement through commercialisation for medical devices, combination products and pharmaceutical services.

E: asmita.khanolkar@smcltd.com

Marta Vilaplana

Marta Vilaplana is a Manager of Device Development with over 15 years of technical experience in the medical device and pharmaceutical industries. She has specialised in the design and development of drug device combination products, leading programmes from early-stage concept through to clinical readiness. Her expertise includes the engineering of precision mechanical systems, device-drug compatibility, and the integration of product and industrial design into robust delivery platforms. Ms Vilaplana has contributed to the development of a broad range of injectable and inhalation systems, with a strong focus on reliability, manufacturability and regulatory compliance. Her current responsibilities include leading combination product programmes that translate complex technical requirements into practical, patient-ready solutions. She continues to focus on advancing delivery system technologies that enhance usability, improve therapeutic outcomes and meet the evolving needs of patients and healthcare providers. Ms Vilaplana graduated from the University of Barcelona (Spain) with a BEng(Hons) in Industrial & Product Design Engineering.

E: marta.vilaplana@smcltd.com

SMC Ltd
330 SMC Drive, Somerset, WI 54025, United States
www.smcltd.com

2026 Event Calendar

PharmaED RESOURCES, INC

Cleaning Validation Summit 2026
February 24-25, La Jolla, CA

Connected Devices & Digital Health 2026
March 24-25, Philadelphia, PA

Extractables and Leachables 2026
April 14-15, Raleigh, NC

Combination Products Summit 2026
May 13-14, Philadelphia, PA

Microneedle & Transdermal Delivery Forum 2026
September 16-17, Philadelphia, PA

Aseptic Processing Summit 2026
October 27-28, Philadelphia, PA

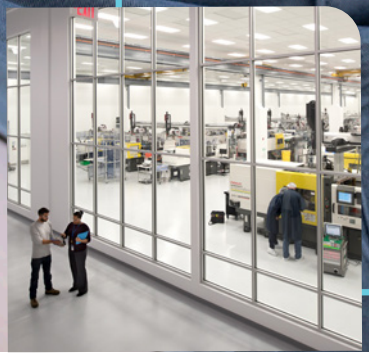
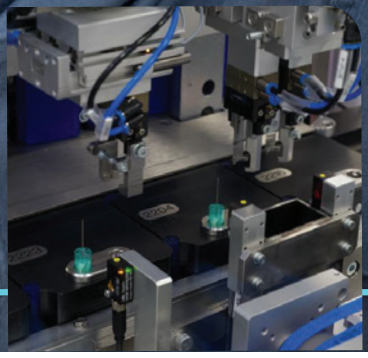
Extractables & Leachables West 2026
November 4-5, La Jolla, CA

Pre-filled Syringes & Injection Devices 2026
December 9-10, La Jolla, CA

CONTACT KIM:
khubbard@pharmaedresources.com
217.721.5774

Stay informed at
www. pharmaedresources.com

PRECISION.
INNOVATION.
CARE.

SMC Ltd. is a trusted global partner for combination product manufacturing, offering full-service capabilities from concept through commercialization. With decades of experience in drug delivery and injection molding, we provide proven expertise to support assembly, labeling, and packaging requirements across standardized parenteral platforms.

Our proprietary autoinjector portfolio is specifically designed to handle the challenges of high-viscosity and large-volume drug delivery. Complementing these platforms, our new fill-finish facility in North Carolina expands capacity to support growing market demand, while our newly expanded Devens, Massachusetts site anchors our U.S. presence.

SMC's global footprint ensures seamless support for bespoke component manufacturing, combination product assembly, and scalable fill-finish solutions.

At SMC, we combine technology, experience, and service to bring your drug delivery innovations to market with confidence.

715.247.3500 SMC® Ltd. www.smcltd.com

ADVANCEMENTS IN INTRADERMAL DELIVERY: FROM HISTORIC TECHNIQUES TO MODERN INNOVATIONS

TERUMO
MEDICAL CARE SOLUTIONS

Michele Guasti at **Terumo** explores the evolution of intradermal delivery methods, comparing historic methods of delivery, such as the Mantoux technique, with modern innovations, such as the Terumo Immucise™ intradermal injection system. The article goes on to discuss the expanding applications of intradermal delivery, including its potential for targeted lymph node delivery.

Intradermal (ID) delivery has long been a critical method in the medical and pharmaceutical fields, offering unique advantages for diagnosis, vaccination and therapeutic applications.

ID delivery involves administering substances directly into the dermis, the skin layer rich in immune cells. This method has been used for over a century, primarily for vaccinations and diagnostic tests. The dermis is extremely rich in various resident and recruited types of dendritic cells, which play a critical role in the human immune response by capturing antigens and presenting them to T cells. ID administration of vaccines can potentially result in quantitatively or qualitatively superior immune responses compared with intramuscular (IM) or subcutaneous (SC) injection.[1]

"ID DELIVERY HAS A RICH HISTORY, WITH SEVERAL TECHNIQUES AND DEVICES DEVELOPED OVER THE YEARS, WITH THE AIM OF IMPROVING THE EFFICACY AND ACCURACY OF SUBSTANCE ADMINISTRATION INTO THE DERMIS."

Terumo Corporation recently announced the commercial launch of its Immucise™ Intradermal Injection System, designed to deliver vaccines and other approved drugs to the dermal layer of the skin. This is a vertical puncture type ID injection device that is applied perpendicular to the surface of the skin in the deltoid region.[2]

This article aims to compare historic ID delivery methods with modern advancements and explore new applications, particularly in the context of targeted lymph node delivery.

HISTORIC ID DELIVERY METHODS

ID delivery has a rich history, with several techniques and devices developed over the years, with the aim of improving the efficacy and accuracy of substance administration into the dermis.

The Mantoux technique, developed in the early twentieth century, is one of the most well-known methods for ID delivery. In the US, the Mantoux tuberculin skin test has been the standard method for detecting latent tuberculosis (TB) infection since the 1930s. To perform the ID injection, the needle is inserted slowly with the bevel against the patient's skin at a 5°–15° angle. The needle bevel is advanced through the epidermis to a depth of approximately 3 mm. The injection will produce inadequate results if the needle angle is too deep or too shallow. The tuberculin solution is then slowly injected and a tense, pale wheal of 6–10 mm in diameter appears over the needle bevel.[3]

The Mantoux technique has several advantages, demonstrated by decades of clinical and epidemiological research in testing for TB in the US, where the technique has shown its simplicity (e.g. no laboratory equipment needed) and low cost.[4] However, the accuracy and the consistency of an ID administration by the Mantoux technique with a standard syringe and needle mostly depend on the performance of the practitioner.[5]

Advancements in technology have led to the development of modern devices aiming to enhance the precision, ease of use and patient comfort in ID delivery.

THE IMMUCISE™ INTRADERMAL INJECTION SYSTEM: CONSIDERATIONS FOR PRACTITIONERS AND PATIENTS

Terumo's Immucise™ Intradermal Injection System has been designed to deliver vaccines and other approved drugs to the dermal layer of the skin. The system is designed to be simple enough to handle easily and is expected to reduce risks of damaging tissues, such as blood vessels and peripheral nerves, due to its thin and short needle.[5] In use, the system has advantages over traditional ID delivery methods.

First, the device is applied perpendicular to the surface of the skin in the deltoid region, supporting precise and consistent delivery.[2] In a US FDA guidance-based human factors engineering study on the Immucise™ Intradermal Injection System, ("*Immucise™ Intradermal Injection System Human Factors and Usability Engineering Study Report*"), conducted by Terumo, a group of healthcare professionals (55 participants, including physicians, primary care nurses and pharmacists) were able to complete an injection using the Immucise™ Intradermal Injection System without use error on critical tasks, without receiving any prior instructions on the system. Furthermore, delivery was conducted without causing serious harm through accidental needlestick injury. This differs from the Mantoux technique, where the accuracy and the consistency of ID administration, by using a standard syringe and needle, mostly depends on the ability of the practitioner.[5]

The needle of the Immucise™ Intradermal Injection System is sized (i.e. outer diameter, bevel and length) so that the needle tip is retained in the dermal layer of the skin. The needle has an outside diameter of 0.2 mm (33G) and is 1.15 mm long, with a bevel length of 0.6 mm (Figure 1).[2]

The Immucise™ Intradermal Injection System is FDA cleared and indicated for ID injections of FDA-approved drugs. The system is to be used in the deltoid region for infants aged two months (excluding low birth weight and/or preterm birth) to adults.

The device is also CE marked and is intended to be used for the ID injection of approved formulations (Figure 2).

Figure 1: The needle-end of the Terumo Immucise™ ID injection system, illustrating the outer diameter of 0.2 mm (33G) and length of 1.15 mm, which is designed to be retained in the dermal layer during delivery.[2]

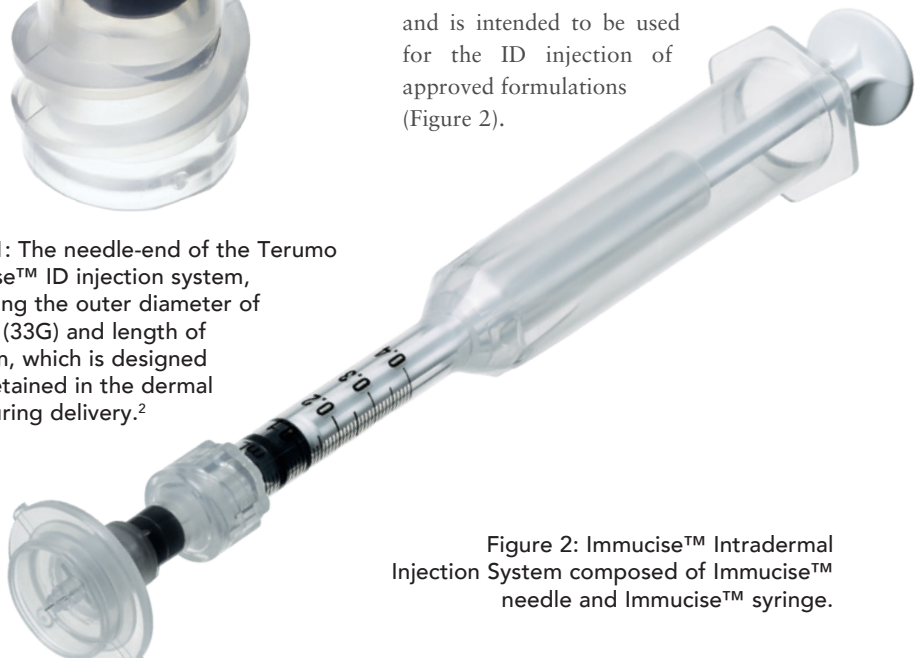


Figure 2: Immucise™ Intradermal Injection System composed of Immucise™ needle and Immucise™ syringe.

ID VACCINATION

Driven by its innate ability to generate an enhanced immune response, dose sparing and the expansion of its use to deliver a wider variety of vaccines and other therapeutics, ID delivery is an increasingly popular route for vaccination.[1]

Enhanced Immune Response

The dermis is extremely rich in various resident and recruited types of dendritic cells, which play a critical role in the human immune response by capturing antigens and presenting them to T cells. ID administration of vaccines can potentially result in quantitatively or qualitatively superior immune responses compared with IM or SC injection.[1]

Dose Sparing

As the ID route enhances immune responses, smaller doses of a vaccine can achieve the same immunogenic effect as higher doses administered through other delivery routes. Numerous studies have demonstrated these dose-sparing effects for ID delivery of several vaccines, such as seasonal influenza and rabies. This is particularly valuable during vaccine shortages or in low-resource settings and allows for dose-sparing, making vaccines more accessible and cost-effective.[1]

Expansion of Use

ID delivery is already used for certain vaccines, such as the rabies and BCG (tuberculosis) vaccines.[1] This established use provides a foundation for expanding ID delivery to other vaccines, using its potential for broader immunisation efforts.

CLINICAL TRIALS

In a paper titled, "Immunogenicity and safety of the new intradermal influenza vaccine in adults and elderly: A randomised Phase 1/2 clinical trial", Ryo Arakane *et al* investigated the immunogenicity and safety of single, two-dose vaccination and three different dose strengths (6, 9 and 15 g HA per dose) of the influenza vaccine using the Immucise™ Intradermal Injection System and compared it with the standard SC vaccine (15 g HA per dose).[5]

The Immucise™ ID injection system showed a similar safety profile to that of SC administration. The seroprotection rate for strain B by ID administration of 15 µg of influenza vaccine was 69.4%, whereas by SC administration the rate was 48.0%. Administration of a 15 µg ID influenza vaccine with Immucise™ Intradermal Injection System showed a higher seroprotection rate compared with 15 µg SC dose in elderly subjects ≥ 65 years in Phase I/II trials trials (Figure 3).[5]

Compared with the SC groups, both the single-dose ID group (until 21 days after administration) and two-dose ID group (until 42 days), showed higher geometric titers (GMT) for two type A strains.[5]

"ID DELIVERY ALLOWS FOR LOCALISED ADMINISTRATION, WHICH CAN BE BENEFICIAL FOR TREATMENTS TARGETING SPECIFIC SKIN CONDITIONS OR LOCALISED IMMUNE RESPONSES."

An additional study reported the GMTs of each strain at 90 and 180 days after vaccination in the elderly subjects.[2] The ID group showed similar or better efficacy than the SC group until 180 days after vaccination in both the single- and two-dose groups. Notably, the GMTs in the B strain were significantly higher in the two-dose ID group than in the two-dose SC group in elderly subjects (p = 0.006 at day 90;

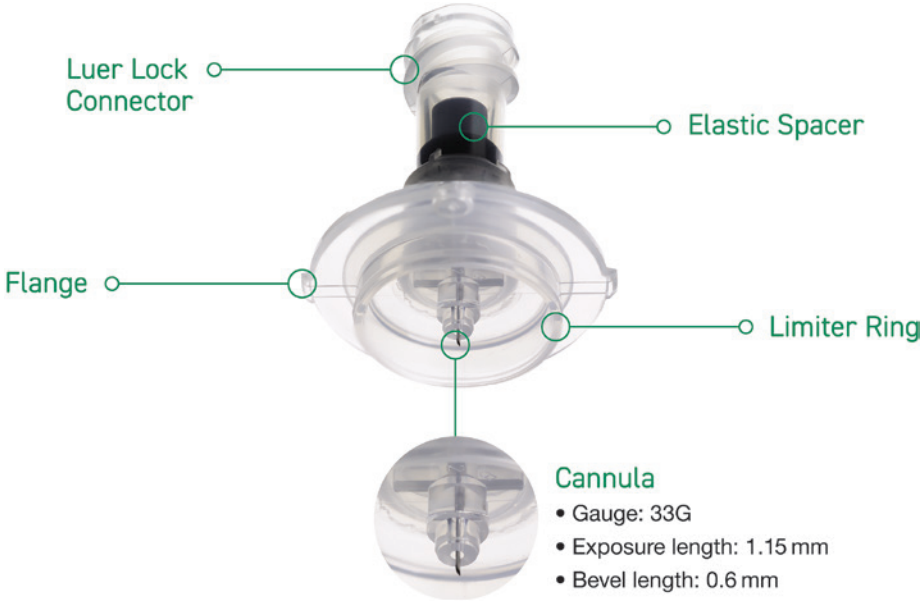


Figure 3: Immucise™ Intradermal Injection System.

p = 0.013 at day 180). These results show that ID administration may induce immunity for a longer period compared with the general administration route.[2]

THERAPEUTICS

Beyond vaccines, ID delivery is being explored for the administration of biologics and other drugs.[6] This method can improve the bioavailability and efficacy of these treatments. ID delivery allows for localised administration, which can be beneficial for treatments targeting specific skin conditions or localised immune responses.

POTENTIAL FOR LYMPH NODE DELIVERY

One of the most promising applications of ID delivery is its potential for targeted lymph node delivery, which may enhance immune responses and therapeutic outcomes.

ID delivery can target lymph nodes by using the rich network of lymphatic capillaries in the dermis.[7] Lymphatic capillaries are 10–60 µm in diameter, around three-times the width of blood capillaries.[8] They also have larger gaps between their endothelial cells compared with blood capillaries, which can expand to allow larger particles, such as proteins, lipids and even pathogens, to enter the lymphatic system.

Furthermore, lymphatic capillaries are designed to absorb interstitial fluid, which includes particles and molecules that have leaked out of blood capillaries. Unlike blood capillaries, lymphatic capillaries have an incomplete, discontinuous or absent basal lamina,[8] and overlapping endothelial cells, which can act like one-way valves to permit the uptake of larger particles. Due to their unique structure, particles with sizes of 10–100 nm are preferentially taken up by the lymphatics.[9]

> "STUDIES HAVE EXPLORED THE POTENTIAL OF ID DELIVERY FOR TARGETED LYMPH NODE THERAPIES, WITH PROMISING RESULTS IN CANCER TREATMENT."

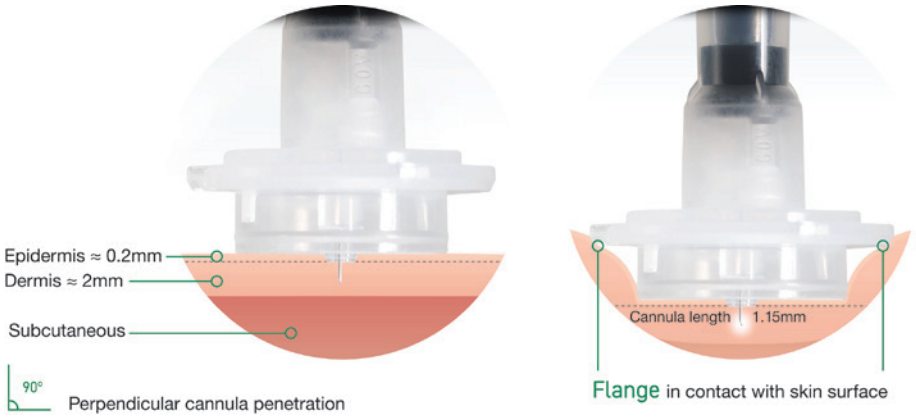


Figure 4: Immucise™ Intradermal Injection System (with dermal layer).

Further Promise for ID Delivery

For immunotherapies, delivering therapeutic agents directly to the lymph nodes can enhance their ability to stimulate an immune response against cancer cells or other pathogens, and studies have explored the potential of ID delivery for targeted lymph node therapies, with promising results in cancer treatment.

Furthermore, ID administration immediately and efficiently delivers antibodies to lymph nodes, whereas little drug is delivered by systemic administration.[10]

Drug delivery to lymph nodes – by changing the route of administration to ID – may improve drug efficacy, and ID administration of anti-PD-L1 antibodies has been found to significantly suppress tumour growth.[10]

Further research in this area is focused on developing methods to optimise the delivery of therapeutic agents to the lymph nodes, improving their efficacy and reducing side effects. Clinical trials are underway to evaluate the effectiveness of ID delivery for various therapeutic applications.

CONCLUSION

ID delivery has evolved significantly from its historic roots, with modern innovations, such as Terumo's Immucise™ Intradermal Injection System, designed to offer enhanced precision and ease of use (Figure 4). Through broadening the application of this method to include a wider range of vaccines and therapeutic agents, ID delivery has the potential to revolutionise healthcare. Future research and development will continue to expand the possibilities of ID delivery, including its potential for targeted lymph node therapy.

Terumo Internal Reference: PM-09811

REFERENCES

1. *"Intradermal delivery of vaccines: A review of the literature and the potential for development for use in low- and middle-income countries". PATH, Aug 2009.*
2. *Shimizu S et al, "Performance and usability evaluation of novel intradermal injection device Immucise™ and reanalysis of intradermal administration trials of influenza vaccine for the elderly". Vaccine, 2022, Vol 40(6), pp 873–879.*
3. *"Mantoux Tuberculin Skin Test Facilitator Guide". PDF, CDC, accessed Sep 2025.*
4. *"Clinical Testing Guidance for Tuberculosis: Tuberculin Skin Test". PDF, CDC, accessed Sep 2025.*
5. *Arakane R et al, "Immunogenicity and safety of the new intradermal influenza vaccine in adults and elderly: A randomized phase 1/2 clinical trial". Vaccine, 2015, Vol 33(46), pp 6340–6350.*
6. *"INTRADERMAL DELIVERY - New Technology Brings Simplicity & Scalability to Intradermal Drug Delivery". Drug Development &*

Delivery, Mar 2018.
7. *Skobe M, Detmar M, "Structure, function, and molecular control of the skin lymphatic system". J Investig Dermatol Symp Proc, 2000, Vol 5(1), pp 14–9.*
8. *Lala PK, Nandi P, Majumder M, "Roles of prostaglandins in tumor-associated lymphangiogenesis with special reference to breast cancer". Cancer Metastasis Rev, 2018, Vol 37(2–3), pp 369–384.*
9. *Bagby TR et al, "Impact of molecular weight on lymphatic drainage of a biopolymer-based imaging agent". Pharmaceutics, 2012, Vol 4(2), pp 276–295.*
10. *Tanaka R et al, "Efficient drug delivery to lymph nodes by intradermal administration and enhancement of anti-tumor effects of immune checkpoint inhibitors". Cancer Treat Res Commun, 2023, Vol 36, art 100740.*

Michele Guasti

Michele Guasti is Global Product Manager at the Pharmaceutical Solutions Division of Terumo Medical Care Solutions. He graduated from the University of Brescia (Italy) and holds a master's degree in mechanical engineering. Mr Guasti has more than 10 years of experience in primary packaging within the pharmaceutical industry. In the last five years, he has acquired expertise in fill-finish processes for injectable drugs and associated technologies. Mr Guasti has extensive experience in establishing strong partnerships and collaborations between companies and supporting pharma customers in finding solutions to their daily challenges. Previously, he worked in strategic product management at Stevanato Group.

E: michele.guasti@terumo-europe.com

Terumo Pharmaceutical Solutions
Interleuvenlaan 40, 3001 Leuven, Belgium
www.terumopharmaceuticalsolutions.com

Quality time for better care

TERUMO
MEDICAL CARE SOLUTIONS

PHARMACEUTICAL

Immucise™ Intradermal Injection System

The new intradermal injection system designed to deliver vaccines & other approved drugs to the dermal layer of the skin.

Immucise™

Intradermal vaccination using Immucise™ induces faster and higher immune response*

*R Arakane et al. Vaccine 33 46 (2015):6340-6350.

PM-09395

WHY YOU CANNOT DESIGN A PREFILLED SYRINGE SYSTEM OUT OF COMPONENTS

Dr Bettine Boltres at **West Pharmaceutical Services** unravels the complexities of bringing a new molecule to market as part of a combination product and rethinks the way that drug-device design could be tackled instead, approaching the system as a whole rather than through individual component development.

Over the decades, the challenges of drug delivery have continually been met with innovation. Problems have been met with solutions. Take prefilled syringes (PFSs) as an example. These devices were first introduced during the Second World War as a mechanism for delivering injections in battlefield settings – an innovative answer to the question of how to administer medication with speed, sterility and dosing accuracy. While the fundamental premise has remained the same, today PFSs have grown in significance and prevalence. Advances in design and materials science ensure that they play a crucial role in the delivery of drugs, especially sensitive biologics, through their ability to preserve the drug's quality, efficacy and safety; deliver highly targeted doses; and support self-administration.

NAVIGATING THE REGULATORY LANDSCAPE

While PFSs might have provided the means to simplify drug delivery, they are part of a highly complex, strongly regulated and traditionally component-driven development programme. Being regulated as combination products adds an additional layer of complexity. For design and development through part selection, verification and manufacturing, there are many critical, often contradictory considerations that must be taken into account to simultaneously ensure the quality, efficacy and safety of a drug within a reliable, functional and usable device. The success of these development programmes is undoubtedly testament to the sector's problem-solving capabilities,

but they also serve to highlight the absence of more efficient top-down, integrated and holistic solutions.

The issue at the heart of the matter is navigating regulatory processes while simultaneously developing numerous components into a combination product. It is therefore typical for development to be a lengthy and highly complex process. In a market increasingly populated by emerging biotechnology companies, the process of taking a molecule from formulation to the market as a final combination product can be a daunting one, with significant challenges.

Currently, these issues are addressed through engagement with external consultancies and a disaggregated network of supply chain partners. The onus is on the drug originator to co-ordinate these moving parts and bring various strands of development together. Indeed, the sourcing and procurement of components demands detailed knowledge of the quality target product profile, critical quality attributes and specialised information to create robust design and development inputs. These are guided by:

- Quality Guidelines Eight and Nine of the Internation Council of Harmonisation (ICH Q8 and Q9)
- GMP regulations across global territories, which include:
  - Part 211 (CGMP for Finished Pharmaceuticals)
  - Part 820 (Quality Management System Regulation) of Title 21 of the Code of Federal Regulations in the US (21 CFR Parts 211 & 820)
  - GMP guidelines in the EU (EU GMP).

STAGES OF PFS DEVELOPMENT

In the very earliest stages of defining the design and development inputs for a PFS, pharma and biotech companies face an almost bewildering array of component choices. For each component, arriving at an optimal decision will require engagement in a time-consuming and highly detailed sourcing process. This involves multiple contacts from a broad range of potential supply partners. Typically, this process will initially require stakeholders to define the component specification before conducting market research to identify possible candidate suppliers. Following completion of this phase, requests for information will be issued to shortlisted providers as part of an evaluation of production capabilities and quality and compliance credentials. Risk assessments and supplier qualification checks will also need to be carried out as part of this comprehensive due diligence process. For each company, this will need to be conducted under the security of a Confidential Disclosure Agreement (CDA) to ensure all parties are legally protected. Furthermore, in some cases, there will be a need to establish more complex three-way CDAs to facilitate discussion between multiple partners.

Taken together, all these stages evidently add up to a significant investment in time, energy and therefore cost for sponsors, who are ultimately responsible for overseeing the device. They face clear pressure in managing supplier relationships effectively and mitigating risk in the interests of final drug quality and continuous improvement. Importantly, this must be considered from the first point of engagement throughout development, design and development verification and validation testing, clinical and human factors studies, technology transfer and commercial manufacturing. This must all occur while also exerting control over change management activities and product quality throughout the lifecycle of the combination product. Finally, the need to align on technical demands must be matched by a shared culture, agreed behaviours and effective communication for this to be achieved with minimal friction.

> "THE SOURCING AND PROCUREMENT OF COMPONENTS DEMANDS DETAILED KNOWLEDGE OF THE QUALITY TARGET PRODUCT PROFILE, CRITICAL QUALITY ATTRIBUTES AND SPECIALISED INFORMATION."

> "IN THE VERY EARLIEST STAGES OF DEFINING THE DESIGN AND DEVELOPMENT INPUTS FOR A PFS, PHARMA AND BIOTECH COMPANIES FACE AN ALMOST BEWILDERING ARRAY OF COMPONENT CHOICES."

Record-keeping and data management can present particular challenges in this multi-stakeholder environment. Sponsors are not only required to evaluate part-level datasets of device components in isolation, but must also ensure performance of a PFS as the final combination product. Ultimately, disparate datasets will need to be compiled into a unified and robust device and development file as part of an electronic common technical document submission to regulatory bodies.

FURTHER CHALLENGES IN PFS DESIGN

Practically speaking, this task is far from straightforward. Take for example, the fact that a rigid needle shield will be supplied with product specifications detailing material attributes for a variety of characteristics. This includes measurements such as pull-off force, endotoxin level, bioburden level and particulate matter – which at West is uniquely reported according to a Proved Clean Index value. The same PFS system will also feature particle data from the glass barrel supplier, reported as a specific percentage based on US Pharmacopeia-National Formulary (USP-NF) General Chapter 788. Meanwhile, the plunger supplier will report on particulate matter in terms of amount per square centimetre of plunger surface area. This places the onus on the applicant to understand the interplay between three different measures, potentially from three separate suppliers, in order to arrive at a robust singular evaluation of particle characteristics at a system level. This is a task that must be repeated for all critical characteristics

of the PFS beyond particulates, amounting to a heavy data-evaluation burden.

There are also inherent challenges regarding stakeholder management where multiple vendors are concerned, each with individual stipulations in terms of minimum order quantity options and with limited guarantees of consistency when it comes to manufacturing processes and quality. Moreover, if complaints later arise in relation to the PFS, accountability cannot likely be attributed to a single supplier, requiring the authorisation holder to detangle and resolve potentially difficult interlinked issues.

Such challenges can be overcome, but resolving them can place additional demands on internal resources. If problems escalate, however, there is a real risk of milestones being missed, unforeseen increases in development costs and potentially delays to product launch. This might be caused, for example, by the need to retrospectively source specific aspects of performance data, the failure to meet in-clinic targets for quality or quantity of supply, or delays to the regulatory approval process.

Delays to the development schedule and launch of a device are well known to have damaging implications. However, translating those problems into a financial cost in the past has stemmed from estimates and anecdotal evidence. But in late 2023, the Tufts Center for the Study of Drug Development grounded this conversation in real-world figures based on empirical research. It concluded that the cost of missing a single day in drug development equates to approximately US$500,000 (£370,000) in lost prescription drug or biologic sales. It also puts an approximate price tag of $40,000 per day on Phase II and III trials, underlining the financial imperative of avoiding issues that have the potential to extend trial schedules.[1]

"APPLYING A SYSTEM-LEVEL APPROACH TRULY HAS THE POTENTIAL TO SHIFT THE CURRENT PARADIGM IN PFS DEVELOPMENT."

CHALLENGING ASSUMPTIONS

For years, this fragile dynamic has been the status quo in the sourcing of PFSs, driven by a component-based approach to device selection and evidencing of system-level performance. Taking a moment to reflect on this situation, it is not unreasonable to question whether drug companies should continue to absorb these pressures as an accepted and unavoidable cost associated with achieving their goal. In an evolving market, is a one-size-fits-all approach optimal for all innovators? Where appropriate, would it not be possible instead to bypass the many points of friction involved in building a system from disparate components and instead employ a ready-made system that has already been verified for the task?

Today, those assumptions are being directly questioned by the groundbreaking introduction of integrated PFS systems. By incorporating pre-verified device constituent parts – syringe barrel, plunger and needle shield/tipcap – these novel systems provide a catalyst for emerging biologic and vaccine innovators to accelerate the journey towards the critical milestone of clinical fill-finish. They provide the means to accelerate PFS selection, simplify vendor management, secure reliable single-source device supply and streamline regulatory submissions through a pre-planned system performance verification data package.

CONCLUSION

As discussed, the current component-driven model introduces the need for sponsors to manage a multiplicity of risks across a disaggregated network of suppliers. Cumulatively, this can represent a potentially insurmountable task for emerging biotechnology companies that are under pressure to deliver their molecule to clinic and progress towards marketing approval. Applying a system-level approach truly has the potential to shift the current paradigm in PFS development.

As with so many examples of impactful innovation, the premise of taking a system-level rather than component-driven approach to PFS development is not reflective of wholesale reinvention or rewriting the rules. Rather, it is about challenging the status quo, addressing underlying flaws and creatively rethinking how to optimise the route to the same destination. It rests on the knowledge that where problems remain unsolved, drug delivery innovators will keep rising to the challenge of developing newer, better and faster ways of bringing therapeutic benefits to the lives of patients.

Dr Bettine Boltres

Bettine Boltres, PhD, Director, Scientific Affairs, Integrated Systems at West Pharmaceutical Services is a recognised thought leader in the industry, fostering scientific exchange between West and the pharmaceutical sector. She possesses extensive knowledge in glass, polymer and rubber materials, which carries over in her expertise in combination products. Dr Boltres is the author of the book "When Glass Meets Pharma" and serves as an expert for the US Pharmacopeia, European Pharmacopoeia and various ISO working groups. Additionally, she plays an active role in the Parenteral Drug Association (PDA) and has served on the PDA Board of Directors since 2019.

E: bettine.boltres@westpharma.com

West Pharmaceutical Services Inc

530 Herman O West Drive, Exton, PA 19341, United States

www.westpharma.com

REFERENCE

1. *Smith ZP et al, "New Estimates on the Cost of a Delay Day in Drug Development". Ther Innov Regul Sci, 2024, Vol 58, pp 855–862.*

SCAN HERE
TO REQUEST A MEETING

Learn more at CPHI Frankfurt
October 28-30 | Stand 8.0H8

ACCELERATING TIME TO MARKET FOR NEW INJECTION DEVICES USING A NOVEL FORCE-MODELLING METHOD AND SOFTWARE

SANNER GROUP
Protecting Health.

Pfizer

Bradley Sawyer, **Elena Guss Tarazona** and **Matthew Latham**, all at **Sanner Group**'s Design Center of Excellence, **Springboard**, and **Charlie Bowen**, **Dr Jay Sayed**, and **Harriet Field**, all at **Pfizer**, describe new software co-developed by the companies to translate syringe test data into injection device performance, and to work backwards from device performance after shelf-life expiration to the maximum forces they can allow in a syringe test.

New injection devices are being asked to deliver larger volume injections, with higher viscosity formulations and increasing user expectations for device aesthetics, simplicity and quality. All injection devices risk performing inadequately when challenged with components, volumes and viscosities at the upper end of their tolerances. This risk of failure is present when developing devices for biosimilars and generics too.

As such, it is becoming ever more important to predict a device's behaviour early in development, as well as to predict the effect of shelf-life ageing. However, with increased drug viscosity and volume comes more complex force requirements, and basic methods of predicting plunger forces are not sufficiently capable. The nightmare scenario is that an injection device is designed, taken through tooling, automation and design verification testing, and then fails its performance requirements at the end of its shelf life.

Sanner Group's Design Centre of Excellence (Springboard) has developed new software that allows the translation of basic syringe test data into injection device performance. The software also enables engineers to work backwards from device performance after shelf life to

the maximum forces they can allow in a syringe test. This can be done early in development to avoid failures late in the programme.

WHY USE BREAK-LOOSE EXTRUSION FORCE DATA?

Break-loose and extrusion force (BLEF) tests are a common way to characterise prefilled syringes with plungers. In a BLEF test, a tensometer drives a plunger at constant speed and measures the (varying) force as the plunger moves down the syringe.

The force-distance chart created in a BLEF test provides useful information – the initial break-loose force of the stationary plunger, the extrusion force (which comprises the dynamic plunger-syringe friction and the drug formulation's back-pressure) and a small dip in force indicative of an air bubble expelled after drug delivery (Figure 1).

ISO 11040-8 mandates that such tests use the complete, final system "as intended for use" and that the designer considers how forces vary with ageing and environmental factors. BLEF testing is valuable for characterising the relationships between forces and plunger speed, syringe or needle dimensions, and fluid properties.

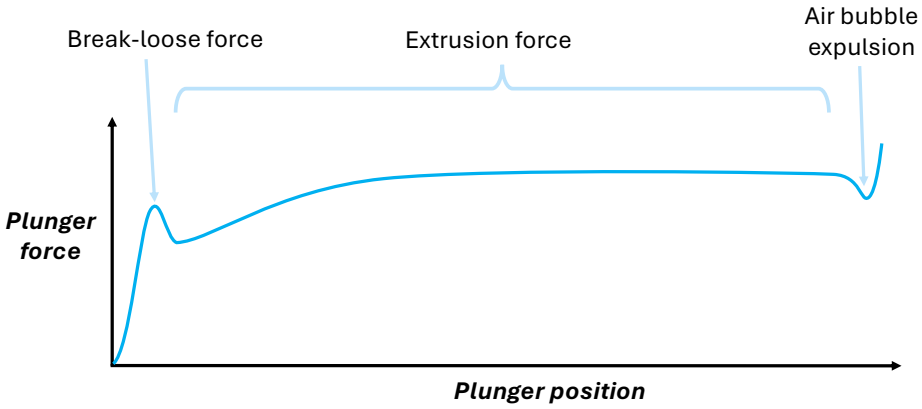


Figure 1: The force-distance chart for a BLEF test.

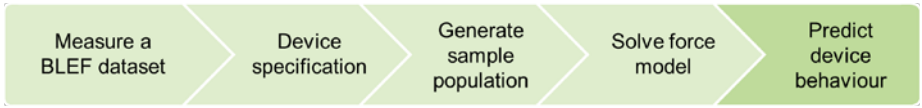


Figure 2: Steps taken to generate BLEF predictive data.

However, it cannot be used to accurately predict injection times for a device because it does not reflect dynamic injection behaviour. Therefore, designers need a tool that can use common BLEF test data to provide accurate predictions for injection device performance.

To address this, Springboard has co-developed advanced modelling software with Pfizer's Devices Centre of Excellence. This software enables device developers to easily forecast injection times, anticipate variation due to ageing and set meaningful specifications early in the development process. The software can bridge the gap between constant-speed BLEF data and dynamic injection device performance without the need for guesswork, reducing the number of slow and costly prototype testing cycles and rework (Figure 2).

A NEW MODEL AND SOFTWARE FOR DEVICE PERFORMANCE

Software users simply upload their own BLEF data into the software and, in a few steps, can generate:

1. A predicted distribution of injection times for their specified device
2. Maximum extrusion force requirement predictions
3. A report for their design history file.

The model behind the software uses a time-stepped approach to break down an injection into discrete, calculable steps (Figure 3). Each loop begins with a known plunger position, which relates to the device's spring length. From this, the spring force is known and is assumed to be approximately equal to the current extrusion force.

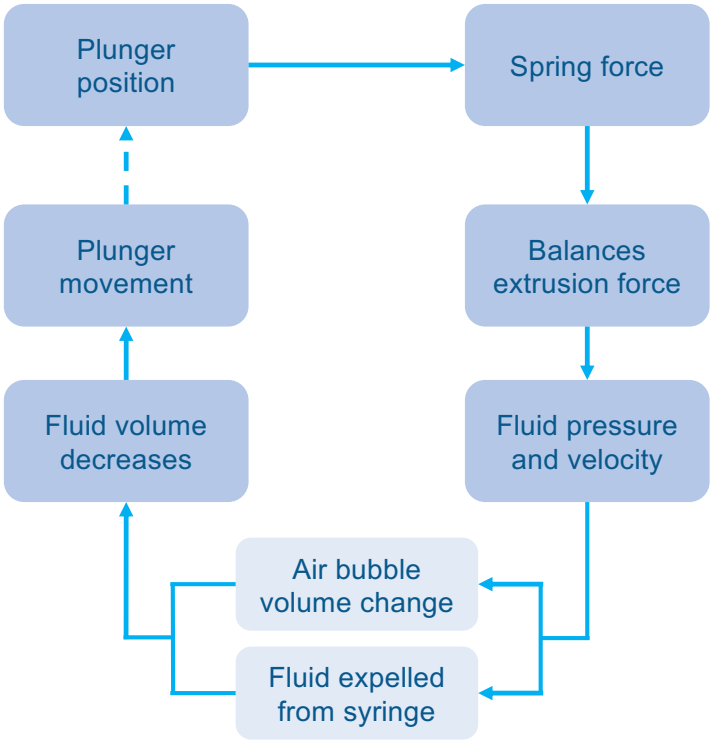


Figure 3: A time-stepped approach to break down an injection.

Using relationships from the user's BLEF data for the modelled syringe, the extrusion force is used to work back to the plunger speed and internal syringe pressure. By calculating the Hagen-Poiseuille equation across the needle, the pressure is related to the velocity of fluid ejected.

The plunger movement can then be calculated due to the reduction in injection volume, while also accounting for any changes in any air bubble volume due to pressure changes – this step is important to capture, but is complex and challenging to address through other predictive methods. The loop is repeated until the full volume has been delivered, with the total time elapsed giving the device injection time.

This software uses the Monte Carlo method to sample the random variation of all input parameters, which include:

1. User-specified tolerances on input parameters
2. The variance of real BLEF data.

COPING WITH DEVICE AGEING

Various factors lead to device performance degradation over time, most notably desiliconisation of the syringe, which leads to increased plunger-syringe friction. After shelf-life expiration, device performance is more likely to fail requirements such as injection time than on the day the device was manufactured. This is bad news for development projects because issues might not be discovered until years into a programme.

"VARIOUS FACTORS LEAD TO DEVICE PERFORMANCE DEGRADATION OVER TIME, MOST NOTABLY DESILICONISATION OF THE SYRINGE, WHICH LEADS TO INCREASED PLUNGER-SYRINGE FRICTION."

Therefore, Sanner Group and Pfizer used newly siliconised and fully desiliconised syringes as best and worst cases for plunger-syringe friction and used desiliconisation as a surrogate for ageing. In practice, while it is safe to say that syringes effectively move away from newly siliconised performance as they age, most will never get near to fully desiliconised, depending on their ageing properties.

The software has been extended to establish ageing trends using a small number of single-speed BLEF tests on aged syringes. This effect is modelled by increasing theoretical BLEFs until devices stall or breach injection time limits. This results in establishing the worst case syringes that can be allowed. Then, by back-calculating from end-of-shelf life performance to initial conditions, the method can define a maximum allowable BLEF result at time zero. This allows engineers to specify the maximum forces allowed on a BLEF test at time zero where they can still be confident that the injection device would perform after shelf-life expiration.

"THE SOFTWARE HAS BEEN EXTENDED TO ESTABLISH AGEING TRENDS."

Bradley Sawyer

Bradley Sawyer is a mechanical engineer at Sanner Group's Design Center of Excellence, Springboard, with particular experience in medical device concept design and injection device verification. He holds an MEng in mechanical engineering from the University of Cambridge (UK).

E: bradley.sawyer@springboard.pro

Elena Guss Tarazona

Elena Guss Tarazona holds a BEng in mechanical engineering from the University of Warwick (UK) and an MRes in medical physics and biomedical engineering from University College London (UK). While at Sanner Group's Design Center of Excellence, Springboard, she has worked on a range of medical devices from early-stage R&D through to forensic engineering, with a focus on feasibility and rapid prototyping.

E: elena.gusstarazona@springboard.pro

Matthew Latham

Matthew Latham, an engineer at Sanner Group's Design Center of Excellence, Springboard, has a background in mechanical and aerothermal engineering. He has worked on a broad range of medical devices across all stages of product lifecycles, with a particular focus on primary packaging, design verification and injection devices.

E: matthew.latham@springboard.pro

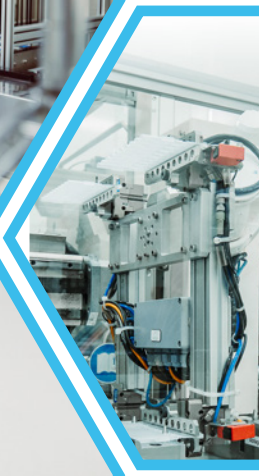
Springboard Ltd – a Sanner Group Company
Platinum Building, St John's Innovation Centre, Cowley Road, Cambridge, CB4 0WS, United Kingdom
www.sanner-group.com

SANNER GROUP

Sanner is a smart, agile and reliable CDMO, providing a full spectrum of services, from the initial design and development phases to mass production of everything from simple, single-use consumables to complex electromechanical devices.

Our agility, scalability and substantial production capacity allows us to cater to a wide range of specific customer needs - whether for small production runs or high-volume manufacturing.

Supported by our state-of-the-art production facilities across Europe, Asia, and North America, Sanner is a strong partner of choice to support our clients to bring medical devices to their local markets efficiently.



28.500 sqm of state-of-the art production space with available capacities. 11.000 sqm cleanroom space Class 7 & 8

Production footprint on three continents: Europa, North America, and Asia

Highest quality level, GMP compliant and DIN EN ISO 9001, ISO 15378, & ISO 13485 production space

150 engineers for design and development of devices and packaging

Contact us today to start your device design and production!

sales@sanner-group.com
www.sanner-group.com

And don't forget to visit us at:

PDA Vienna, #150 hall X2
PODD Boston, #26
CPHI Frankfurt, #0J92 hall 8

SANNER GROUP

Protecting Health.

PRECISION ENGINEERED – SEAMLESSLEY DELIVERED

As user expectations for device aesthetics, simplicity and quality continue to rise, the pressure on the medical device industry intensifies. Sanner empowers pharmaceutical and healthcare companies to meet these demands by uniting world-class design expertise, global manufacturing capabilities, regulatory know-how and operational excellence. From next-generation injection systems and drug delivery devices to innovative diagnostics and connected health solutions, Sanner delivers a comprehensive, single-source approach that accelerates time to market. Built on a foundation of quality, trust and shared purpose, Sanner stands ready to shape the future of medical device development in close partnership with its customers.

Charlie Bowen

Charlie Bowen is a mechanical engineer at Pfizer, with a passion for developing medical devices. For the past three years, Mr Bowen has been developing combination products for Pfizer at the Devices Centre of Excellence in Cambridge (UK).

T: +44 1304 640538
E: charlie.bowen@pfizer.com

Dr Jay Sayed

Jay Sayed, PhD, Principal Device Development Scientist at Pfizer, is a medical engineer with over 10 years of experience in drug-delivery device development. Based at Pfizer's Devices Centre of Excellence in Cambridge, Dr Sayed is focused on the development and manufacture of spring-driven autoinjectors.

T: +44 7590 537503
E: jay.sayed@pfizer.com

Harriet Field

Harriet Field, Laboratory Science Apprentice, has been working at Pfizer since 2021 through the Level 6 Laboratory Scientist apprenticeship programme. Ms Field joined the Device Centre of Excellence in 2024 and previously worked in Chemical R&D. As part of her apprenticeship, Ms Field is studying part-time towards a BSc chemistry qualification, and is now in her final year.

E: harriet.field@pfizer.com

Pfizer Inc
235 East 42nd Street, New York, NY 10017, United States
www.pfizer.co.uk

SUMMARY

If injection time performance is not properly predicted (including predictions for after shelf life), a device programme risks substantial cost and time overruns. The cost and time come from having to implement time-consuming and expensive component modifications and reverification testing.

Instead, device developers can use the new model described here to change the physical build-and-test loop into a mathematical model, which specifies acceptable force limits for easy BLEF tests early in the programme. These predictive tools will become increasingly essential for efficient and reliable device development as drug delivery systems evolve to accommodate more demanding formulations. The modelling software offers a practical solution by translating BLEF test data into more accurate forecasts of injection performance over a device's lifespan.

"DEVICE DEVELOPERS CAN USE THE NEW MODEL DESCRIBED HERE TO CHANGE THE PHYSICAL BUILD-AND-TEST LOOP INTO A MATHEMATICAL MODEL, WHICH SPECIFIES ACCEPTABLE FORCE LIMITS FOR EASY BLEF TESTS EARLY IN THE PROGRAMME."

MORE THAN THE SUM OF ITS PARTS: HOW SUPPLIER COLLABORATION DRIVES SUCCESSFUL COMBINATION PRODUCTS

gerresheimer
innovating for a better life

SHL MEDICAL

Aptar pharma

Bernd Zeiss of **Gerresheimer**, **Lucy Lee** of **SHL Medical** and **Sébastien Cordier** of **Aptar Pharma** discuss the multitudinous advantages of collaboration between suppliers and pharma partners, from boosting innovation to optimising component choices for device development early on, all while ensuring compliance with global regulatory standards.

In the dynamic field of pharmaceutical combination products, synergy between component suppliers and between suppliers and pharmaceutical companies is essential. Collaboration is especially crucial in the development of prefilled syringes (PFSs) for integration into autoinjectors. Such relationships go beyond simple transactions; they are true partnerships that enhance product performance, ensure regulatory compliance and anticipate future needs. Successful partnerships ultimately result in patient-centric combination products that are greater than the sum of their parts.

With the introduction of new industry guidance, such as the US FDA's Essential Drug Delivery Outputs (EDDO) for Devices Intended to Deliver Drugs and Biological Products,[1] close collaboration between companies is more critical than ever for the successful development of combination products.

Given the essential role each component supplier plays in creating robust systems, the key question becomes: how can we reduce R&D burden for pharmaceutical partners, minimise the risk of product failure during development and, at the same time, accelerate time to market? In response to this question,

Gerresheimer, Aptar Pharma and SHL Medical collaborated to collect functional and performance data on an autoinjector system (Figure 1). The system incorporated Gerresheimer's premium quality Gx® Elite syringe and an Aptar Premium Coat® plunger stopper within the Molly® autoinjector platform from SHL Medical. This joint effort exemplifies how shared expertise and early-stage data generation can streamline development and support pharma companies to achieve optimal outcomes for their combination products.

ENSURING COMPLIANCE AND PERFORMANCE IN AUTOINJECTOR-BASED COMBINATION PRODUCTS

Incorporating a PFS into an autoinjector presents unique challenges, as a high level of precision, reliability and seamless integration of components is required. Each element, such as the syringe barrel, elastomer and autoinjector mechanism, must function together to ensure the overall safety and effectiveness of the final combination product. Component suppliers play a critical role by proactively testing and validating their products against international standards, including the new United States Pharmacopeia (USP) <382> and USP <1382> chapters, ISO 11040-8 for PFSs, ISO 11608-1 and 11608-5 for autoinjectors and the FDA's EDDO.[1]

USP <382>

This general chapter addresses the fitness-for-use functional requirements for packaging/delivery systems that are intended for parenteral dosage forms and include primary packaging components partially or completely made of elastomeric material. With regards to PFSs, break-loose and gliding forces (BLGF), needle shield functionality, plunger seal integrity, as well as integrity testing, are all within the scope of USP <382>.

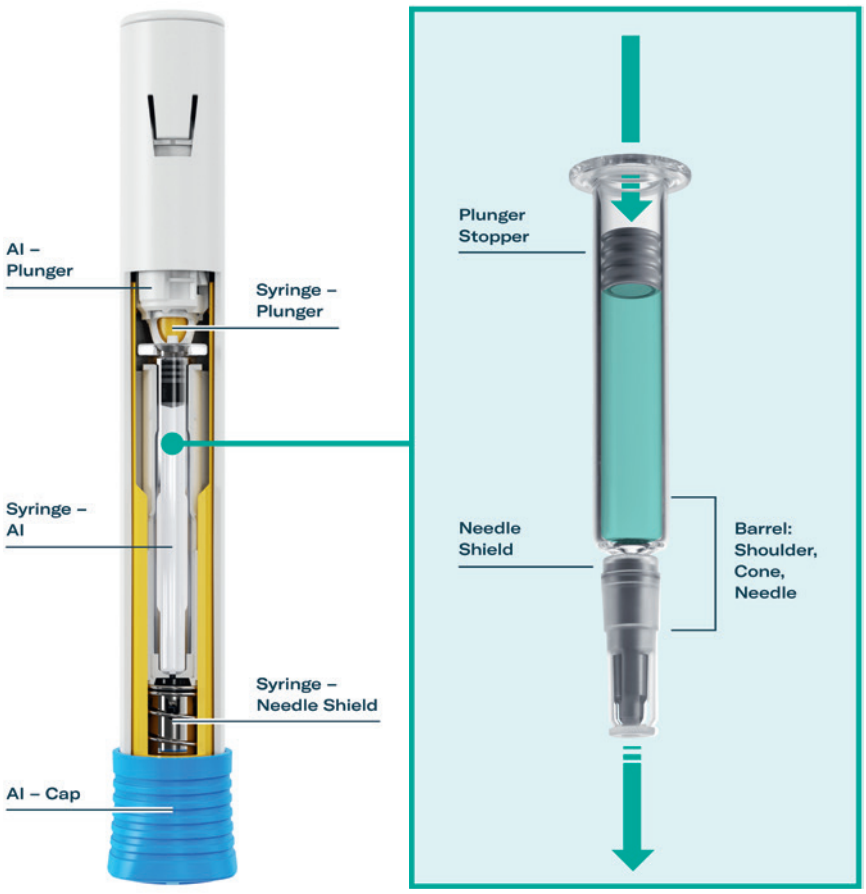


Figure 1: Interface between the autoinjector, syringe, needle shield and plunger stopper. The image shows SHL Medical's Molly® modular platform autoinjector with Gerresheimer's Gx® Elite 2.25 mL long glass syringe and Aptar Pharma's PremiumCoat® plunger stopper.

ISO 11040-8

ISO 11040-8 is part of the ISO 11040 series, which focuses on packaging systems and components for pharmaceutical use. ISO 11040-8 deals specifically with "finished PFSs" used to deliver medications. This norm covers design, functionality, safety and materials of PFSs to ensure that they meet the requirements necessary for safe and effective use without compromising safety or integrity. It includes aspects such as dimensional requirements, performance testing and usability features critical to healthcare professionals and end-users.

ISO 11608-1 and ISO 11608-5

The ISO 11608 series, especially Parts 1 and 5, addresses functional requirements and test methods for automated functions in needle-based injection systems. The standards outline the necessary criteria to evaluate devices that incorporate automated features such as dose delivery and needle insertion. Key elements covered in this norm include dose delivery mechanisms, performance testing, safety, usability and mechanical requirements. It helps manufacturers to design and develop reliable and safe devices for self-administering drugs, facilitating regulatory approval and enhancing user trust in automated medical devices.

FDA EDDO for Devices Intended to Deliver Drugs and Biological Products

When developing devices intended for the delivery of drugs and biological products it is, of course, critical to consider essential drug delivery outputs for efficacy, safety and

"THIS JOINT EFFORT EXEMPLIFIES HOW SHARED EXPERTISE AND EARLY-STAGE DATA GENERATION CAN STREAMLINE DEVELOPMENT AND SUPPORT PHARMA COMPANIES TO ACHIEVE OPTIMAL OUTCOMES FOR THEIR COMBINATION PRODUCTS."

regulatory compliance. The FDA provides guidance on these aspects. Suppliers can pre-test some EDDO aspects to reduce burden at later stages of combination product development. These include dose accuracy and precision, rate of delivery, user interface and usability, reliability and robustness, safety and risk mitigation.

"BY PROVIDING SUCH COMPREHENSIVE DATA, SUPPLIERS HELP PHARMACEUTICAL COMPANIES SELECT OPTIMAL COMPONENTS WITHOUT STARTING DEVELOPMENT FROM SCRATCH, WHICH CAN ACCELERATE TIMELINES AND REDUCE RISK."

LAYING THE FOUNDATION FOR SUCCESSFUL COMBINATION PRODUCT DEVELOPMENT THROUGH SYSTEM INTEGRATION

Based on their knowledge and experience of the system's physical performance, component suppliers can generate valuable, drug-agnostic platform data by making informed assumptions about typical use cases. This approach enables performance verification of autoinjector systems and syringe components through key tests, including:

- **Needle-shield Pull-off Force (PoF):** Assessing ease of removal while maintaining sterility.
- **BLGF:** Simulating injection forces with model liquids.
- **Autoinjector Fit:** Ensuring dimensional and functional compatibility.

By providing such comprehensive data, suppliers help pharmaceutical companies select optimal components without starting development from scratch, which can accelerate timelines and reduce risk. In addition to platform development, supplier-affiliated or independent laboratories can conduct stability studies, clinical simulations and human factors testing. Such a collaborative, forward-looking approach lays the foundation for successful combination product development and regulatory design verification.

Risk assessment also plays a crucial role in system testing. Suppliers must evaluate the risk of component failure and develop mitigation strategies. For instance, the predictability of BLGFs is generally high, and the spring force of the autoinjector can be adapted to meet specific performance requirements (Table 1).

Interface of Syringe Barrel and Elastomer Components

The interfaces between the syringe barrel and elastomer caps/needle shields, as well as the elastomer plunger stopper, are critical for the device's physical functionality. Figure 1 shows physical influencing factors, which can be either drug dependent or drug agnostic.

System performance	Essential performance requirements	Risk of failure – supplier assessment	Contributing part of the system			Risk of failure	Risk-mitigation strategies through supplier collaboration
			Components	Syringe	Autoinjector		
Break-loose and gliding force	Forces enable manual injection or autoinjector integration	Mostly predictable based on solution properties	✓	✓	(✓)	Low to moderate	Generate platform datasets to predict real case results. Spring force of autoinjector can be adapted for compatibility with gliding and break-loose forces
Finger flange and cone break	PFS resistance higher than spring force	Drug independent		✓	✓	Low	Comparison of PFS and autoinjector specifications. Resistance tests
Needle shield and cap removal force	Cap gripping force higher than RNS pull-off	Drug independent	✓	✓	✓	Low	Determination of RNS pull-off force, and comparison with autoinjector specification
Dimensional fit into autoinjector	Compatibility of key dimensions	Drug independent		✓	✓	Low	Comparison of key dimensional requirements and tolerances
Administration time	Acceptable time for subcutaneous injection	Mostly predictable based on solution properties	✓	✓	✓	Low to moderate	Integration of multiple parameters to anticipate results (BLGF, needle length, needle diameter, drug viscosity, etc.)

Table 1: Example of risk assessments conducted by component suppliers for autoinjector-based combination products.

"BLGF CURVES FROM TEST LABS, LIKE THOSE AT GERRESHEIMER AND APTAR PHARMA, HELP IN SELECTING THE OPTIMAL COMPONENTS."

USP <382> and USP <1382> chapters address and give guidance for the functionality data of these components. As a pharma company brings the final drug product to the market, it is ultimately their responsibility to comply with these standards. However, component suppliers can pre-test important drug-agnostic functional aspects of the device. These tests can include bracketing assessments with syringes filled with water for injection, or other model liquids to establish baseline performance data. Bracketing in this context means that well-functioning combinations will be suggested to pharma partners as a platform, while less optimal systems will not be recommended in the first place. Testing and evaluating various syringe barrel-to-elastomer interfaces help define the container, which eventually gets assembled inside the autoinjector. Such platform test data are invaluable for defining the best primary packaging combination mounted inside the device according to its intended use. For example, BLGF curves from test labs, like those at Gerresheimer and Aptar Pharma, help in selecting the optimal components.

Drug-Agnostic Versus Drug-Dependent Syringe Features

Reliable testing of basic requirements can be carried out by component suppliers if they work collaboratively. Some tests are entirely independent from the drug properties and mainly material-related. They can easily be carried out by suppliers alone. System requirement tests depend on the properties of the liquid but are mainly physical by nature. Hence, tests can be carried out with model liquids so the device as a system can be adapted by suppliers prior to drug substance exposure. Data from supplier co-operation help to identify the optimal syringe system and autoinjector layout. When it comes to the finished drug product of a PFS or a syringe mounted into an autoinjector, true drug-dependent testing needs to be performed, which can only be undertaken in pharma labs (Figure 2).

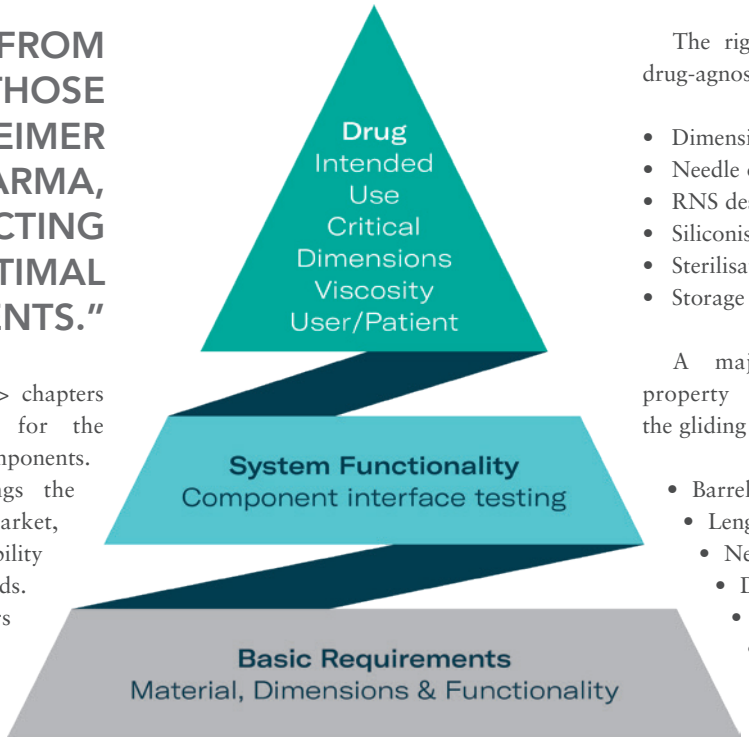


Figure 2: Three levels of syringe and device functionality: alongside basic material information, suppliers can contribute to general functionality by providing platform test data prior to testing the finished drug product.

The rigid needle shield (RNS) PoF is drug-agnostic by nature, which depends on:

- Dimensions of the cone
- Needle outer diameter (OD)
- RNS design and material
- Siliconisation
- Sterilisation influence
- Storage time and conditions.

A major liquid-dependent syringe property is combined BLGF. Mainly, the gliding force is strongly influenced by:

- Barrel material
- Length and inner diameter (ID)
- Needle length and ID
- Drug viscosity
- Elastomer type and design
- Siliconisation type and amount
- Stoppering method
- Storage time and conditions
- Speed parameters applied.

To assess gliding force without a defined drug product, syringe suppliers can generate orientating data with model liquids that simulate drug properties.

Gerresheimer and Aptar Pharma conducted a series of tests (Figure 3) of the 2.25 mL Gerresheimer Gx® Elite syringe to show general performance of the syringe system. Often, autoinjectors are stored at lower temperatures, for example, in a patient's fridge before use. Thus removing the cap can lead to unacceptably high PoF. Tests show that storage at 5°C has no significant influence on PoF after adapting

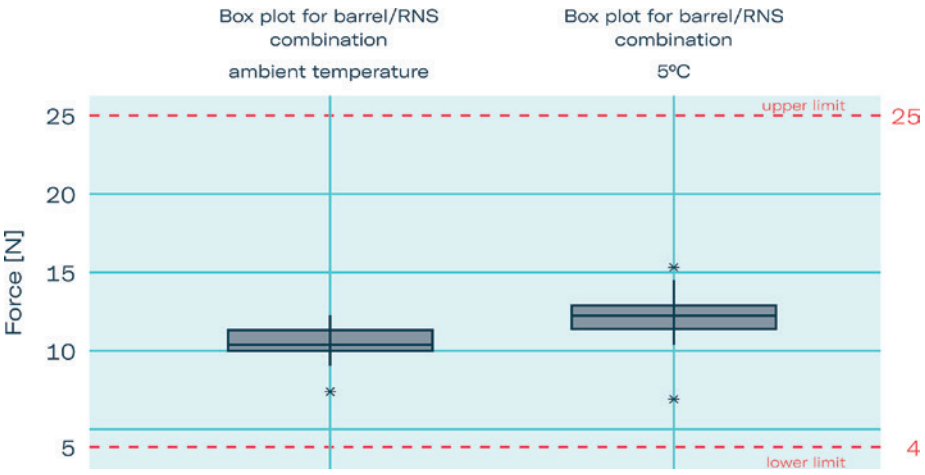


Figure 3: Box plot showing RNS pull-off force with optimised cone/RNS interface, ambient temperature versus cold storage 5°C (worst case).

the cone-elastomer interface. RNS PoF with optimised cone/RNS interface was tested at room temperature with a mean of 10.59 N and in cold storage at 5°C with a mean of 12.16 N. These were considered to be good results, as standard PoF values for PFSs today are 30 N or higher.

Interface of PFS and Autoinjector

Achieving seamless integration between a syringe barrel and autoinjector is essential, as it directly impacts the functionality, safety and reliability of the final combination product. Some performance parameters are drug-agnostic and can be pre-assessed early in development. These include factors such as needle-shield removal force, activation force and overall mechanical compatibility between components. More functional parameters such as BLGF, or injection time are dependent on the physical properties of the drug formulation. They can also be pre-assessed by suppliers with information provided by pharma partners.

Such pre-assessments allow suppliers to identify potential risks, optimise component fit and ensure compliance with relevant standards before drug-specific testing begins (Figure 2). By using platform performance data, suppliers can recommend the most suitable materials and components for the combination product. These shared, early-stage data not only streamline development but also de-risk the pharmaceutical company's choice of primary container, reducing costly design iterations and accelerating time to market.

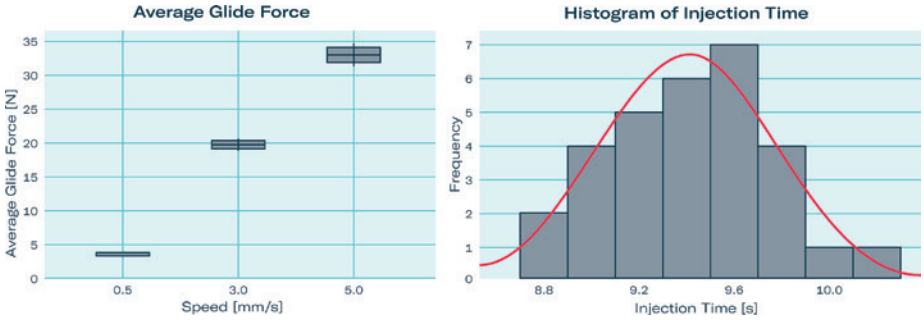


Figure 4: Liquid-dependent performance features: average glide force (1) and injection time (2) of a 2.25 mL Gx® Elite syringe 27 G thin wall, ID 0.28 mm, with PremiumCoat® plunger mounted in SHL Molly; tested with 15 cPs water-based solution.

Drug-Agnostic and Liquid-Dependent System Features

There are basic liquid-agnostic features of PFSs in autoinjectors that need to be tested and approved, such as dimensional fit, needle-shield removal force, activation force (choosing fitting spring) and penetration force (needle OD and gauge). More complex are liquid-dependent syringe-autoinjector system features, such as dose accuracy, delivered dose, average glide force and injection time. Needle ID, drug viscosity, drug density and temperature, as well as needle extension, can heavily affect the system's functionality.

The liquid-dependent performance features of average glide force and injection time were tested by Gerresheimer, SHL Medical and Aptar Pharma in a joint study. As with the PoF tests shown in Figure 3, a 2.25 mL Gx® Elite syringe with 27 G thin wall and 0.28 mm ID was used for testing. The syringe was filled with a glycerin solution of 15 cP, stoppered with the PremiumCoat® plunger from Aptar Pharma and assembled into the Molly® autoinjector from SHL Medical. Average glide force was 3.66 N at 0.5 mm/s and 33.01 N at a higher injection speed of 5 mm/s. With this system layout, injection time was measured at 9.41 s, which is a frequently used target value for autoinjector applications (Figure 4).

CONCLUSION

SHL Medical, Aptar Pharma and Gerresheimer demonstrate the critical role of collaboration between pharmaceutical companies and component suppliers in the successful development of autoinjector-based combination products. The more

"PRE-ASSESSMENTS ALLOW SUPPLIERS TO IDENTIFY POTENTIAL RISKS, OPTIMISE COMPONENT FIT AND ENSURE COMPLIANCE WITH RELEVANT STANDARDS BEFORE DRUG-SPECIFIC TESTING BEGINS."

"THE MORE LIQUID-RELATED INFORMATION AVAILABLE EARLY ON, THE EASIER IT IS TO RECOMMEND AN AUTOINJECTOR SYSTEM."

liquid-related information available early on, the easier it is to recommend an autoinjector system. From syringe barrels and elastomeric components to the autoinjector itself, each element must be precisely engineered and seamlessly integrated to meet the stringent performance and regulatory requirements of today's combination drug delivery systems.

Close co-operation between suppliers and pharmaceutical partners enables early identification of liquid-agnostic performance factors. It also supports comprehensive risk assessments and provides access to robust platform data. This not only helps to de-risk the selection of components – such as plunger stoppers, needle shields and primary containers – but can also accelerate development timelines and reduce the need for costly, late-stage redesigns.

By applying their respective areas of expertise, suppliers can recommend optimal materials and configurations tailored to pharmaceutical needs. Pharma companies benefit from data-driven decisions and more efficient progression through development and regulatory milestones. Ultimately, the final combination products are not only safe and effective, but also patient centric and commercially viable.

In short, seamless collaboration between device, component and pharmaceutical stakeholders establishes a foundation for innovation, efficiency and long-term success – delivering solutions that are truly greater than the sum of their parts.

REFERENCE

1. *"Guidance for Industry: Drug Delivery Outputs for Devices Intended to Deliver Drugs and Biological Products". US FDA, Jun 2024.*

Bernd Zeiss

Bernd Zeiss is Head of Scientific Affairs & Applied Technologies at Gerresheimer. A biologist by education, he graduated from the University of Göttingen, Germany. After several years working as a biostatistician, in lab automation, pharma sales and technical support, he now focuses on medical devices for injectables and has deep expertise in drug-container interactions, device functionality and fill-finish.

T: +49 5223 164 309
E: bernd.zeiss@gerresheimer.com

Gerresheimer
Erich-Martens-Strasse 26-32, 32257 Bünde, Germany
www.gerresheimer.com

Lucy Lee

Lucy Lee is an Associate Director of Product Management at SHL Medical, leading the global product management of SHL's Molly modular platform autoinjectors. She brings with her more than 13 years of experience in autoinjector research and development, programme management of innovation projects, as well as manufacturing know-how.

T: +1 954 725 2130
E: lucy.lee@shl-medical.com

SHL Medical
588 Jim Moran Boulevard, Deerfield Beach, FL 33442, United States
www.shl-medical.com

Sébastien Cordier

Sébastien Cordier is Technical Product Manager at Aptar Pharma's Injectables division. A graduate of MINES ParisTech and EDHEC Business School in France, Mr Cordier spent over 15 years in the automotive industry, where he developed a strong expertise in plastics and elastomers, before joining Aptar Pharma in 2020. In his current role, Mr Cordier is responsible for the PreFilled Syringe Platform, which includes PremiumCoat® syringe plungers and is dedicated to supporting customer development projects with coated elastomeric solutions.

T: +33 6 3170 5278
E: sebastien.cordier@aptar.com

Aptar Pharma
12 14 Rue Louis Blériot, 92500 Rueil Malmaison, France
www.aptar.com

Gx® Elite Syringe Platform

Best-in-class SIN syringes designed to administer biologics and highly sensitive drug molecules

CPHI Worldwide I October 28–30, 2025 | Frankfurt, Germany I Booth #8.0G8

Ultra low tungsten levels to lower protein interaction risk

Optimized design for best AI compatibility

Comprehensive test data on performance and interactions

Optimized siliconization options: very low silicone-oil, silicone-oil-free and baked-on

gerresheimer.com

gerresheimer
innovating for a better life

CUSTOM METAL SOLUTIONS FOR EMERGING CHALLENGES IN AUTOINJECTOR SYSTEMS

Iker Ibisate, **Álvaro García Nograro** and **Irakusne Incierte**, all at **RPK Medical**, address the complex manufacturing challenges posed by increasingly sophisticated autoinjector devices and introduce RPK Medical's approach as a technical partner in overcoming these challenges through the tailored design and manufacture of functional metal components, such as precision springs and stamped parts.

The autoinjector device market is experiencing rapid growth, driven by the increasing demand for home-based treatments, biologic therapies and greater patient autonomy. These increasingly sophisticated devices pose complex engineering challenges related to miniaturisation, the delivery of highly viscous drugs, precise flow control, safe skin contact and digital connectivity. RPK Medical's solutions not only address these challenges but also significantly contribute to the clinical and commercial success of next-generation drug delivery devices, positioning the company as a key player in the industry.

The autoinjector market is expanding at a double-digit rate, primarily driven by the growth of biologic therapies and the increasing preference for self-administration outside hospital settings. These devices must be safe, user-friendly and compatible with increasingly complex drug formulations. Simultaneously, they must meet new demands surrounding portability, sustainability, connectivity and regulatory compliance.

In this context, precision mechanical engineering plays a pivotal role. Components such as compression springs, stamped parts or metal contacts are no longer mere structural aids; they perform critical functions, including needle deployment, plunger actuation, flow control and dose delivery. With its extensive expertise in designing and manufacturing metallic components for medical devices, RPK Medical provides tailored solutions

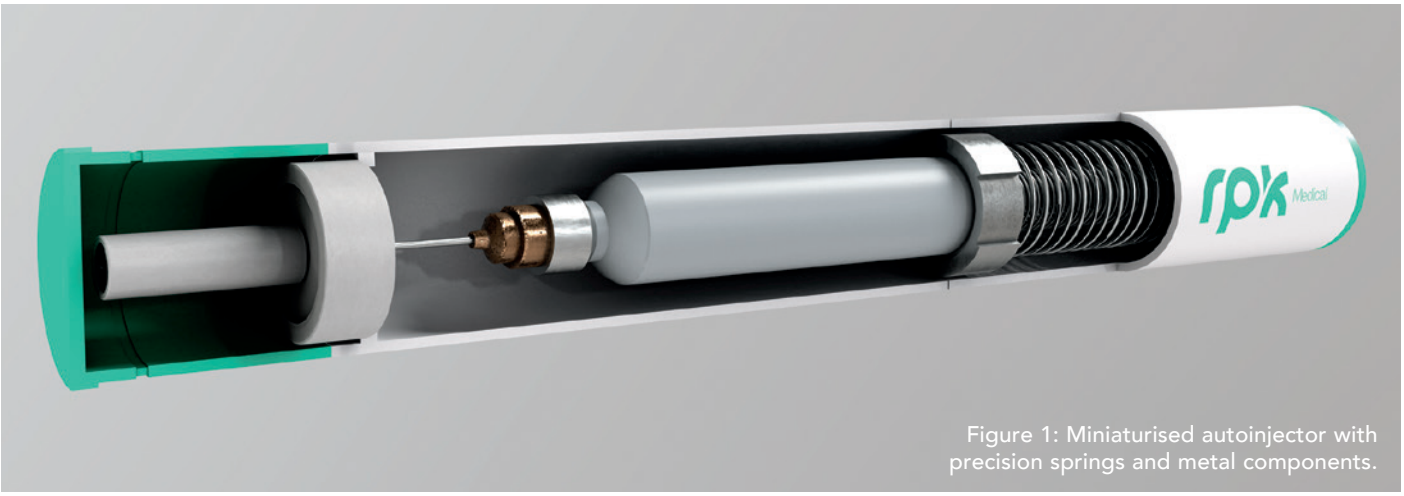


Figure 1: Miniaturised autoinjector with precision springs and metal components.

"WITH ITS EXTENSIVE EXPERTISE IN DESIGNING AND MANUFACTURING METALLIC COMPONENTS FOR MEDICAL DEVICES, RPK MEDICAL PROVIDES TAILORED SOLUTIONS THAT EFFECTIVELY AND RELIABLY ADDRESS THESE CHALLENGES, INSTILLING CONFIDENCE IN THE COMPANY'S ABILITY TO MEET CLIENT NEEDS."

that effectively and reliably address these challenges, instilling confidence in the company's ability to meet client needs.

MINIATURISATION: FUNCTIONALITY IN COMPACT FORMATS

The trend towards more ergonomic, portable and sustainable autoinjectors requires a significant reduction in component size and volume, without compromising critical functions, such as activation, needle retraction, sensor integration or visual/acoustic indicators, posing a significant engineering challenge. Miniaturisation addresses the clinical need for discreet, user-friendly and easily disposable devices, enhancing patient satisfaction and overall experience (Figure 1).

However, reduced space makes the inclusion of essential safety mechanisms – such as needle locks or post-use protection features – difficult, demanding optimal use of every single millimetre of internal design. This need for precision requires components to be manufactured to extremely tight tolerances to ensure precise assembly and reliable operation in compact devices. Some of the technical challenges include:

- Space limitations for critical mechanisms
- Strict dimensional tolerances to prevent assembly errors
- Co-existence with electronics, batteries or actuators in constrained areas.

RPK Medical's solutions include:

- Micro-springs optimised for compact geometries using finite element analysis
- Multifunctional stamped parts combining structural and mechanical roles
- Rapid prototyping and co-engineering for agile design iteration.

DELIVERY OF HIGHLY VISCOUS DRUGS

Modern biologic therapies – such as monoclonal antibodies and advanced treatments for immune, oncologic or neurodegenerative conditions – are often highly viscous, making them difficult to administer with conventional autoinjectors. They require greater plunger force and precise speed control to prevent pain, dosing errors or incomplete injections. These concentrated formulations offer more capable, longer-acting treatments, but they require injection solutions adapted to their rheological properties (Figure 2).

Delivering highly viscous fluids requires overcoming greater resistance and carefully modulating the flow to avoid discomfort or underdosing – especially during slow subcutaneous injections that last 30 seconds or more. It is crucial to prevent both flow drops and pressure spikes, as these can compromise patient experience or treatment efficacy. The core challenge is designing mechanisms capable of delivering these formulations reliably, safely and almost imperceptibly to the user.

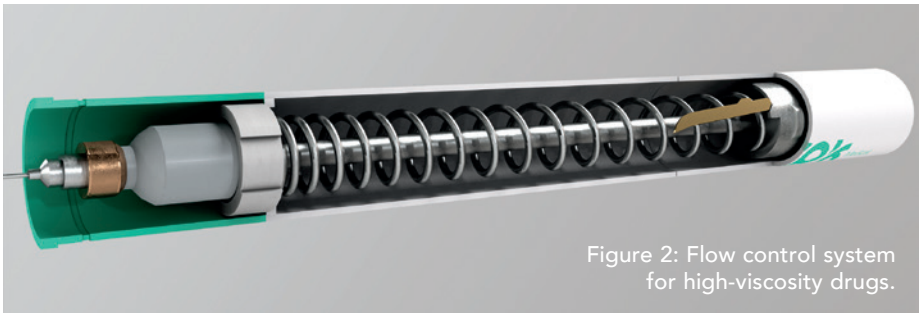


Figure 2: Flow control system for high-viscosity drugs.

Some of the technical challenges include:

- High plunger resistance
- Risk of interrupted or partial dosing
- Need to maintain comfort and pressure control throughout administration.

RPK Medical's solutions include:

- High-force springs in 17-7PH stainless steel or other specialised alloys
- Multistage mechanisms (e.g. concentric or telescopic springs) to modulate energy
- Rheological simulation and testing to match component behaviour to drug profiles.

FLOW CONTROL: STABILITY AND THERAPEUTIC EFFECTIVENESS

Maintaining a consistent injection flow rate is crucial for both therapeutic efficacy and patient comfort, as abrupt flow variations can lead to pain, bruising, poor absorption or subtherapeutic dosing. Unstable flow profiles may affect both the effectiveness of the drug and user acceptance of the device, eroding trust in treatment. This requirement becomes even more critical for smart autoinjectors and wearable systems (on-body delivery systems), which must deliver medication predictably over set intervals – from seconds to minutes – in accordance with clinical guidelines.

Patient comfort depends on smooth, uninterrupted delivery, while regulatory standards require consistent flow performance across all devices and uses, presenting major design, validation and quality control challenges. Some of the technical challenges include:

- Internal pressure variability due to changes in viscosity or temperature
- Limited space for active controllers
- Regulatory demands for flow reproducibility.

RPK Medical's solutions include:

- Constant-force springs for stable plunger actuation
- Calibrated stamped parts used as flow restrictors, passive valves, or energy dissipators
- Mechanical alternatives to electronic pumps or actuators.

"PATIENT COMFORT DEPENDS ON SMOOTH, UNINTERRUPTED DELIVERY, WHILE REGULATORY STANDARDS REQUIRE CONSISTENT FLOW PERFORMANCE ACROSS ALL DEVICES AND USES, PRESENTING MAJOR DESIGN, VALIDATION AND QUALITY CONTROL CHALLENGES."

RELIABLE SKIN CONTACT

The interaction between the autoinjector and the skin is a critical clinical and technical factor. Poor contact may result in failed administration, surface injury or loss of user confidence. Devices must adapt to varying body morphologies, applied pressure levels and application zones (such as the abdomen, thigh and arm), all with different curvatures and mobility, while preventing slippage or accidental triggering. The challenge intensifies in unsupervised home settings or among vulnerable populations (e.g. the elderly or those with limited mobility), where application errors may have a serious impact on health. Therefore, the physical interface must be designed with maximum ergonomics and safety in mind, ensuring the device only activates when optimal skin contact is achieved – accounting for skin thickness, hair, sweat and irregular surfaces (Figure 3). Some of the technical challenges include:

- Anatomical variability and inconsistent manual pressure
- Risk of incomplete or accidental activation
- Need for clear mechanical feedback to the user.

RPK Medical's solutions include:

- Calibrated springs ensure consistent skin contact pressure
- Sensor-stamped parts that only trigger activation under optimal conditions
- Passive fixation systems or mechanical suction cups for wearable applications.

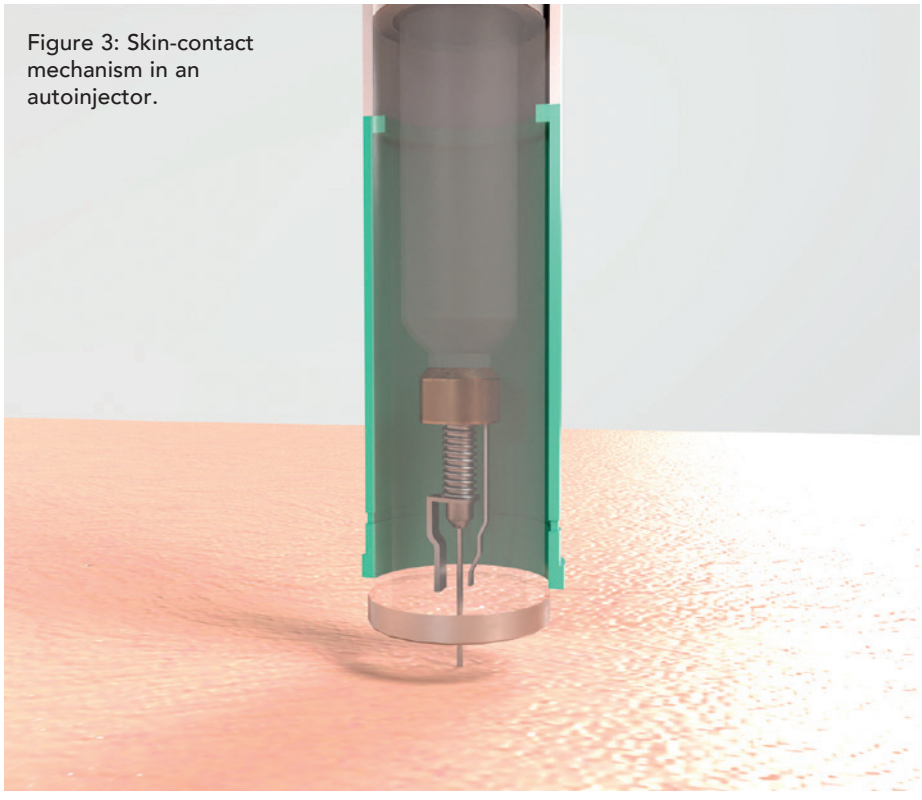


Figure 3: Skin-contact mechanism in an autoinjector.

CONNECTIVITY AND DIGITAL INTEGRATION

The digital evolution of next-generation autoinjectors – featuring sensors, data logging and wireless connectivity – enables usage tracking, personalised dosing and app integration, aligning with trends in telemedicine and remote monitoring (Figure 4). However, this shift creates technical challenges that require electrically reliable, electromagnetic interference (EMI)-compatible metal components to integrate seamlessly within the electronic architecture.

Traditional elements, such as springs, must now serve additional functions – conducting signals or acting as antennas – while maintaining their mechanical roles. This necessitates careful consideration of conductivity, inductance and shielding. Electrical reliability is critical – issues such as poor contact or corrosion could compromise data transmission, dose logging or even treatment safety. Devices must also resist electrostatic discharge (ESD) from users or the environment, without unintentional activation or damage, placing precision engineering at the core of hybrid, connected systems. Some of the technical challenges include:

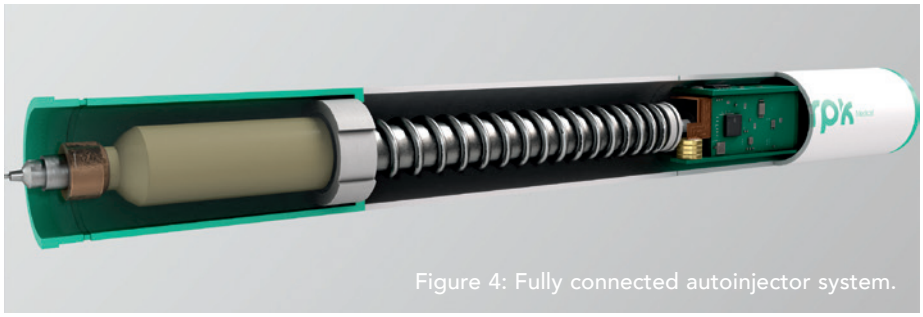


Figure 4: Fully connected autoinjector system.

- Space constraints amid increased electronic integration
- Demands for durable, stable electrical contacts
- EMI/ESD compatibility requirements.

"THE DIGITAL EVOLUTION OF NEXT-GENERATION AUTOINJECTORS – FEATURING SENSORS, DATA LOGGING AND WIRELESS CONNECTIVITY – ENABLES USAGE TRACKING, PERSONALISED DOSING AND APP INTEGRATION, ALIGNING WITH TRENDS IN TELEMEDICINE AND REMOTE MONITORING."

RPK Medical's solutions include:

- Low-resistance, high-repeatability contact springs
- Conductive or shielded stamped parts to minimise interference
- Integrated electromechanical subassemblies through automated assembly.

CONCLUSION

These challenges demonstrate that precision mechanics are fundamental to modern autoinjector design. As drug delivery evolves, devices must be as dependable as the therapies they deliver. Collaboration between system designers and component manufacturers enables the development of more efficient, safe and compliant devices. Co-engineering, combined with the use of structural simulation or rapid prototyping, allows early-stage iteration and validation before full-scale production.

The development of next-generation autoinjectors requires innovation not only in electronics and software but also in the mechanical design of their core components. Emerging challenges, including miniaturisation, viscosity, flow control, safety and connectivity, must be addressed holistically, with precision metal engineering playing a central role. The technical solutions outlined in this article – from specialised micro-springs to multifunctional stamped components – demonstrate how tailored mechanics can solve complex problems while enhancing safety and therapeutic performance.

The transition to smaller, connected devices suited for advanced therapies will only succeed if the underlying mechanical challenges are solved. RPK Medical delivers custom metal solutions for each of these challenges, enabling the development of safe and effective devices aligned with the future of personalised medicine. With a global footprint and ISO 13485 certification, RPK Medical is a strategic partner for drug delivery engineering – from design to series production.

Iker Ibisate

Iker Ibisate serves as Head of Stamped and Formed Products for Medical Applications at RPK Medical, bringing over 20 years of experience in product development engineering. He specialises in designing and manufacturing metal components from strip materials, including steel, aluminium and conductive alloys, using advanced multislide forming technologies. Combining deep technical expertise with a collaborative, client-focused approach, he helps optimise both design and production costs. His leadership enables RPK Medical to deliver precision-engineered solutions for complex challenges in autoinjectors, such as miniaturisation, controlled drug flow and seamless integration of electronic components, ensuring the safety, reliability and performance of next-generation medical devices.

T: +34 945 276 050
E: i.ibisate@rpk.es

Álvaro García Nograro

Álvaro García Nograro, a Key Account Manager in the Sales Department at RPK Medical, is a specialist in the medical sector. His international experience in the Americas and Asia has equipped him with a deep understanding of diverse markets. Mr Nograro's role involves managing components for medical devices, such as autoinjectors, inhalation devices and surgical tools. His multidisciplinary background enables him to collaborate closely with R&D, engineering and operations teams, delivering high-quality solutions tailored to the needs of global customers. His primary focus is on building long-term partnerships, supporting innovation and contributing to the advancement of medical technologies worldwide.

T: +34 619 210 881
E: alvaro.garcia@rpk.es

RPK Medical
Portal de Gamarra 34, 01013 Vitoria-Gasteiz, Spain
www.rpk-medical.com

Irakusne Incierte

After 15 years of working in Mexico across various industrial sectors, Irakusne Incierte has served as a Business Developer in the medical division of the RPK Group in North America since 2023, focusing on the drug delivery and medical devices markets. She holds a master's degree in International Trade from the prestigious ICEX-CECO business school, which is part of the Ministry of Economy, Trade and Industry of the Spanish Government.

T: +52 1 461 346 6297
E: irakusne@rpk.com.mx

RPK Medical
Oriente 5 No. 132, Cd Industrial, Emiliano Zapata, 38010 Celaya, Guanajuato, Mexico
www.rpk-medical.com

Excellence for your autoinjectors and peninjectors

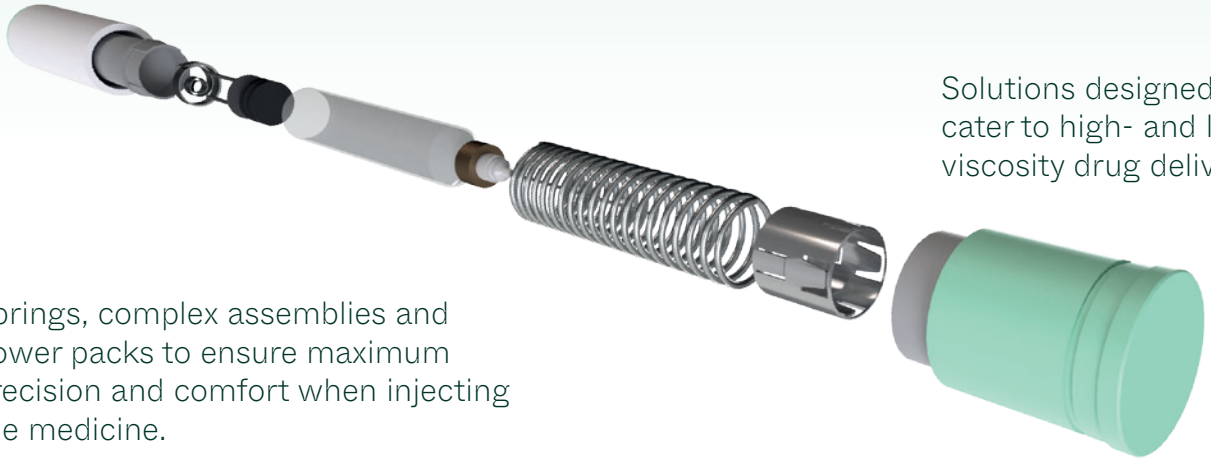
Join us at PDA, PODD and Pharmapack!

Tailor-made solutions in springs, stamping & bending and assemblies for enhanced autoinjector and pen injector performance and patient safety.

Precision components for 2- or 3-step autoinjectors that provide clear, audible, visual and tactile feedback.

Ensure maximum accuracy in every dose with our springs and metal parts.

Automatic spring-based needle shielding before and after the injection.



Solutions designed to cater to high- and low-viscosity drug delivery.

Springs, complex assemblies and power packs to ensure maximum precision and comfort when injecting the medicine.

rpk-medical.com

rpk Medical

HOW COC SYRINGES ARE SHAPING THE FUTURE OF INJECTABLE DRUG DELIVERY

Tom Van Ginneken of **Wirthwein Medical**

explores the advantages of cyclo-olefin copolymer syringes, including where they outperform glass, which applications benefit most and why many common objections are outdated or debunked by current data, market adoption and technological advances.

In the ever-evolving landscape of injectable drug delivery, packaging and injection products play a crucial, yet often underappreciated, role in ensuring product safety, stability, usability and manufacturability. While borosilicate glass syringes have served the pharmaceutical industry well for multiple decades, new biologics, personalised therapies and complex drug formulations are demanding more and more from their delivery systems. Enter cyclo-olefin copolymer (COC) syringes – a modern, high-performance polymer-based alternative designed to meet the needs of both today's and tomorrow's drug products.

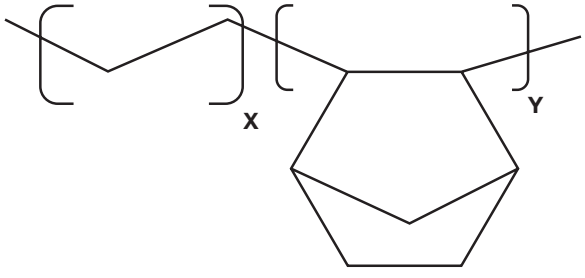


Figure 1: Chemical structure of cyclo-olefin copolymer.

WHAT SETS COC APART AS A PACKAGING MATERIAL?

COC is a high-performance polymer that has gained widespread acceptance in pharmaceutical packaging due to its outstanding functional properties (Figure 1). Originally

developed in the early 1990s as a new class of amorphous olefin-based polymers, COC has since evolved into a leading material platform for parenteral packaging, particularly for prefilled syringes and other drug delivery systems.

COC is composed of cyclic and linear olefins, polymerised to form a rigid, non-reactive structure. It offers an exceptional combination of features that make it highly suitable for sensitive and high-value drug products:

- **Superior Barrier Properties**: COC exhibits low permeability to moisture and oxygen, offering effective protection for moisture-sensitive APIs and biologics, while supporting an extended shelf life.
- **Chemical Inertness and Low Extractables**: Unlike glass, COC contains no heavy metals or ions, eliminating the risk of ion leaching, thereby maintaining drug purity.
- **No pH Shift**: COC does not interact with aqueous drug solutions in a way that alters pH, maintaining formulation integrity over time – a critical factor for stability in biologics and vaccines.
- **Excellent Optical Clarity**: The material's high transparency enables easy visual inspection of the filled product, meeting strict quality control requirements.
- **Dimensional Stability and Precision**: COC's robust mechanical properties allow for high-precision injection moulding, ensuring consistent part geometry with tight tolerances and overall little product variation.
- **Hydrophobic Surface**: COC's non-polar, hydrophobic nature reduces protein adsorption, preserving the structural integrity of protein-based drugs and minimising aggregation risks.

WHY CONSIDER COC SYRINGES?

When choosing a primary container for parenteral drug delivery, COC syringes offer more than just material advantages. Their comprehensive system design – inert material, cutting-edge cross-linked siliconisation, fully automated cleanroom production, high-quality rubber components and breakage-free performance – makes them an ideal solution for ensuring patient safety, drug stability, product integrity and manufacturing efficiency.

"ORIGINALLY DEVELOPED IN THE EARLY 1990S AS A NEW CLASS OF AMORPHOUS OLEFIN-BASED POLYMERS, COC HAS SINCE EVOLVED INTO A LEADING MATERIAL PLATFORM FOR PARENTERAL PACKAGING, PARTICULARLY FOR PREFILLED SYRINGES AND OTHER DRUG DELIVERY SYSTEMS."

Cross-Linked Siliconisation

Cross-linked siliconisation is a next-level innovation that significantly reduces and immobilises the free silicone oil. This approach lowers sub-visible particle counts and minimises drug–silicone interactions, making COC syringes especially suitable for sensitive biologics and high-viscosity formulations.

Fully Automated, Human-Free Production

COC syringes are manufactured using a fully automated process, with no manual handling throughout production. This not only increases consistency and reduces variability but also eliminates the risk of human error and contamination.

Cleanroom Manufacturing for Ultra-Low Contamination

Every production step – from moulding to siliconisation and packaging – takes place within an ISO-classified cleanroom environment (Figure 2). This ensures the lowest possible bioburden and particulate contamination, aligning with the strictest regulatory and quality requirements.

Precision Moulding and Dimensional Accuracy

The injection-moulding process used for manufacturing COC syringes provides tight tolerances and excellent product reproducibility, which supports reliable functional performance as well as device integration in injection devices, infusion pumps and wearable drug delivery systems.

Figure 2: Production of COC syringes in a cleanroom – ensuring maximum product safety under controlled conditions.

ADVANTAGES OF COC SYRINGES OVER GLASS SYRINGES

Inert and Non-Reactive Container System

The borosilicate glass frequently used for pharmaceutical packaging is inorganic in nature, but multiple chemical elements are added to the silicon dioxide structure to make the glass more processable. These ions, such as sodium, can leach out of the glass structure and interact with the drug solution, potentially changing the pH of the solution. The hydrophilic, charged nature of the glass surface also promotes protein adsorption and aggregation, increasing the risk of denaturation and loss of drug efficacy. These interactions make borosilicate glass less ideal for modern biologic and high-value drug products.

COC, on the other hand, is free from ions and metal oxides, which eliminates the risk of drug interaction seen in some borosilicate glass compositions. Its non-polar, hydrophobic surface dramatically reduces the adsorption of proteins, peptides and other sensitive molecules, which is key for preserving drug stability, especially in sensitive biologic molecules and other advanced therapies.

Dimensional Precision and Consistency

Unlike glass syringes, which are subject to bigger tolerances inherent to the process of hot-forming the syringes out of glass tubes, COC syringes benefit from being manufactured using precision injection-moulding processes. This ensures tight dimensional tolerances, improving the consistency of product functionality and reducing mechanical failures in combination products such infusion pumps or injection devices.

Break Resistance and Patient Safety

COC syringes are shatter-proof, offering a clear safety advantage over glass, especially in home, paediatric or high-volume healthcare settings, reducing the risk of glass particulates, product recalls and potential patient harm. Furthermore, COC syringes are injection-moulded as a single piece, resulting in superior mechanical stability and structural integrity. Unlike glass syringes, where the Luer lock is added separately, the integrated Luer lock in COC syringes eliminates the risk of component separation or "needle pop-off" during injection or device use.

Low Drug Interaction with Cross-Linked Siliconisation

Cross-linked siliconisation is an advanced surface treatment used in COC syringes to ensure smooth gliding performance while minimising the drawbacks associated with traditional silicone oil lubrication. In this process, a silicone layer is chemically bonded and cross-linked to the inner surface of the syringe barrel, creating a stable, immobilised coating. Unlike conventional free silicone oil, which can migrate into the drug solution and lead to the formation of sub-visible particles, the cross-linked layer remains fixed in place,

significantly reducing the risk of particle generation and drug–silicone interaction.

Greater Design Freedom

COC syringes offer greater design freedom due to being manufactured via injection moulding, which allows for highly precise and customisable geometries. Unlike glass, which has limitations in shaping and tolerance control, COC can be moulded into complex, integrated forms with tight dimensional accuracy. This enables the creation of features such as customised integrated Luer locks, optimised finger flanges or custom barrel designs tailored to specific drug delivery devices. Greater design flexibility supports better device integration, improved ergonomics and enhanced functionality for autoinjectors, wearable systems and specialised applications.

Safe and Reliable Performance in Cold Storage

In contrast with glass syringes, where leakage occurs after reaching a certain low temperature, COC syringes have been tested down to -180°C and still maintain their normal functionality and container closure integrity. The careful combination of COC (which has similar thermal expansion coefficient properties to halobutyl rubber), plunger rubber formulation, tight control of the syringe's inner diameter and cross-linked silicone can ensure that even the lowest temperatures do not affect COC syringes.

WHEN IS A COC SYRINGE THE RIGHT CHOICE?

Neither glass syringe nor COC syringes are perfect. Both have their strengths and weaknesses, and both have their merits in the right conditions (Table 1). Therefore, understanding the requirements and the intended use is paramount when choosing the right syringe for a given application. The following are some common applications where COC syringes might be chosen over glass syringes:

Biologics and Biosimilars

COC's inertness, low protein adsorption and particle control make it ideal for use with monoclonal antibodies, fusion proteins and complex formulations that would otherwise bind to or degrade in glass.

mRNA Therapies and Other Low-Temperature Storage Drugs

With messenger RNA (mRNA) vaccine storage often requiring cold-chain or cryogenic conditions, COC's thermal stability and container closure integrity outperform glass. COC has been successfully used for deep-freeze applications.

Silicone-Sensitive Formulations

For silicone-sensitive biologics, the immobilised silicone in cross-linked siliconisation reduce risks of aggregation or immune responses compared with free silicone oil.

Hyaluronic Acid and Other Aesthetic Injections

COC syringes are ideal for aesthetic applications, such as dermal filler injections, where safety, precision and comfort are critical. Their integrated Luer lock prevents needle pop-off, ensuring secure administration and enhanced patient safety. The homogenous cross-linked siliconisation and precisely controlled inner syringe diameter enable smooth, consistent dosing, while ergonomic design features support user comfort and control during high-force injections, benefiting both patient and practitioner.

IV Drugs

Unlike glass syringes, where incompatibility with needleless intravenous (IV) access systems can cause leakage and, in the worst cases, cone breakage, COC syringes provide a safe and reliable injection solution for all IV injections.

ADDRESSING COMMON OBJECTIONS TO POLYMER SYRINGES

Despite the growing adoption of COC syringes, some objections persist. Let us address them head-on:

"Polymers Are Too New"

COC is not new; it has been around for 30 years. Regulatory approvals for polymer syringes began more than 20 years ago, and they now support over 80 marketed drugs – including blockbusters – in over 90 regulated markets. This is not a leap into the unknown, it is a step towards proven innovation.

"Polymer Syringes Are Too Expensive Compared with Glass"

The assumption that polymers cost "several times more" than glass is outdated. Today, polymer syringe pricing is on par with standard biotech-grade glass syringes.

Glass Syringe	COC Syringes
• Known, traditional material • Market standard • No organic leachables • Great barrier properties • Multiple supply sources • Less scratch sensitive (e.g. during filling)	• No ion or heavy metal leaching • Low protein adsorption • No breakage • Maintain container closure integrity, even at extremely low temperatures • Very low contamination and sub-visible particles from siliconisation and production processes • Broad sterilisation options available (steam, ethylene oxide and irradiation) • Better compatibility with needleless access devices (e.g. IV connectors) • Dimensional accuracy and small tolerances • Greater design freedom for customisation (e.g. adaptation to cone, Luer lock or even bigger syringe formats)

Table 1: The respective strength of glass versus COC syringes.

When factoring in lower defect rates, fewer recalls, reduced breakage and improved device performance, the total cost of ownership can be significantly lower.

"Oxygen Permeation is a Major Issue in Polymers"

While it is true that COC is more permeable than glass, it is manageable. High-performance barrier labels, foil overwraps or secondary packaging can reduce oxygen ingress to acceptable levels, even for oxidation-sensitive molecules. These solutions are affordable and widely validated.

"Our Manufacturing Line is Built for Glass"

Many pharma companies have successfully adapted glass-compatible lines to handle COC syringes. With support from suppliers, often including technical assessments and change control documentation, polymer integration is frequently more feasible than assumed.

"The Supply Chain for Polymers is Too Risky"

This is not true anymore. The polymer syringe market now includes multiple qualified suppliers, including a second-source option using the same drug-contacting materials as the market leader. This allows for dual sourcing, reducing supply risk and enhancing flexibility.

THE BOTTOM LINE: FIT FOR THE FUTURE

Pharmaceutical development is advancing towards more complex, sensitive and patient-centric products. The delivery systems used must evolve in parallel. COC syringes offer:

- Superior safety through break resistance and low particulates
- Improved drug compatibility via inert surfaces and low adsorption
- Precision fit for high-tech devices
- Proven scalability and support for manufacturing and regulatory success
- Customisation to support safe and convenient patient-centric solutions.

While glass remains suitable for many conventional drugs, its limitations are being increasingly exposed by new therapeutic formats. COC syringes do not replace glass universally, but they offer a modern, performance-driven alternative where it matters most.

Figure 3: WIM Ject® COC syringes in a tub: A break-resistant and cross-linked silicone alternative to conventional glass syringes.

"WHILE GLASS REMAINS SUITABLE FOR MANY CONVENTIONAL DRUGS, ITS LIMITATIONS ARE BEING INCREASINGLY EXPOSED BY NEW THERAPEUTIC FORMATS."

Wirthwein Medical helps pharmaceutical manufacturers find the ideal syringe for their application by either offering a standardised COC syringe – WIM Ject® (Figure 3) – or go one step further and offer individualised syringe solutions depending on the drug and specific needs of the application. Whether it is building up a second source for an already commercial COC syringe or finding the right syringe for a new application, Wirthwein Medical is able and happy to support.

Tom Van Ginneken

Tom Van Ginneken, Head of Business Development, currently leads the business development activities at Wirthwein Medical, focusing on innovative solutions for pharmaceutical primary packaging. With over 20 years of experience in the pharma and healthcare industry, he has spent the majority of his career developing syringe systems and, over the last decade, has been a key driver in the adoption of COC syringes for a broadening range of applications. Mr Van Ginneken holds a degree in Chemical Engineering from the University of Antwerp (Belgium) and an MBA from the University of St Gallen (Switzerland).

E: tom.van-ginneken@wirthwein-medical.com

Wirthwein Medical GmbH & Co KG

Bahnhofstraße 80, 64367 Mühltal/Nieder-Ramstadt, Germany

www.wirthwein-medical.com

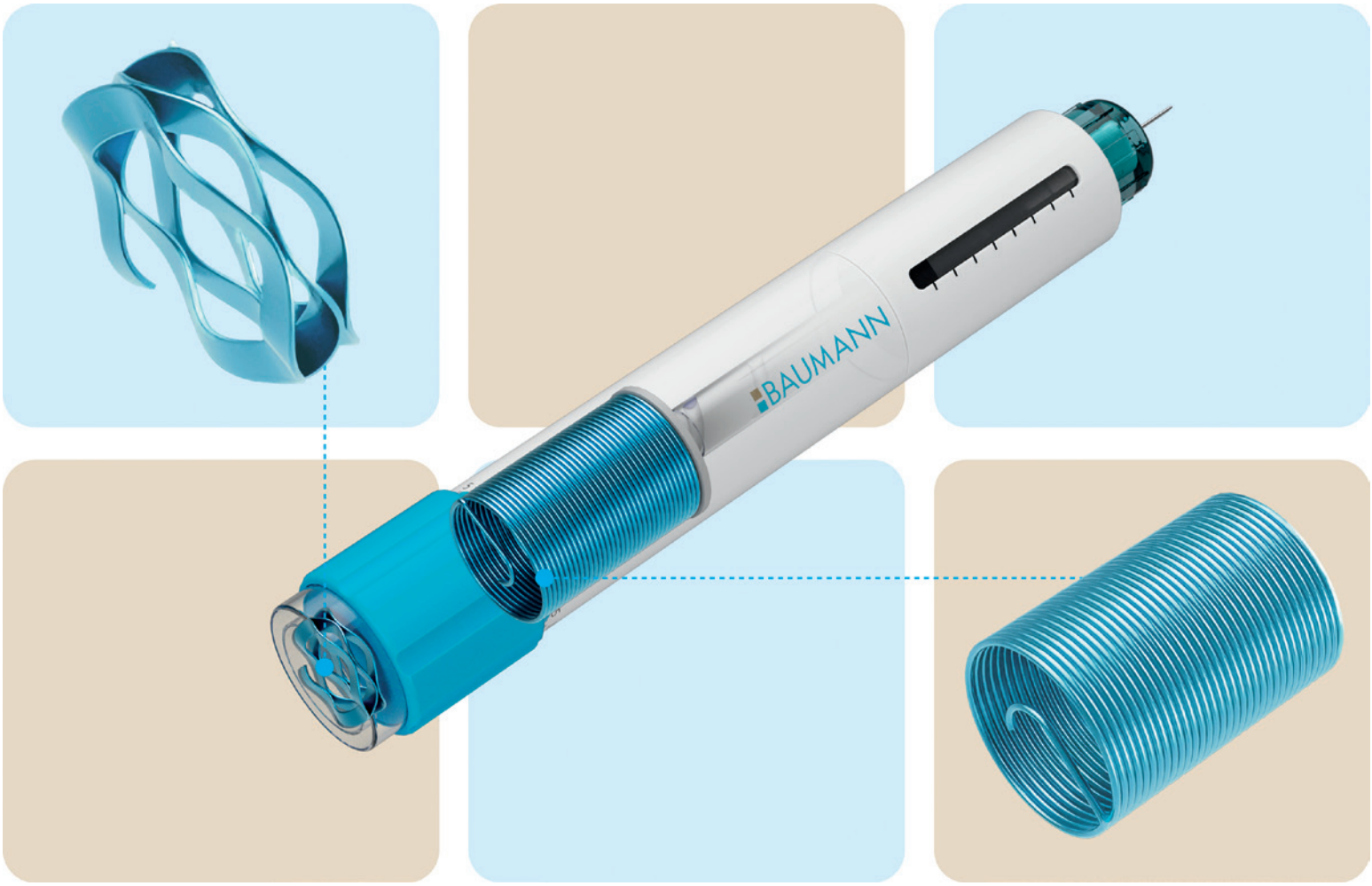
WIRTHWEIN

INJECTING CONFIDENCE WITH EVERY DOSE

WIMJect® - The prefillable COC syringe is a safe and reliable choice for drug storage and delivery, offering superior protection and drug stability for a broad range of drug applications.

Wirthwein Medical GmbH & Co. KG ▪ Bahnhofstraße 80 ▪ 64367 Mühltal

www.wirthwein-medical.com



ENSURING EXCELLENCE IN MANUFACTURING

David Pircher, **Pavel Zahradník** and **Maxime Ludwig**, all of **BAUMANN Medical**, discuss the medical mindset in the context of quality and present examples and tools that are used in practice.

A strong quality culture is the foundation of ensuring consistent product performance and customer satisfaction. Adherence to key principles such as zero defects, zero compromises and continuous improvement is central to maintaining high standards across all operations (Figure 1). When it comes to manufacturing, the focus should be on minimising variations and defects through stringent regulatory compliance, advanced quality control measures and process optimisation. Every employee within the company should be empowered to uphold quality standards, with ongoing training and development supporting this commitment. Risk management should be integrated throughout, using tools such as statistical process control (SPC) and failure mode

Figure 1: BAUMANN Medical adheres to key principles of zero defects, zero compromises and continuous improvement.

"BEYOND THE PILLARS OF ZERO DEFECTS, ZERO COMPROMISES AND CONTINUOUS IMPROVEMENT, BAUMANN MEDICAL HAS ESTABLISHED A DEDICATED FRAMEWORK THAT REFLECTS ITS MEDICAL MINDSET AND GUIDES THE PURSUIT OF QUALITY EXCELLENCE."

and effects analysis (FMEA) to proactively identify and mitigate risks.[1] This approach fosters a culture of excellence, ensuring that products consistently meet regulatory, safety and customer requirements, while also driving continuous innovation and improvement (Figure 1).

CORE QUALITY CULTURE

BAUMANN Medical's commitment to delivering high-quality products with minimal batch variation and competitive pricing is rooted in its core values. Consistent quality can reduce the total cost of a product by minimising scrap and rework, directly supporting efficient customer assembly and long-term savings.

This quality mindset is deeply embedded in the company's culture. Every employee – regardless of role – is empowered to uphold quality standards. In the Medical division, this is reinforced by GMP-compliant environments,[2] validated processes and a focus on clean manufacturing. From precision component design to service delivery, quality is integrated into all operations, adhering to ISO 13485 standards.

Beyond the pillars of zero defects, zero compromises and continuous improvement, BAUMANN Medical has established a dedicated framework that reflects its medical mindset and guides the pursuit of quality excellence.

Employees

Quality emanates from the expertise and dedication of BAUMANN Medical's team, guided by both corporate and individual values. Committed to medical standards, the company exemplifies a medical mindset to deliver best practices and exceptional service. By prioritising onboarding, continuous training and talent development, BAUMANN Medical fosters a culture of excellence that maintains high standards, ensures seamless services and guarantees top-quality products. This enables the team to deliver exceptional results with responsibility, professionalism and care (Figure 2).

Regulatory and Standards

BAUMANN Medical adheres to strict regulatory standards, emphasising product safety through validation processes, digitalised in-process controls (IPC/SPC) and meticulous documentation. The company's commitment is solidified by compliance with ISO 13485 and 14001 guidelines and regular customer and internal audits. And, of course, it strictly adheres to the appropriate GMP/GDP regulatory standards.

Stability

BAUMANN Medical prioritises precision and stability, maintaining assembly and production stability. The company follows the "Four Eyes" principle for data transfer, batch release and thorough line clearance, as well as adhering to logbook documentation standards. BAUMANN Medical considers the production and specification stability of products to be essential, especially when it comes to supporting the assembly line with high overall equipment effectiveness through its high-quality products.

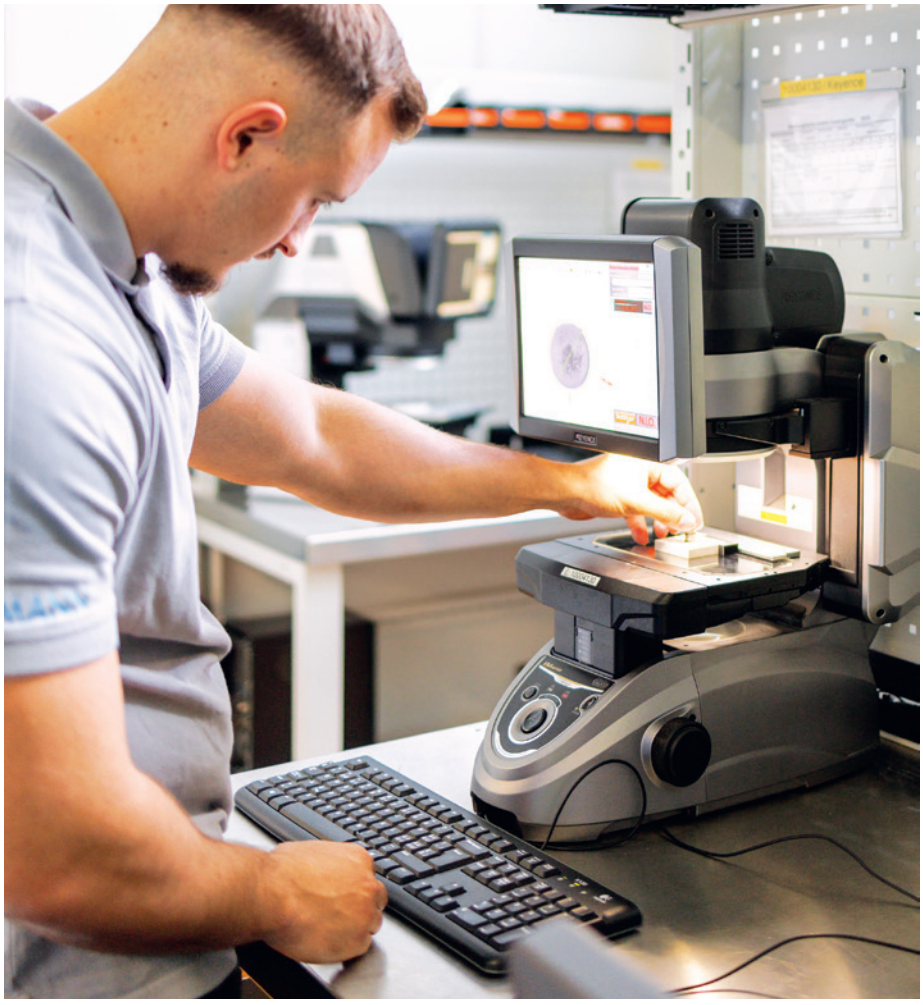


Figure 2: BAUMANN Medical's employees demonstrate professionalism and care.

Risk Management

The company employs a risk-based approach for key elements such as control charts, FMEA and design of experiments. Looking at the bigger picture, BAUMANN Medical is driven by its risk process at all business levels, ensuring that the company is optimally positioned and able to mitigate risks in a situational manner.

ZERO DEFECTS – A COMMITMENT TO EXCELLENCE

First, at BAUMANN Medical, "zero defects" is not just a target – it is a core policy that guides every process. Quality is defined as consistently meeting customer expectations, driven by a relentless focus on excellence in design, manufacturing and service. Through stringent quality controls and advanced technologies, BAUMANN Medical ensures defect-free operations to the highest possible level.

In medical applications, zero defects becomes critical. A minor deviation – such as in a spring for an inhaler or stamping in a continuous glucose monitor – can affect patient safety. BAUMANN Medical uses SPC, real-time monitoring and root cause analysis to detect and resolve deviations before defects occur.

BAUMANN Medical monitors processes in its production SPC through control charts.[3] This enables the company to address any issues before the process drifts out of specification. Samples are measured all along the production of an order at regular intervals. This monitors the production output and reacts by correcting the influence parameters on the machine to bring the outputs back towards their target values (Figure 3).

Targeting a zero-defect production, BAUMANN Medical places high significance on its sampling strategy for production inspections. The sampling sizes and frequencies are determined by an internal guideline that adheres to VDA 6.3 and ISO 2859 standards. The sampling depends on the project phase, the type of inspection and the criticality of the characteristics. The zero acceptance method is used, which allows optimal sampling sizes – smaller sizes, selected at timely intervals.

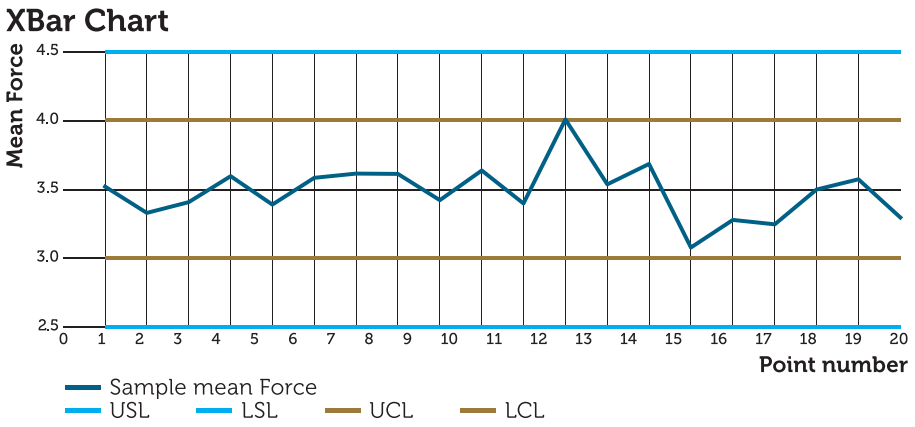


Figure 3: Control chart of force of 100 SPC measurements with sample size five. Point 12 has an average value higher than upper control limit, which triggers correction of the machine settings, and the average value of the next point reverts back to the target average.

As an example, let's consider a customer who requires an accepted quality level (AQL) of 0.04% on inspection level II for the inner diameter of a spring. The lot size for this product is 20,000 parts. ISO 2859 provides a sampling size of 315 parts to be checked for the whole lot to ensure the target AQL level. A production lot of 20,000 parts of this article requires 20 hours for production. In 20 hours, 10 SPC points are recorded. The inspection plan contains a minimum of 10 x 32 (315/10 = 31.5 (~32)) parts measured to achieve the AQL level. Once a single component fails to meet the specification, the lot is rejected.

ZERO COMPROMISES – REGULATORY AND CUSTOMER REQUIREMENTS, ADHERENCE AND RESPONSIBILITY

The second pillar of BAUMANN Medical's quality policy is "zero compromises". The company's policy is that no compromise is made on key principles at any stage of the product creation process – especially in the areas of quality, safety, compliance, environment and ethics. This means doing things right the first time, even if it is more difficult, time-consuming or expensive. This is how BAUMANN Medical ensures that it adheres to GMP standards within the medical environment. The company starts with unconditional adherence to regulatory requirements, goes above and beyond the 100% compliance standard for customer requirements and, should any cause for deviation arise, follows state-of-the-art customer complaint and notification handling procedures.

BAUMANN Medical makes zero compromises for medical production:

- **Adherence to Regulatory**: In the medical industry, "zero compromises" also means unwavering adherence to regulatory standards. Whatever is needed to support ISO 13485, US FDA or the EU's Medical Device Regulation (MDR) approvals for medical devices, BAUMANN Medical can assist with clean and professional documentation that is required from medical device manufacturers. The company's documentation corresponds to reality – no retroactive filling in and no modification of records.

- **Adherence to Customer Requirements**: Every customer request and all feedback is evaluated by BAUMANN Medical's quality teams for feasibility, regulatory compliance and technical impact. Requirements, such as 100% inspection, are integrated into the system and followed without exception, ensuring strict compliance.

"TARGETING A ZERO-DEFECT PRODUCTION, BAUMANN MEDICAL PLACES HIGH SIGNIFICANCE ON ITS SAMPLING STRATEGY FOR PRODUCTION INSPECTIONS."

- **Complaint Handling**: For claims and notifications, BAUMANN Medical systematically uses the "8D" problem-solving method, including correction and prevention of reoccurrence, lessons learned and best practices shared with other plants. For customer claims or notifications, the BAUMANN Medical mindset to solve the problem sustainably is independent of the type of claim (official or notification).

As an example, let's imagine that some deformed springs were found in a bag unit. The number of springs found deformed in the bag did not violate the specification. However, BAUMANN Medical built an 8D team (D1) and defined and analysed the problem (D2) following 8D methodology (Figure 4):

- D1 – Form a multidisciplinary team, including different functional experts
- D2 – Define the problem (deformed springs in bag)
- D3 – Containment action to ensure that no parts are affected in production, in storage or at the customer site
- D4 – Analysis of the root causes for occurrence and not detection (in this case, a design optimisation was found in the transport system)
- D5 – Choose and verify permanent corrective actions (design modification of the transport system)
- D6 – Implement permanent corrective actions (implement D5)
- D7 – Prevent recurrence (the design modification was shared with all BAUMANN Medical locations that have similar transport systems)
- D8 – Recognise and celebrate (close the case in form of an 8D report).

CONTINUOUS IMPROVEMENT – DEDICATED CUSTOMER SUPPORT AND ADVANCING THROUGH INNOVATION

The last of the three pillars, continuous improvement, is a key driver at BAUMANN Medical. The company systematically optimises processes, enhances systems and fosters innovation. This is embedded in the company's culture – every employee is encouraged to contribute, challenge

Figure 4: BAUMANN Medical follows an 8D methodology to analyse and resolve any manufacturing issues.

norms and refine even well-functioning processes. With an agile approach to risk and opportunity management, BAUMANN Medical remains flexible and responsive to changing market needs. The company is committed to minimising risk and delivering benchmark-quality products. Robust management systems are developed in line with international standards, legal requirements and customer expectations, and are regularly reviewed to ensure improvement.

Products and Processes

BAUMANN Medical improves processes using data from machines, maintenance and production. Discrepancies and deviations are analysed to find root causes, not just symptoms. Tools such as SPC help to prevent issues early. Procedures are reviewed regularly – what was "good" yesterday may not meet today's standards. Instructions, layouts and processes are regularly refined. Successful improvements are standardised and shared across sites. Ideas from all levels – operators, technicians and inspectors – provide valuable insights. Continuous improvement, without compromising quality, is part of the company's DNA – driven by optimisation.

To ensure compliance and continuous improvement, BAUMANN Medical analyses process capability from prototype to series.[4] Beyond compliance, process capabilities provide valuable insights for improvement, such as comparisons between machines, raw materials and product ranges.

Figure 5 provides an example of process capability for comparing raw material

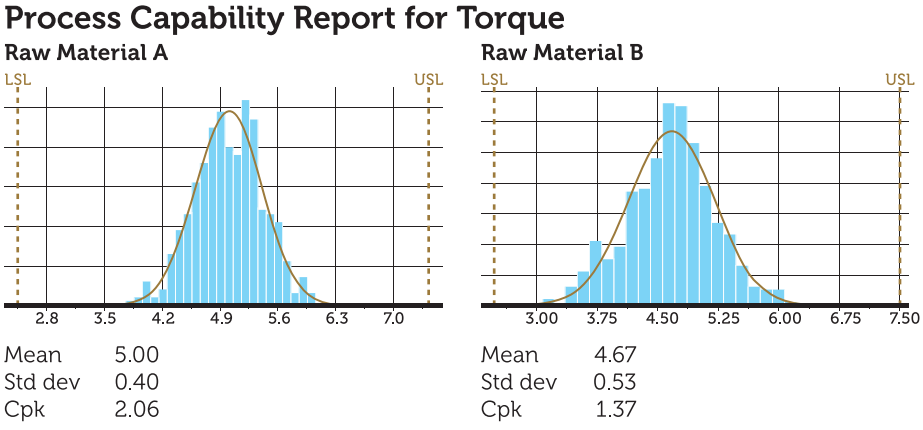


Figure 5: Comparison of raw material suppliers within product specifications.

suppliers of the same article, both being compliant to specification. It shows that Raw Material A has a very centred torque output with a tight distribution. Whereas Raw Material B has a less centred and less tight torque distribution. There is potential for improvement with the supplier of raw material B by implementing actions to tighten and shift the distribution towards the middle of the specification limits (USL, LSL). For such an improvement project, BAUMANN Medical often uses the data-driven "Six Sigma" approach.[5]

Risk-Management Processes

Risk management aligns strategy, ensures compliance and enables informed decisions with stakeholders. BAUMANN Medical promotes risk awareness across all levels, ensuring timely identification and mitigation. Integrated with strategy, internal controls and documentation, the company supports audits and regulatory alignment. Standardised processes improve clarity. BAUMANN Medical ensures ongoing risk assessment, giving leadership a global view of critical risks. Participation is mandatory at all sites, with tailored activities and documentation.

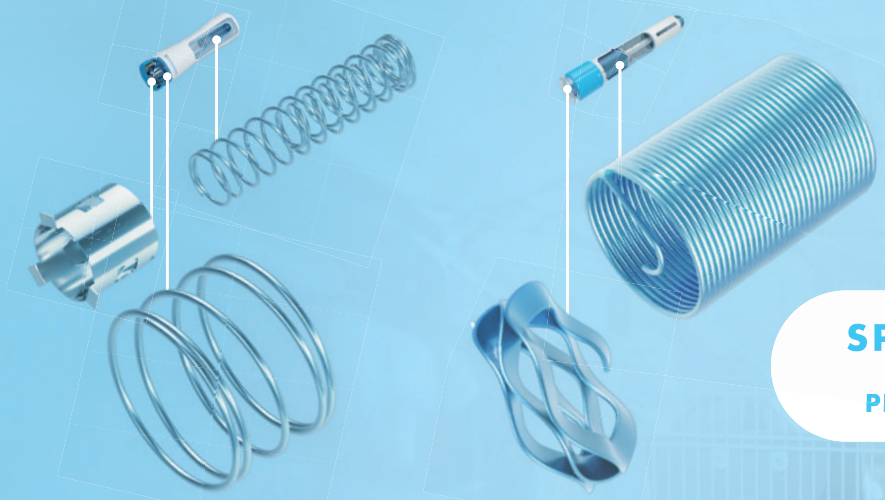
"BAUMANN MEDICAL PROMOTES RISK AWARENESS ACROSS ALL LEVELS, ENSURING TIMELY IDENTIFICATION AND MITIGATION."

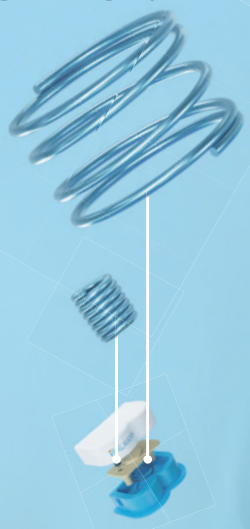
One example of how BAUMANN Medical follows a risk-based approach, as required by ISO 13485, is the use of process failure mode and effect analysis (PFMEA) for risk analysis over the whole process. This method allows the company to identify internal risks by understanding the customer's point of view. It also assists with planning validations for new products by providing a risks assessment on all processes of the article's manufacture (from the arrival of raw material to shipment of finished goods) and a prioritised list of actions required to mitigate risks in production, both related and unrelated to production processes. PFMEAs are living documents, updated based on learnings in production, engineering and customer feedback.

As an example of an action taken following PFMEA analysis, BAUMANN Medical noticed that a cutting process was lacking stability and detection after receiving customer feedback about a prototype order. The original PFMEA foresaw the risk but did not identify it as high priority. Following customer feedback, the occurrence and detection of the failure assessment was re-rated and action was taken to create a safe launch concept for the product during the validation process with a high focus on the cutting step of the manufacturing process.

Need reliable, custom-made springs and stampings for your medical devices or pharmaceutical applications?

As a trusted global partner, we deliver precision springs and stampings tailored to your medical device or pharmaceutical applications needs. Our ISO 13485-certified facilities and experienced team ensure exceptional quality, performance, and competitive pricing.





SPRINGS & STAMPINGS
FOR MEDICAL DEVICES & PHARMACEUTICAL APPLICATIONS

How can we support you in the early stages of development?

Please contact us:

BAUMANN Springs Ltd.
+41 55 286 81 11
medical@baumann-group.com

baumann-medical.com

BAUMANN MEDICAL

CONCLUSION

BAUMANN Medical's commitment to quality is reflected in its three foundational pillars: zero defects, zero compromises and continuous improvement. By embedding these principles into its culture and operations, the company ensures that it consistently meets the highest standards and remains a trusted partner across industries. With a focus on sustainability, safety and innovation, BAUMANN Medical is well-equipped to thrive in an ever-changing market while continuing to deliver exceptional value to its customers.

Nowhere is this commitment more critical than in the medical industry, where the integrity of each component can directly influence therapeutic outcomes. By applying rigorous standards, design expertise and technical innovation, BAUMANN Medical delivers safe, reliable and high-performance solutions that help shape the future of drug delivery and patient care.

REFERENCES

1. *"FMEA". ASQ, 2020.*
2. *"5 main components of GMP: A comprehensive guide". SciLife, Feb 2025.*
3. *"What is Statistical Process Control?". ASQ, 2021.*
4. *"VDA 6.3 Volume 4: Process Audit – Statistics (Control Chart and Process Capability)". VDA QMC, 2021.*
5. *Harry M, Shroeder R, "Six Sigma: The Breakthrough Management Strategy Revolutionizing the World's Top Corporations". Crown Currency, 2026.*

David Pircher

David Pircher is the Global Head of Business Development in the Medical Division at BAUMANN Group. He holds an EMBA, an MAS in Business Consulting and an Engineering degree. As a member of the executive medical board, he is responsible for strategy, marketing and business intelligence. Mr Pircher has over 25 years of professional experience, with more than 15 years in senior management roles.

T: +41 55 286 8814
E: david.pircher@baumann-group.com

Maxime Ludwig

Maxime Ludwig is BAUMANN's Head of Quality Operations (Switzerland) for the Medical Division. Mr Ludwig is originally from France and holds a master's degree in Material Science, having gained his professional experience over the last 10 years in manufacturing engineering and quality management. In his career, he has specialised in continuous improvement with the Lean Six Sigma method and in problem solving based on the 8D method, helping to maintain a co-operative customer relationship.

T: +41 55 286 8111
E: medical@baumann-group.com

Pavel Zahradník

Pavel Zahradník is the Quality Assurance Manager for BAUMANN's Medical Division. He is a system-oriented specialist with 15 years of experience in quality. Originally from the Czech Republic, he has gained extensive expertise in both automotive and medical industries. As a certified internal auditor for ISO 13485, he supports quality assurance across the entire division. He is a reliable partner in raising quality to the next level.

T: +41 55 286 8111
E: medical@baumann-group.com

BAUMANN Springs Ltd
Fabrikstrasse 1, 8734 Ermenswil, Switzerland
www.baumann-group.com

LAUNCHING A LARGE-VOLUME PREFILLABLE GLASS SYRINGE SYSTEM: RELIABLE SUBCUTANEOUS DRUG DELIVERY

SCHOTT PHARMA

Isabelle Jeangoudoux and **Sven Pohle** introduce **SCHOTT Pharma**'s new syriQ BioPure® 5.5 mL staked-needle prefillable glass syringe and explain how this solution meets the growing need for large-volume subcutaneous drug delivery.

Subcutaneous (SC) drug delivery is growing as an alternative to intravenous (IV) delivery. It supports the trend to decentralised care, allowing injection therapy to take place outside of the hospital and potentially in the home. Using prefilled syringes (PFSs) as an alternative to vials for SC formulations reduces manual preparation steps and minimises medication errors during administration, further supporting at-home injections and providing a patient-centric solution with greater convenience and comfort. Handheld autoinjector devices designed for use with PFSs have been instrumental in shifting the point of care from hospital to home and have become a preferred solution for safe and effective self-administration.[1]

Where SC dosing volumes had previously been limited to 1 mL and later 2.25 mL, new co-formulation and enabler technologies have been developed that allow the injection of larger volumes, exceeding this range significantly. Since high-dose drug applications are usually associated with higher viscosities of the formulations, new requirements are now being placed on large-volume drug delivery solutions.

MEETING THE NEEDS OF A GROWING MARKET

The advances in drug formulation development and new therapy concepts are reflected in a growing pipeline of large-volume SC drugs. A recent review identified 182 approved or clinical-stage

"A PROVEN CONTAINER PLATFORM CAN FACILITATE A SHORTER TIME TO CLINICAL TRIALS."

large-volume drugs either currently using the SC route or with high potential to use this administration route. Of these, 31 were approved large-volume SC agents and 83 were clinical-stage candidates, demonstrating the potential for significant growth in this area.[2] Another 68 IV formulations were identified by the study authors as potential candidates for transition from an IV to an SC route. The review found that of these 182 drugs, 81 had a volume range between 2–5 mL, while the remainder had even larger volume ranges. These trends indicate a significant need for large-volume container solutions that can handle volumes exceeding 2 mL at a wide range of viscosities and that are compatible with SC injection devices, such as autoinjectors.

Time-to-market is critical for biopharma companies, and because clinical testing is a lengthy process, companies want to reach this step as quickly as possible. A proven container platform can facilitate a shorter time to clinical trials. This makes available multiple configurations of the primary packaging to best meet specific customer needs and provide a prequalified route to easy sampling, regulatory filing and commercial supply. Alongside this, there is a need for dependable production capacity as well as technical and regulatory support for biopharma companies and CMOs entering the growing market of large-volume SC drug delivery.

The latest solution from SCHOTT Pharma is the syriQ BioPure® 5.5 mL staked-needle glass PFS, designed to meet the growing need for large-volume SC drug delivery (Figure 1). SCHOTT Pharma brings all the knowledge gained from the established 1 mL long and 2.25 mL PFS glass platforms for biologics to the development of the 5.5 mL format.

When developing a PFS, the needs of all stakeholders should be taken into account. Firstly, drug compatibility and safety must be ensured. Secondly, the patient and user needs are key, including comfort and ease of use, as well as considering how to build confidence for the user. Processability throughout fill-finish and final assembly stages must be evaluated, as well as business aspects, such as speed of implementation and lowering development risks. For a PFS designed for use in an autoinjector, collaboration between the container and device developers is crucial. In the holistic development of the new 5.5 mL staked-needle glass PFS, SCHOTT Pharma considered all these factors and collaborated with its partners to identify the best solution.

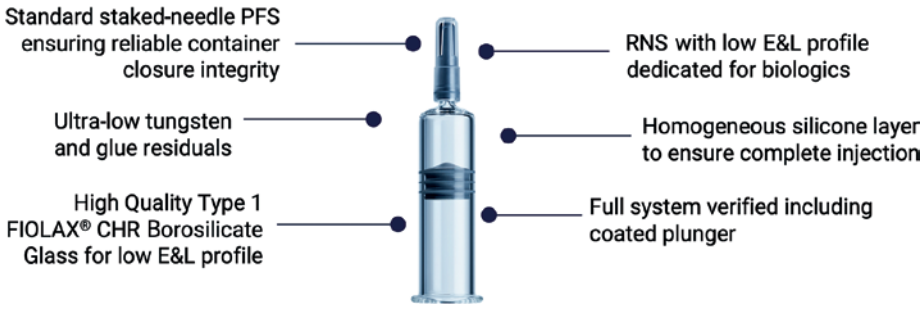


Figure 1: Key features of the syriQ BioPure® 5.5 mL prefillable syringe, a new, large-volume drug delivery solution in the syriQ BioPure® platform that builds on the proven success of the 1.0 mL and 2.25 mL syringes.

PURITY FOR SENSITIVE DRUG FORMULATIONS

Minimising interaction between the drug and the container is of primary importance and a key pharmaceutical requirement. A low extractables and leachables (E&L) profile of all components of the primary packaging is crucial for many drugs used in SC drug delivery because these biopharmaceutical formulations may be sensitive to extractables from the glass or the elastomeric closures. Therefore, first class components and materials have been chosen for the design of syriQ BioPure® 5.5 mL.

The glass barrel uses Type I FIOLAX® CHR Borosilicate Glass that has been designed for controlled hydrolytic resistance of the inner surface of the container. In addition, SCHOTT Pharma's converting processes for high-value prefillable glass syringes enable ultra-low tungsten levels. This is essential because tungsten oxide is a critical residue for some biological drugs; even amounts in the nanogram range can cause aggregation, denaturation or precipitation of proteins, such as monoclonal antibodies, which might increase the risk of immunogenicity.[3,4] In principle, tungsten residues may originate from the forming pins during hot forming of the syringe cone. Through the development of an alternative pin alloy, SCHOTT Pharma has established a high-quality forming process for the whole syriQ BioPure® platform so that an ultra-low tungsten specification can be ensured.

For the elastomeric components, state-of-the-art materials were selected, such as Aptar's (IL, US) Rigid Needle Shield (RNS) 4900GS. This uses a modern styrene butadiene rubber material with a type I classification according to EP 3.2.9 and US Pharmacopoeia Chapter <381> and a fit-for-biologics positioning. Datwyler's (Altdorf, Switzerland) latest plunger development for large-volume PFSs was also selected, which is a NeoFlex™ plunger coated with a protective fluoropolymer layer, typical for use with biologics to minimise interactions with sensitive drugs.

"IN THE HOLISTIC DEVELOPMENT OF THE NEW 5.5 ML STAKED-NEEDLE GLASS PFS, SCHOTT PHARMA CONSIDERED ALL THESE FACTORS AND COLLABORATED WITH ITS PARTNERS TO IDENTIFY THE BEST SOLUTION."

FUNCTIONALITY IS KEY FOR PATIENT-CENTRIC DRUG DELIVERY SYSTEMS

To address user needs in terms of confidence and ease of use, the syriQ BioPure® 5.5 mL syringe system was carefully designed for reliable functionality over its entire shelf life. One essential requirement is, of course, that the patient receives the full injection from the autoinjector. Therefore, the gliding performance of the plunger in the spray-coated syringe barrel must be reliable and consistent over its shelf life. Exemplary results for water-filled syringes stored for up to six months at 5°C and 25°C are shown in Figure 2. Average and maximum gliding force did not change significantly during storage at either temperature or compared with initial performance. The test gives confidence that the new 5.5 mL syringe and the large-volume NeoFlex™ plunger from Datwyler meet the requirements for gliding force throughout its shelf life and function as a reliable container system in the autoinjector.

For the application of more viscous drugs, the needle's inner diameter plays a crucial role, as it impacts the hydrodynamic extrusion force significantly. Therefore, the syriQ BioPure® 5.5 mL features a high quality, 27G ½-inch special thin wall needle. To reduce the extrusion force, this needle has an increased inner diameter compared with a standard 27G thin wall type.

Another important factor for the user experience is the removal of the autoinjector cap. In addition to specific design requirements for the device, the interaction of the RNS with the syringe cone is also relevant here – a low RNS pull-off force supports a low cap removal force with the autoinjector. Verification studies confirmed that the 4900GS RNS meets the quality requirements.

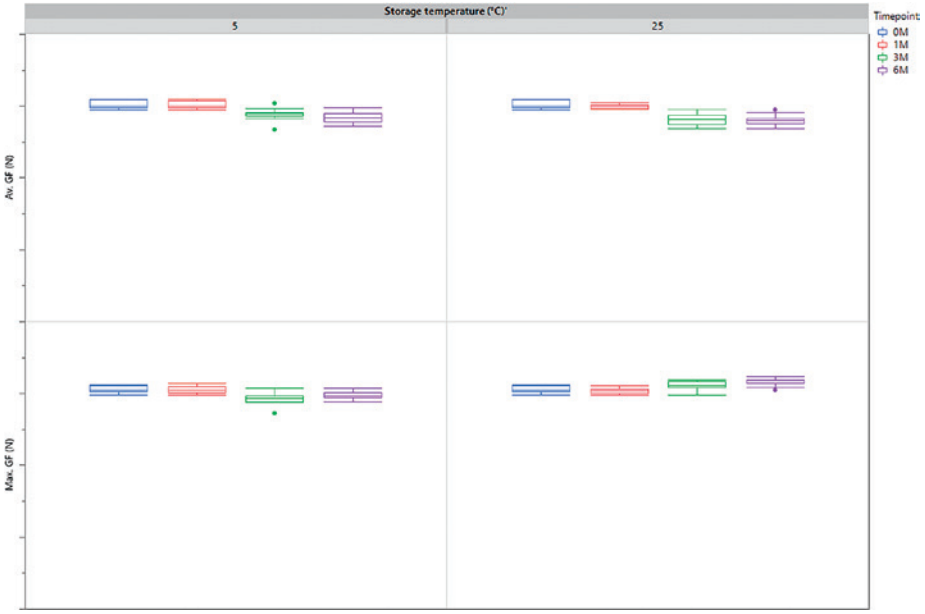


Figure 2: The gliding force (GF) for water-filled 5.5 mL syringes was tested on a universal test machine directly after filling (0 m) and after 1, 3 and 6 months of storage at 5°C and 25°C. The syringes were stoppered with a Datwyler NeoFlex™ plunger.

Furthermore, dosing accuracy is an important user requirement. The syringe system contributes to this with a minimal residual volume smaller than 20 µL, which is <0.4% of the total syringe volume. This low residual volume has been achieved by an ideal match of barrel shoulder dimensions with Datwyler's large-volume NeoFlex™ plunger. The plunger design incorporates a dome and optimised dimensions allowing it to fit perfectly into the syringe barrel design.

CO-DEVELOPING WITH AN AUTOINJECTOR

Autoinjector devices are commonly used for at-home injection. The interplay of device and container is crucial to ensure safe and reliable drug administration during self-medication. Therefore, the interfaces between autoinjector and PFS must be clearly matched and understood as a system that, as a whole, ensures essential performance requirements are met.

> "THE TEST GIVES CONFIDENCE THAT THE NEW 5.5 ML SYRINGE AND THE LARGE-VOLUME NEOFLEX™ PLUNGER FROM DATWYLER MEET THE REQUIREMENTS FOR GLIDING FORCE THROUGHOUT ITS SHELF LIFE."

SCHOTT Pharma and Ypsomed (Burgdorf, Switzerland) collaborated to co-develop the new syriQ BioPure® 5.5 mL PFS and the YpsoMate® 5.5 autoinjector. As part of this co-development process, the critical syringe dimensions for autoinjector use and optimal performance criteria were determined and included in a joint interface specification. Precision is a key requirement for the container-device interaction, as it ensures reliable processability in the syringe-to-device assembly, as well as functionality and ease of use. In addition to the interface specification, compatibility tests were performed at Ypsomed during the development process, to ensure that the two parts would function together smoothly.

SIMPLIFYING FILL-FINISH PROCESSES

Thinking in systems means considering the whole ecosystem of a PFS. Therefore, it is important to assess the impact of the new large-volume syringe on the fill-finish landscape. Firstly, the design of syriQ BioPure® 5.5 mL allows the use of SCHOTT Pharma's standardised secondary packaging, the SCHOTT iQ® platform. All three syringe formats of the biologics PFS glass platform – 1.0 mL long, 2.25 mL and now 5.5 mL – are packaged in a

standardised 3" tub for simple incorporation into existing fill-finish systems. The new 5.5 mL design fits 42 syringes in the standardised tub (Figure 3). Secondly, throughout industrialisation of syriQ BioPure® 5.5 mL, various partners in the fill-finish sector have successfully conducted technical test runs and begun introducing the new large-volume syringe format.

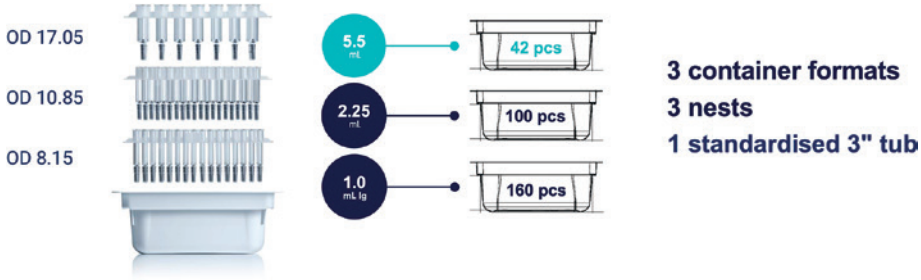


Figure 3: The syriQ BioPure® platform uses a standardised 3" tub for all three volumes of pre-sterilised, nested prefillable syringes, designed to facilitate automated fill-finish. The tub is sealed with a Tyvek® sheet and packaged in a double-bag configuration. OD: outer diameter of the glass barrel.

CONCLUSION

SCHOTT Pharma's syriQ BioPure® 5.5 mL is the first large-volume staked-needle glass PFS designed for SC drug administration of biologics. The new PFS, co-developed to be compatible with the YpsoMate® 5.5 autoinjector, enables a broader design space for formulation development and improved patient-centric drug delivery for large-volume SC therapies. These advances reduce the treatment burden for patients by allowing fewer injections at home for greater comfort and convenience. As part of a proven PFS platform, this new large-volume syringe offers reliable performance in terms of drug compatibility, safety, functionality and processability in final assembly and fill-finish. The platform approach allows a fast time to market and comes with reduced risks for combination product development. SCHOTT Pharma provides expertise in large-volume container fill-finish, along with regulatory support, so that biopharma companies and CMOs can quickly come up to speed with this new format and achieve fast implementation with low risk. This new PFS provides a solution for the growing pipeline of large-volume SC drugs, ultimately enabling solutions that reduce the treatment burden for patients.

SCHOTT Pharma is currently in the industrialisation phase. Not-for-human-use samples of the 5.5 mL PFS are available for testing and feasibility studies. The commercial launch of for-human-use product is expected by the end of 2025.

Isabelle Jeangoudoux

Isabelle Jeangoudoux is the Head of Global Product Management for the Glass Syringe portfolio at SCHOTT Pharma. She started her career in international product management in the automotive industry before transferring to the medical devices industry in 2008. She joined SCHOTT Pharma in 2023 to support innovations, product strategy and device partnerships for glass syringes. Ms Jeangoudoux graduated from ESCEM School of Management Tours (France) with a degree in International Management and Marketing and holds a Master of Arts in Business and Administration from Bradford University School of Management (UK), Audiencia School of Management (France) and Deusto University (Spain).

E: isabelle.jeangoudoux@schott.com

Sven Pohle

Sven Pohle is Global Product Manager for Glass Syringes at SCHOTT Pharma, where he is responsible for portfolio management, component partnerships, technical trainings and the launch of product innovations. Prior to that, Mr Pohle worked for over 10 years in various R&D positions in the medical device industry. He holds a PhD in Polymer Chemistry from Technical University of Braunschweig, Germany.

E: sven.pohle@schott.com

SCHOTT Pharma AG & Co KGaA
Hattenbergstraße 10, 55122 Mainz, Germany
www.schott-pharma.com

REFERENCES

1. *Schneider A et al, "Autoinjectors for large-volume subcutaneous drug delivery: a review of current research and future directions". Expert Opin Drug Deliv, 2023, Vol 20(6), pp 815–830.*
2. *Green P et al, "Navigating large-volume subcutaneous injections of biopharmaceuticals: a systematic review of clinical pipelines and approved products". MAbs, 2024, Vol 16(1).*
3. *Bee et al, "Precipitation of a Monoclonal Antibody by Soluble Tungsten". J Pharm Sci, 2009, Vol 98(9), pp 3290–3301.*
4. *Seidl A et al, "Tungsten-Induced Denaturation and Aggregation of Epoetin Alfa During Primary Packaging as a Cause of Immunogenicity". Pharm Res, 2012, Vol 29(6), pp 1454–1467.*

Introducing syriQ BioPure® 5.5 ml

SCHOTT Pharma's syriQ BioPure® 5.5 ml is the company's first large-volume staked-needle glass syringe, specifically engineered for the subcutaneous delivery of biologics. Co-designed for seamless compatibility with the YpsoMate® 5.5 autoinjector from Ypsomed*, this innovative container expands the formulation design space, enabling the administration of high-volume drugs that reduce treatment burden by requiring fewer injections, enhancing patient safety, comfort, and convenience at home. The syriQ BioPure® 5.5 ml offers proven functionality and processability during fill-and-finish and final assembly. It supports the transition from intravenous to subcutaneous administration, streamlining clinical workflows by reducing preparation steps and minimizing the risk of medication errors. With validated component compatibility, it meets the growing demand for subcutaneous biologics delivery and paves the way for pharmaceutical innovation and development.

Further information at www.schott-pharma.com/syriq-biopure

Available now! Meet us at CPHI Frankfurt, booth 8.0L24.

SCHOTT PHARMA

*YpsoMate® is a brand owned by the Ypsomed Group.

INSIDE A TRACK-AND-TRACE SYSTEM FOR MEDICAL MOULDS: A MODEL FOR HEALTHCARE MANUFACTURING

Twan Mertens and **Floor Verhorst-Willems** of **IGS GeboJagema** explore how the company provides comprehensive visibility into every aspect of its operations with a 100% control track-and-trace process, spanning from initial sales discussions through to final validation and beyond.

Today's drug delivery devices are marvels of precision engineering, requiring dozens of specialised suppliers and hundreds of individual components. This complexity underscores the immense challenge of ensuring that they are manufactured with zero defects and incidents, as every component and every link in the supply chain is a potential point of failure that could compromise patient safety.

When quality issues arise or incidents occur, the ability to trace the root cause rapidly is critical. Without comprehensive traceability, a single compromised component can trigger widespread recalls, cause production shutdowns and, most importantly, put patient safety at risk. This is why track and trace does not stop at the pharmaceutical company's door. To guarantee the integrity of their products, these companies need partners throughout their supply chain who share their commitment to comprehensive documentation and process visibility.

> "WITHOUT COMPREHENSIVE TRACEABILITY, A SINGLE COMPROMISED COMPONENT CAN TRIGGER WIDESPREAD RECALLS, CAUSE PRODUCTION SHUTDOWNS AND, MOST IMPORTANTLY, PUT PATIENT SAFETY AT RISK."

With decades of experience serving the healthcare industry, high-precision injection mould maker IGS GeboJagema has built its operations around this fundamental principle. The company understands that manufacturing medical device tooling requires more than technical excellence – it demands complete transparency and accountability at every step of the process. By documenting and tracking each measurement and every action taken for every single mould component throughout its workflow, IGS GeboJagema ensures that pharmaceutical clients can maintain complete confidence in the integrity of their manufacturing tools and, ultimately, their products.

SALES AND PROJECT MANAGEMENT

IGS GeboJagema builds the foundation of their track-and-trace system before any designs are modelled or steel is cut (Figure 1). It starts with the sales team creating a request for quotation where every customer requirement, specification and commercial consideration is meticulously documented. This goes beyond capturing technical specifications – it is about creating a permanent record of what the customer wants to achieve, why they need it and how success will be measured. During the hand-off between sales and project management, extensive order documents are created that establish clear expectations for both parties and provide the reference point for all subsequent decisions throughout the mould development process.

> "THE ENGINEERING TEAM WALKS THROUGH EVERY DETAIL WITH THE CUSTOMER TO ENSURE THAT ALL SPECIFICATIONS MEET THEIR EXACT REQUIREMENTS."

ENGINEERING AND DESIGN QUALIFICATION

Once project requirements are established, IGS GeboJagema's engineering team translates customer needs into manufacturable designs (Figure 2). This phase generates extensive documentation, starting with the project kick-off sheet that formally transitions the project from commercial to technical execution. The engineering team walks through every detail with the customer to ensure that all specifications meet their exact requirements.

A comprehensive suite of technical documentation captures every design decision and specification. The team creates detailed hot-runner design specifications and servo design specifications that define the precise requirements for these critical mould systems. Product variants are documented to ensure consistency across different configurations, while design review checklists provide systematic verification that all technical requirements have been addressed.

A critical step during engineering is a comprehensive design failure mode and effects analysis (FMEA) where the engineering team identifies potential issues and their impact. This systematic risk assessment examines every aspect of the mould design from material flow dynamics to ejection mechanisms, evaluating how each element could potentially affect the final drug delivery device's performance. The FMEA process creates a permanent record of identified risks and the design choices made to mitigate them.

The engineering phase concludes with formal design approval documents that represent management sign-off on the complete design package. These documents confirm that all customer requirements have been addressed, all identified risks have been mitigated and all manufacturing processes have been validated for repeatability and control, creating a clear milestone that locks in the design for all subsequent manufacturing activities.

Figure 1: Pre-production track-and-trace steps.

Figure 2: Engineering track-and-trace steps.

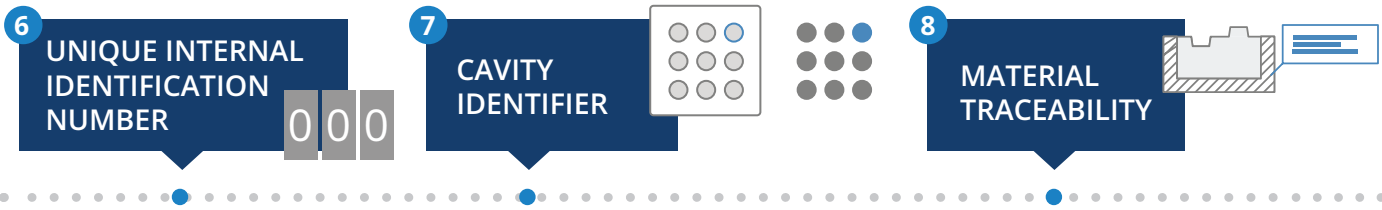


Figure 3: Production track-and-trace steps.

TOOL SHOP

As a project enters the tool shop, maintaining traceability becomes even more complex as hundreds of components move through different processes (Figure 3). Every component receives a unique internal identification number from the moment it enters production (Figure 4), facilitating an internal tracking system that allows complete visibility into each component's journey through manufacturing, validation and delivery. Each mould cavity also carries a cavity identifier that transfers to the final moulded products. This marking allows any moulded product to be traced back not only to a specific mould but to the exact cavity that produced it.

"THESE COMPREHENSIVE REPORTS BECOME PART OF THE DELIVERABLES FOR CUSTOMERS, PROVIDING COMPLETE VISIBILITY INTO HOW EACH COMPONENT WAS MANUFACTURED AND VALIDATED."

Throughout the manufacturing process, IGS GeboJagema employs a 100% control approach, with every manufacturing step and every measurement documented under the component's internal identification number. These comprehensive reports become part of the deliverables for customers, providing complete visibility into how each component was manufactured and validated. The depth of this documentation extends to even seemingly minor details – for example, bolt-tightening torques are specified and recorded, recognising that assembly variations can affect mould performance and product quality.

Figure 4: Every component receives a unique internal identification number.

IGS GeboJagema also tracks components from suppliers, such as hot runners, servo systems and other high-value commercial parts, assigning each a unique internal identification number. Material traceability is ensured through supplier-provided certificates for steel batches, coating processes and heat treatment procedures. This documentation creates a robust audit trail that connects material properties to final mould performance.

VALIDATION

With the mould manufactured and assembled, IGS GeboJagema transitions into the critical validation phase (Figure 5). This phase requires its own dedicated documentation system – a comprehensive scientific moulding workbook created in addition to the main project document. This second document captures every aspect of the qualification process.

There are multiple factors during the moulding process that can influence product quality. IGS GeboJagema employs a scientific moulding approach during validation to optimise these parameters systematically. Using advanced process-optimisation software that was developed in-house, IGS GeboJagema's team goes through a rigorous process to identify the ideal settings to achieve target product weights and quality specifications with minimal shot-to-shot variation.

During this process, every parameter is monitored and recorded with precise time registration, creating a detailed timeline of the validation process. Shot-by-shot data capture ensures that process variations are identified and documented, while every measurement is linked back to the specific cavity that produced it. The extensive documentation at this stage includes first article inspection reports, first-off inspection reports and corrective action

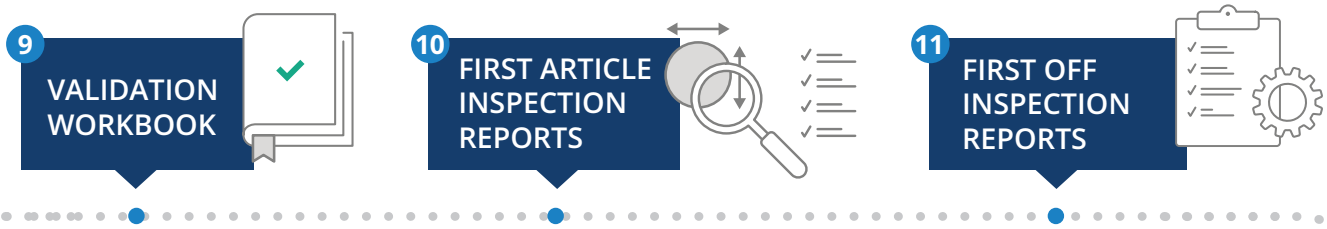


Figure 5: Validation track-and-trace steps.

Figure 6: Delivery track-and-trace steps.

Figure 7: Post-delivery track-and-trace steps

plans that document the problems identified and the specific steps taken to resolve them, creating a permanent record of process improvements.

In short, in line with IGS GeboJagema's 100% control approach, every single action taken or decision made during the qualification process is documented.

"IN SHORT, IN LINE WITH IGS GEBOJAGEMA'S 100% CONTROL APPROACH, EVERY SINGLE ACTION TAKEN OR DECISION MADE DURING THE QUALIFICATION PROCESS IS DOCUMENTED."

The validation phase concludes with factory acceptance test documents that formally transfer responsibility from IGS GeboJagema to the customer. These documents demonstrate that the mould consistently produces parts meeting all specified requirements under controlled conditions. The comprehensive reports generated during this phase enable complete traceability – any component can be traced back not only to its specific cavity but to the exact process conditions under which it was produced.

DELIVERY

The final stage of IGS GeboJagema's track-and-trace process involves delivering the comprehensive documentation to the customer (Figure 6). This goes far beyond simply providing a data dump of project information. Instead, IGS GeboJagema follows Good Documentation Practice and Good Manufacturing Practice standards to create professional, clear documentation packages designed to align perfectly with customer needs and regulatory requirements. In fact, the documentation delivered is so comprehensive and professionally structured that many customers use it directly instead of creating their own internal documentation.

The result is a complete documentation package that provides customers with everything needed to maintain traceability throughout the mould's operational life – one of IGS GeboJagema's unique selling points.

IGS GeboJagema ensures that the digital thread established during manufacturing continues unbroken into the customer's facility and production processes.

SERVICE AND REFURBISHMENT

IGS GeboJagema's commitment to traceability extends even beyond mould delivery (Figure 7). The company maintains a "mould passport" that captures all service interventions and refurbishments. By linking this to the original manufacturing records, both IGS GeboJagema and its customers are able to maintain complete visibility into the tool's history and current condition throughout its operational life.

BUILDING TRACK AND TRACE INTO YOUR DNA

This article outlines how IGS GeboJagema realises track and trace throughout its production process. However, comprehensive track and trace cannot be implemented as a project or bolt-on system – it must be ingrained into every aspect of a company's culture. Underlying all of IGS GeboJagema's methods and systems is a culture of extreme precision and an eye for detail.

The success of any system or approach depends on the actions of individual people and their understanding of the importance of what may seem like insignificant details. Sales teams must capture every detail during initial customer discussions, understanding that incomplete requirements documentation will cascade through the entire project. Engineers must document not just what they designed but why specific decisions were made and how they impact patient safety. Machinists must document every time a component is touched, even if that means an urgent order will take slightly longer.

In short, the level of documentation and precision required in healthcare manufacturing demands a fundamental shift in how every employee approaches their daily work. Organisations that want to realise a comprehensive track-and-trace system cannot simply implement new systems and procedures – they must build it into their DNA.

Twan Mertens

Twan Mertens serves as Operations Manager at IGS GeboJagema. With hands-on production experience as a miller and grinder, as well as holding degrees in mechanical engineering and commercial economics, he brings a comprehensive perspective to his role, in which he focuses on optimising automated Industry 4.0 production processes, quality control and delivery performance.

T: +31 40 264 7500
E: twan.mertens@igsgebojagema.nl

Floor Verhorst-Willems

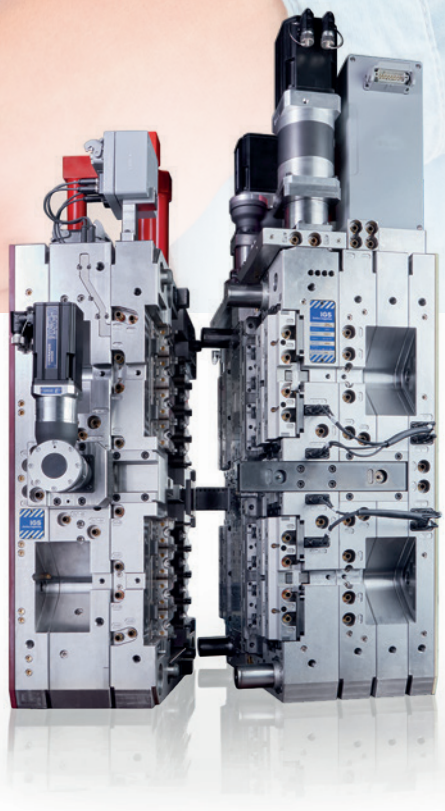
Floor Verhorst-Willems serves as the Strategic Business Development Manager at IGS GeboJagema. In her position, she focuses on expanding international strategic partnerships, accelerating innovation in medical technology, new business and securing IGS GeboJagema's position as a global leader in precision medical moulds. Her collaborative approach has been crucial in fostering early engagement with medical original equipment manufacturers, setting the stage for the development of pioneering moulding solutions.

T: +31 40 264 7500
E: floor.verhorst@igsgebojagema.nl

IGS GeboJagema
Esp 430, 5633 AJ Eindhoven, The Netherlands
www.igsgebojagema.nl

Our work touches billions of people's lives everyday

Combining a **passion for precision** with **responsibility**



Specialised in high precision moulds for pen injectors

IGS GeboJagema is the world's leading high precision mould manufacturer. Recognised and appreciated by all global industry experts. Based in the heart of the most prominent technology hub of Europe, and with a state-of-the-art plant in the USA.

Visit us at:

K Fair	Oct. 08th – 15th	Düsseldorf, Germany
PDA	Oct. 21st – 22nd	Vienna, Austria
PODD	Oct. 27th – 28th	Boston (MA), USA
CPHI	Oct. 28th – 30th	Frankfurt, Germany

www.igsgebojagema.nl

IGS GeboJagema

HIGH-SPEED ASSEMBLY OF NEEDLE SHIELDS FOR PREFILLED SYRINGES

CONTEXO automation

Matthias Müller of **Contexo** discusses the factors that set exceptional manufacturing equipment apart from the rest and how the company's new machine for assembling needle shields with prefilled syringes meets all these expectations.

Over 25 machines leave Contexo's production facilities every year. The company's medical device business is especially important and is growing continually. There is good reason for this – Contexo's decade-long experience of building highly efficient machines, coupled with its inventiveness, produces assembly solutions that satisfy even the toughest requirements while remaining fairly priced. "Everything in-house" is the Contexo way. The challenge is to build a machine with a small footprint that is effective, reliable and fast, and Contexo consistently rises to the occasion.

CONTINUOUS MOTION TECHNOLOGY

As the demand for prefilled syringes continues to rise, so does the need for needle shields. Contexo is currently developing a continuous-motion machine for assembling needle shields as part of its commitment

> "THE CHALLENGE IS TO BUILD A MACHINE WITH A SMALL FOOTPRINT THAT IS EFFECTIVE, RELIABLE AND FAST, AND CONTEXO CONSISTENTLY RISES TO THE OCCASION."

Figure 1: Continuous motion assembly machines.

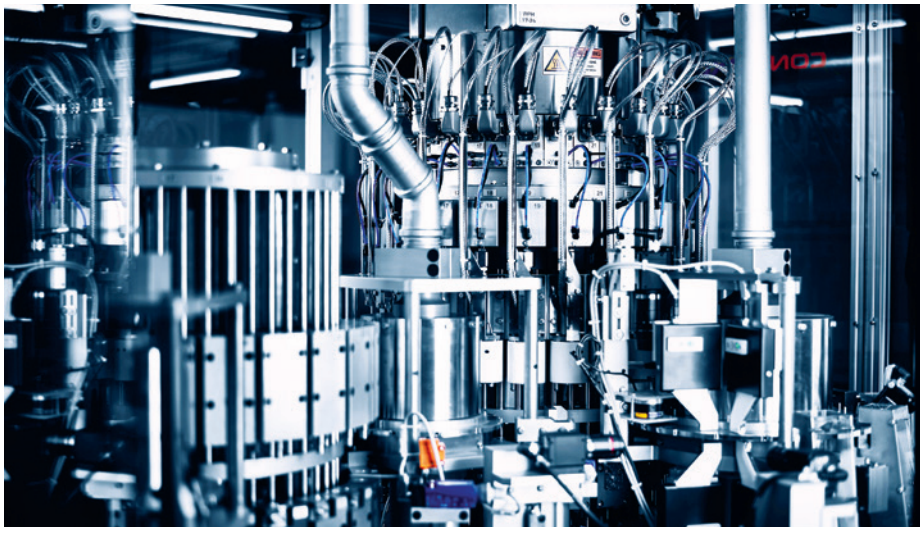


Figure 2: Thermoforming tower.

Figure 3: 100% in-line vision inspection – zero defects.

"CONTEXO HAS DEVELOPED A STANDARD PLATFORM ON WHICH ASSEMBLY MACHINES FOR RIGID OR SOFT NEEDLE SHIELDS CAN BE BUILT QUICKLY AND EFFICIENTLY."

to providing the medical sector with fast and reliable solutions. Working with these products requires in-depth knowledge and experience. Contexo has developed a standard platform on which assembly machines for rigid or soft needle shields can be built quickly and efficiently. The core of this system is the continuous motion technology (Figure 1), which assembles and crimps using two central towers. This enables the system to supply large quantities using stable, reliable processes.

It is essential that the process is well controlled, robust and repeatable. After the cover and needle shield have been fed in smoothly, both parts are pressed and passed on to the thermoforming tower. Since the crimping of the needle shields is critical, this process must meet the highest standards. Consequently, the machine has been designed so that each temperature value in the thermoforming tower can be set individually (Figure 2). This key process is constantly monitored.

Quality control is performed 100% in-line via visual inspection; three cameras perform the various tests (Figure 3). At the end of the process, all product-relevant features are checked again using open and transmitted light controls, and the parts are separated into good and bad. Contact-free inspection and control systems ensure zero contamination.

LONG LIFESPAN

The machine is designed for long-term use and has been built to be robust from the ground up. The use of mechanical components guarantees years of optimal performance and an almost fault-free system. This results in low maintenance

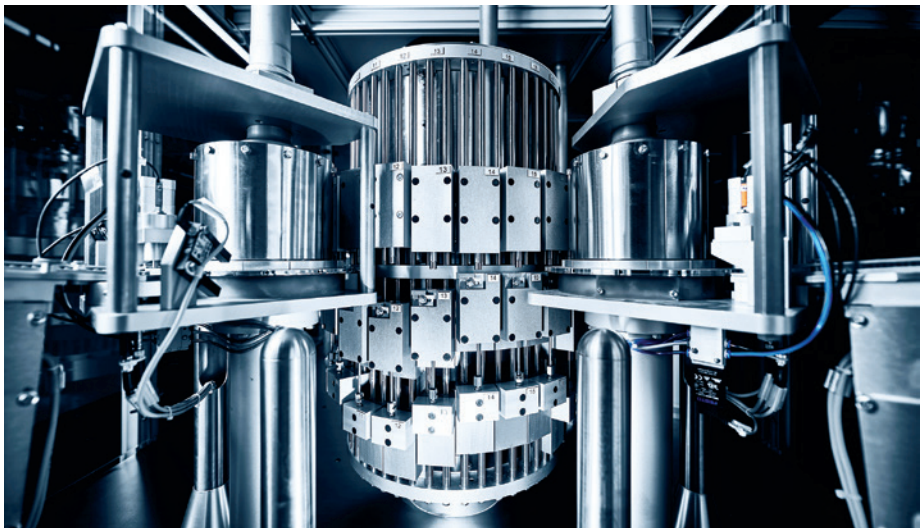


Figure 4: Stainless steel cleanroom production.

"WHEN MANUFACTURING IN CLEANROOM CONDITIONS, IT IS ESSENTIAL FOR PRODUCTION TO REMAIN COST-EFFECTIVE WHILE ALSO FULLY COMPLYING WITH THE RELEVANT REGULATIONS."

requirements and a long service life. The components are made of stainless steel and have been encapsulated to facilitate hygienic cleanroom production (Figure 4).

Operation, maintenance and care have been incorporated into the design from the outset. All surfaces are easy to clean and readily accessible. The space-saving machine concept minimises costs (Figure 5). When manufacturing in cleanroom conditions, it is essential for production to remain cost-effective while also fully complying with the relevant regulations. In addition to the minimal footprint, it is crucial for the system to be flexible. In line with this requirement, the machine can be easily adjusted to new requirements and be flexibly adapted to meet the needs of different products.

FULL GMP QUALIFICATION

It is mandatory for machines in the medical industry to be qualified. Contexo offers comprehensive and up-to-date GMP

"CONTEXO OFFERS VARIOUS SOLUTIONS THAT ARE ALL IN ACCORDANCE WITH CURRENT INTERNATIONAL STANDARDS AND PROVIDES A COMPREHENSIVE GMP PACKAGE, INCLUDING LOG GENERATION, TEST EXECUTION AND DOCUMENTATION OF RESULTS."

compliance. GMP qualifications for production, assembly or quality control processes require an expanded GMP-compliant qualification document to be created. Contexo offers various solutions that are all in accordance with current international standards and provides a comprehensive GMP package, including log generation, test execution and documentation of results.

SHORT PROJECT TIMES

In addition to its reliable technology, Contexo impresses with its short project times. Contexo is well prepared and provides companies with its full range of experience – it is ready to go and its products can be used very quickly. Manufacturers benefit from rapid, professional implementation, enabling them to market and supply their products swiftly.

Figure 5: High-speed assembly.

Matthias Müller

Matthias Müller is the Chief Commercial Officer of Contexo, which he runs together with his two brothers. His father founded the company in 1975 and the brothers took over the management together in 2011.

T: +49 7181 606 100
E: info@contexo-gmbh.de

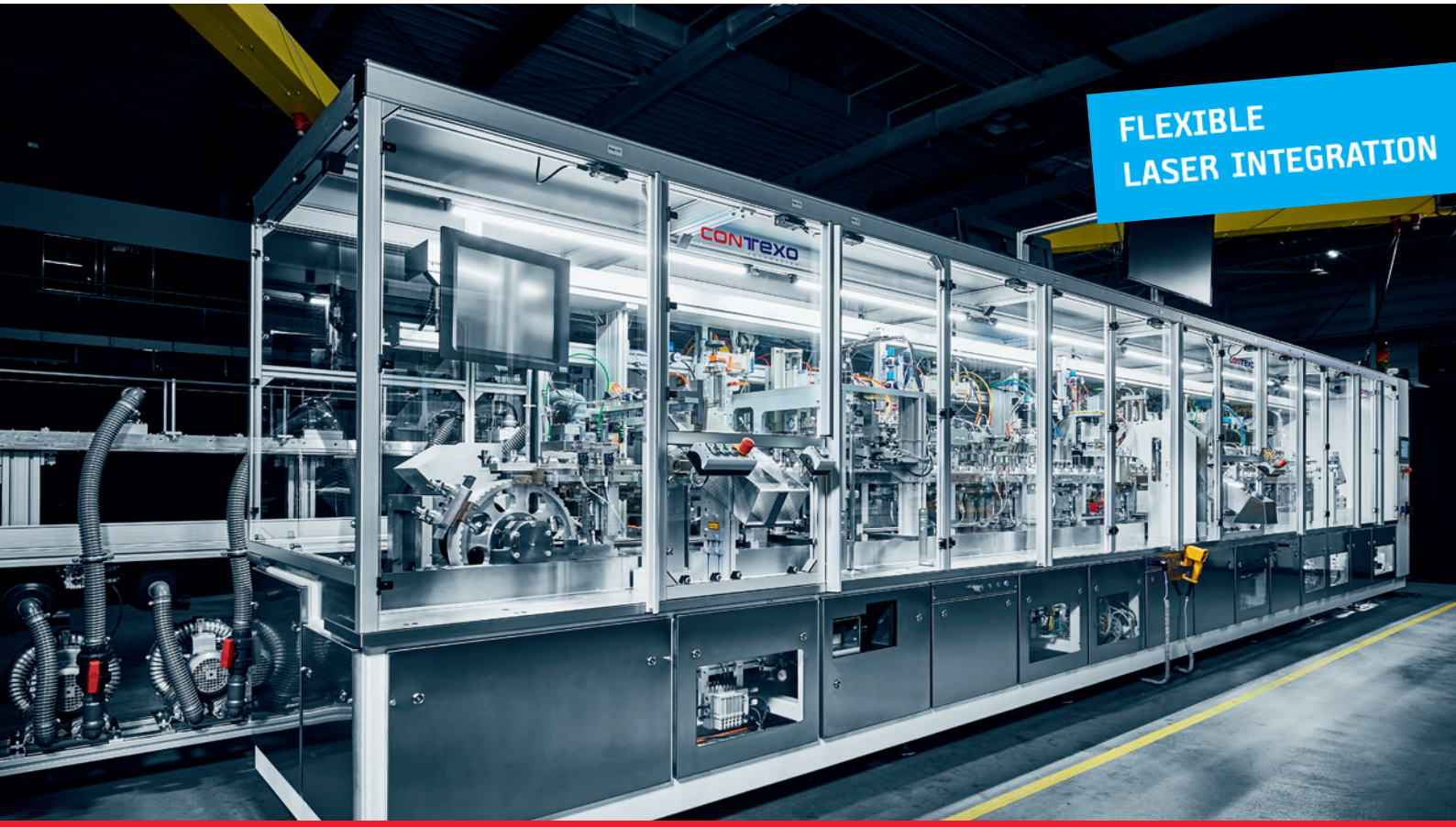
Contexo
Herrenäckerstr. 7-9, 73650 Winterbach, Germany
www.contexo-automation.de

WHERE CONTENT MEETS INTELLIGENCE

ON drugDELIVERY

SCAN TO SUBSCRIBE FREE

CONTEXO
automation



HIGHSPEED ASSEMBLY MACHINES

FOR MEDICAL DEVICES: PRIMARY PACKAGING & DIAGNOSTICS

- FULL PROCESS INTEGRATION
- HIGHEST OUTPUT CAPACITIES
- FLEXIBLE MACHINE CONCEPTS
- GMP FULL SERVICE

www.contexo-automation.de

CONTEXO GmbH Herrenäckerstr. 7-9 73650 Winterbach Germany Tel.+49(0)7181 / 606-100 info@contexo-gmbh.de

FROM CARTRIDGE TO COMMERCIALISATION – UNDERSTANDING THE FILL-FINISH PROCESS

Chelsea Keeton of **Grand River Aseptic Manufacturing** digs into the challenging yet often overlooked process of fill-finish, discussing the particular hurdles and considerations that come with filling drug products into primary containers, with a particular emphasis on cartridges and their role in an injectables landscape increasingly influenced by the needs of biologics.

Developing and manufacturing a drug delivery device is a notoriously difficult process. From initial design work and prototyping through to full-scale commercial production, there are a plethora of individual aspects that all require specialist expertise and know-how to get right, let alone excel at. And, as time goes on, the process is only becoming more complex, with challenging APIs, such as biologics and monoclonal antibodies, demanding that the industry adapt to handle higher viscosities and fill volumes. Simultaneously, pressure is mounting on drug and device developers to create more patient-centric therapies suitable for self-administration as healthcare moves out of the clinic into patients' homes.

With such high demands placed on the industry, it is no surprise to see the prevalence of CDMOs and specialist partners on the rise. Gathering together all the necessary expertise to get a drug-device combination product from concept to market all under one roof is becoming less and less feasible. In an industry as rigorously regulated as pharma, specialist CDMOs can offer the deep institutional knowledge required to de-risk development and smooth the journey from early design to commercialised product.

In the injectables space, a critical area of expertise is fill-finish operations. Prefilled syringes, autoinjectors, wearable injectors and other ready-to-use devices are only continuing to gain relevance, driven by an industry-wide push towards at-home self-administration in an effort to alleviate some of the strain on healthcare systems,

decrease costs and improve patients' quality of life. As an expert CDMO in fill-finish processes, Grand River Aseptic Manufacturing (GRAM) is a leading partner for pharma companies looking to navigate this complex and challenging field.

THE FILL-FINISH PROCESS

Before any new filling line can begin commercial operations, it must undergo and pass a series of rigorous quality checks and validation steps. Experienced CDMOs follow established procedures to ensure that the equipment delivers accurate fill volumes, operates, reliably, maintains sterility, performs consistent in-line inspections and meets regulatory compliance. Understanding what is required of a filling line and how the machinery interacts with the drug formulation and primary container is critical for ensuring smooth operation and minimising waste – a particular concern when dealing with novel biologics.

Regulatory Compliance

A key factor that needs to be considered at this stage is regulation. Fill-finish sites must meet strict requirements set out by various regulations, including the US FDA's 21 CFR Part 11, EU GMP Annex 1 and ISO 13485. This is particularly relevant when considering sterilisation and cleanroom processes for aseptic filling, which are both subject to stringent standards and require specialist infrastructure that may not be readily available to pharma in-house. Working with a specialist fill-finish CDMO can make meeting these requirements significantly easier, as they can use their in-house expertise and specialist facilities to ensure compliance in an efficient manner from a project's beginning, de-risking the process.

"UNDERSTANDING WHAT IS REQUIRED OF A FILLING LINE AND HOW THE MACHINERY INTERACTS WITH THE DRUG FORMULATION AND PRIMARY CONTAINER IS CRITICAL FOR ENSURING SMOOTH OPERATION AND MINIMISING WASTE – A PARTICULAR CONCERN WHEN DEALING WITH NOVEL BIOLOGICS."

Figure 1: Specialist isolator technology may be required when filling highly sensitive biologics.

Sterility

Once a line has been validated and approved, aseptic filling can begin. This is an involved and complex process where a multitude of factors demand attention. First and foremost, it is absolutely vital to prevent any form of contamination entering the formulation, be it particulate or microbial. As such, aseptic filling mandates the use of cleanroom environments in accordance with ISO 14644 regulations.

In some cases, such as with highly potent or complex biologics, traditional cleanrooms may not be sufficient to fulfil this requirement – specialist isolator technology may be needed (Figure 1), which can present a significant up-front cost for companies that have not already made that investment. Additionally, maintaining sterility only becomes more challenging as a filling operation scales up from clinical to commercial scale and batch sizes increase.

Automation

Scale-up is challenging in more ways than just sterility concerns, however. At the small-batch level for early clinical trials, it is possible to rely on manual and semi-automatic processes, but this approach becomes increasingly infeasible at commercial scales. Commercial filling requires the inclusion of automation and robotics across filling, stoppering, inspection and labelling. To successfully automate a filling line requires both expertise to design the line and the mechanical know-how to maintain the line and ensure minimal downtime. GRAM specialises in scale-up and is able to seamlessly transition to larger scales as a drug progresses through the development programme, maintaining flexibility in the early phases and smoothly moving to high-volume manufacture for commercialisation.

Formulation Concerns

It can be easy to overlook the nuances of how the physical properties of a formulation can affect the filling parameters. However, these considerations are critical to ensuring that the drug is filled accurately and reliably into each container. For example, the viscosity of a formulation can dictate the height from which it can be dispensed into a cartridge without splashing, which may lead to rejections during visual inspection if

uncontrolled. Another factor here is bubble formation – if the machinery is incorrectly set up, it can increase the likelihood of the filled liquid containing bubbles, especially for more viscous formulations. Some formulations, such as many advanced biologics, can also be sensitive to shear forces and oxygen exposure, so these factors may need to be tightly controlled during the filling process as well.

Inspection Systems

A filling line must also be able to catch these defects, meaning that they need to include inspection procedures – preferably multiple. Inspection can be performed manually by trained staff or automatically using in-line detection equipment and specialist software (Figure 2). To be as thorough as possible, inspection can go beyond visual inspection by eye or by camera to include additional processes, such as headspace gas analysis, to ensure that the product is filled exactly as required.

Stoppering, Labelling and Storage

Filling the drug substance into the chosen primary container is just the beginning of the fill-finish process. Once the drug is filled, the container must be stoppered, labelled and packaged, each step presenting its own technical challenges and regulatory requirements. Labelling requires careful attention, as regional regulatory variations must be addressed based on the intended market for each batch.

When setting up the filling line, a decision must be made as to what stoppering process to use. The stoppering process will depend on both the type of primary container, such as vials or cartridges, and the needs of the formulation. For cartridges, the standard method is to mechanically insert the stopper with a rod and a vent tube, which prevents the stopper from backsliding. However, in cases where headspace needs to be minimised or the cartridge needs to be free of oxygen, vacuum stoppering may be more appropriate.

Figure 2: GRAM's focus on quality ensures that products are inspected by both trained staff and automated in-line inspection systems.

"IT PAYS TO BRING FILL-FINISH EXPERTS ON BOARD SOONER RATHER THAN LATER TO MAKE THE MOST OF THEIR INSIGHT AND BEGIN PREPARING FOR FILL-FINISH AS EARLY AS POSSIBLE."

During vacuum stoppering, the stopper is placed inside a vacuum chamber connected to the cartridge and then pushed into the cartridge once the correct pressure is reached, causing the stopper to descend right down to the surface level of the filled drug.

Finally, it is important to consider the primary containers themselves throughout the process. If mishandled, glass containers could be scratched or broken, leading to rejections. Then, once filled, stoppered and labelled, the containers need to be stored and transported. It is important to control the conditions that the filled containers are kept in, such as temperature, especially in the case of sensitive biologics.

Partnering for Success

Considering these factors at an early stage of product development can lead to significant savings further down the line in terms of both time and cost. Therefore, it pays to bring fill-finish experts on board sooner rather than later to make the most of their insight and begin preparing for fill-finish as early as possible. Doing so creates the opportunity to circumvent future problems by identifying them before they occur and applying fixes pre-emptively, which can significantly reduce costs in the long term.

GRAM is a leading provider of fill-finish services, with established facilities that have access to state-of-the-art equipment and

Figure 3: GRAM's specialist syringe and cartridge filling centre.

world-class experts in the field, positioning it to be a leading partner for ensuring a smooth and painless fill-finish process (Figure 3).

CONSIDERING CARTRIDGES

A staple primary container format for injectables today is the cartridge, which has become a mainstay of advanced injection devices due to the numerous advantages they offer. However, filling cartridges is a different beast to filling vials, which have historically been the de facto container for injectables. As an expert in fill-finish operations for injectables, GRAM has a wealth of experience and understanding with this format and is able to help its partners through the fill-finish process from clinical trials to commercial scale-up.

For decades, the expectation for injectable drug delivery was that a healthcare professional would administer injections to their patients in a clinical setting using a standard vial and syringe filled at the point of injection. However, the industry has been striving to update this paradigm, first by innovating with prefilled syringes and now with increasingly advanced injection devices, ranging from autoinjectors to wearable devices. The trends driving this shift are manifold, ranging from the drive to shift healthcare from the clinic to the home – requiring devices that are user-friendly enough for laypeople to master – to needing devices that can meet the needs of challenging biologic therapies.

The Advantages of Cartridges

Many of these advanced delivery devices rely on cartridges as their primary container. Cartridges offer unique flexibility to designers compared with vials or syringes as part of an injection device, allowing for both prefilled and user-loaded designs. Cartridges fit easily into a variety of designs and device types compared with other primary containers, due in large part to their more variable form factor, range of volumes and ability to work with custom fluid paths.

Using a cartridge as the basis for a drug delivery device, be it reusable or disposable, provides a baseline assurance of drug sterility compared with requiring the user to fill it from a vial, especially with non-professional users such as patients and carers. Because a cartridge is filled aseptically and directly connected to the fluid path without any need for the user to transfer the liquid, it eliminates the risk of exposing the drug to contaminants during administration.

Beyond these benefits, cartridges are also more efficient than vials, as they eliminate the need for overfilling. To ensure that the listed number of doses can be delivered, vials are typically filled with an excess of drug so that there is no risk of being left with a partial final dose. Cartridges, on the other hand, dispense drug by depressing a plunger like a syringe, so this need is entirely obviated, which can lead to cost savings for expensive biologics. Furthermore, this delivery method allows for precise dosing, unlocking further potential for device designers.

The Challenges for Cartridge Fill-Finish

With these advantages in mind, it is no wonder that device designers are increasingly using cartridges. However, this shift presents challenges to fill-finish providers. There are long established procedures for traditional primary container formats such as vials and 1 mL syringes. Conversely, no such standards exist for larger-volume cartridges – and with devices such as wearable injectors pushing up to 3, 5 and even 10 mL fill volumes, there is a distinct lack of pre-existing infrastructure available.

The increasing use of novel container formats requires fill-finish specialists such as GRAM to adapt with precision and agility. Manufacturing lines must be specifically designed and qualified to accommodate non-standard cartridges with variable fill volumes, while maintaining full compliance with stringent regulatory requirements such as EU GMP Annex 1.

Furthermore, as these programmes progress through the development journey, their fill-finish partners must remain flexible to meet the evolving needs of the novel formulations and devices. This flexibility must be maintained while also planning for eventual scale-up and commercialisation, all of which must be done at a rapid pace as the industry pushes forwards to meet the demands of the moment. Needless to say, this is not a task to be taken lightly – it will require rich expertise and experience to surmount.

EXPERTISE MAKES EVERYTHING EASIER

Fill-finish is both critical and non-trivial – a specialist discipline with its own regulatory demands, challenges and best practices. However, in today's drug delivery landscape, there is no need to try to tackle it alone. Partnering with an expert CDMO with a proven track record, such as GRAM,

"FILLING CARTRIDGES IS A DIFFERENT BEAST TO FILLING VIALS, WHICH HAVE HISTORICALLY BEEN THE DE FACTO CONTAINER FOR INJECTABLES."

can make understanding and navigating the world of fill-finish significantly easier. What could be a challenging and risky road if travelled alone can be made so much simpler by relying on the proven experience of an expert partner in the field.

GRAM prides itself on developing deep and rich partnerships with its collaborators, based on open and frank communication. This transparent approach leads to lower risk and better outcomes, smoothing the development journey from early small-scale production through to full commercial manufacture. GRAM not only has the essential infrastructure already established at its facilities in Grand Rapids (MI, US), but also the institutional knowledge and experience to adapt to the specific needs of a given drug and device. Working together with GRAM, fill-finish can be demystified and scale-up made seamless.

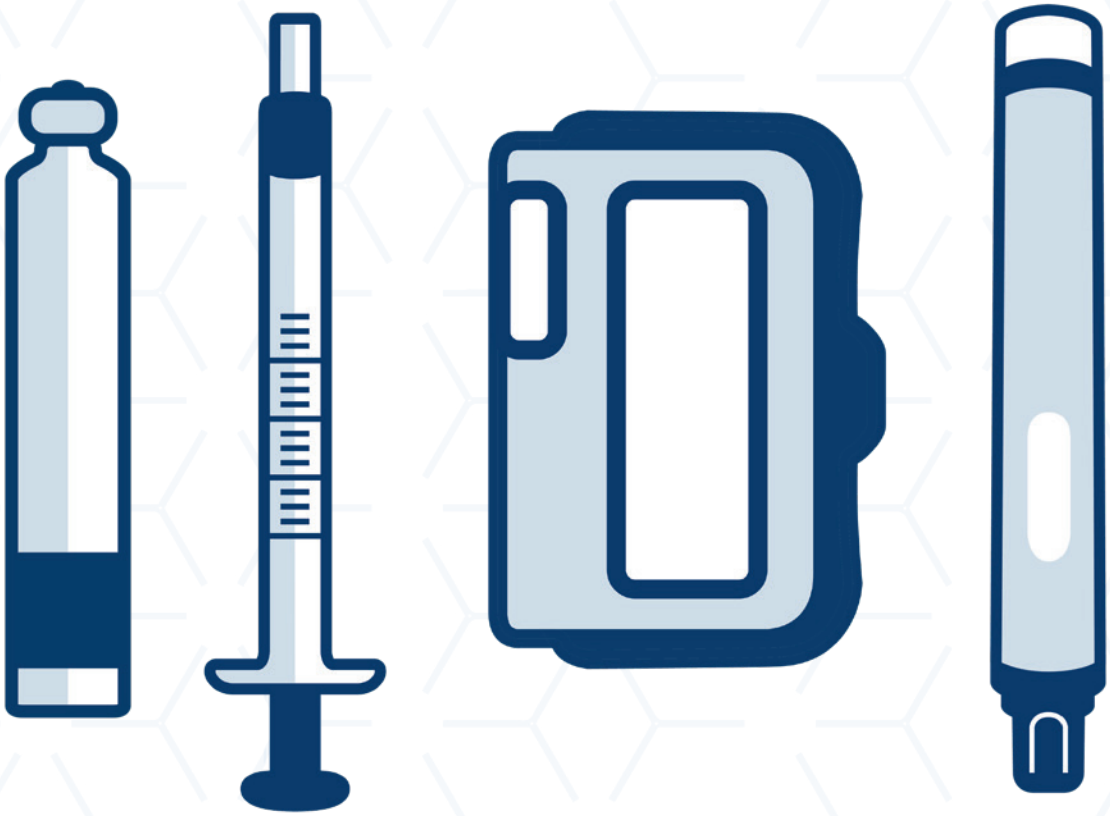
Chelsea Keeton

Chelsea Keeton, Director, Marketing, at Grand River Aseptic Manufacturing (GRAM), has a strong background in marketing and communications and has been an integral part of GRAM since 2019. In her role, she has effectively shared the GRAM story, showcasing the company's innovations and achievements to the industry, customers and stakeholders alike. From spearheading communication efforts, establishing GRAM's brand presence in the market and managing strategic partnerships with industry innovators, Ms Keeton has consistently highlighted GRAM's commitment to excellence. Her passion for innovation, coupled with her commitment to driving growth, makes her a dynamic force in the ever-evolving CDMO landscape.

T: +1 616 678 2400 ext 939
E: ckeeton@grandriverasepticmfg.com

Grand River Aseptic Manufacturing
140 Front Avenue SW, Grand Rapids, Michigan 49504, United States
www.grandriverasepticmfg.com

GRAND RIVER
ASEPTIC MANUFACTURING



Fill-finish CDMO dedicated to supporting advancements in patient care

Grand River Aseptic Manufacturing provides sterile filling and finishing for **syringes, cartridges, and vials** used in drug delivery devices. We are committed to working closely with our customers to develop solutions that meet the evolving needs of patients. We invite conversations on how we can best support your product requirements.

www.grandriverasepticmfg.com

NOLATO'S VIRTUAL FACTORY IN ACTION: ACCELERATING DRUG DELIVERY INNOVATION

Patrik Ingvarsson of **Nolato** discusses the company's virtual factory methodology, wherein embedded technical experts help drug delivery device developers reduce risk, costs and time to market through intelligent application of simulations to facilitate smoother and more robust development cycles with fewer iterations required.

DELIVERING RELIABLE DEVICES FASTER

In the development of complex drug delivery devices, achieving a combination of innovation, quality and speed to market is increasingly critical. Whether it is an autoinjector, pen injector or prefilled syringe, pharmaceutical companies are looking for more effective ways to manage risk, reduce costs and ensure robust manufacturing from the outset.

Nolato addresses this challenge through its virtual factory methodology, designed to improve and de-risk the product development journey. By combining simulation-driven design with manufacturing expertise and global scalability, Nolato offers a structured path from concept to commercial high-volume production.

This front-loaded, simulation-first approach is driven by the company's technical design centres (TDCs), which operate as embedded partners within

> "BY WORKING SIDE BY SIDE WITH CUSTOMER TEAMS, EMBEDDED ENGINEERS CAN GAIN DEEP CONTEXTUAL UNDERSTANDING THAT CAN BE CRUCIAL IN FAST-PACED DEVELOPMENT ENVIRONMENTS."

customer development teams. From concept to industrialisation, Nolato provides digital tools, manufacturing insights and design support to help bring safe and reliable products to market more quickly and with fewer iterations than conventional methods. This proactive involvement enables a more stable and transparent development process, ultimately improving both predictability and performance.

EMBEDDED ENGINEERING: CLOSING THE GAP BETWEEN DESIGN AND PRODUCTION

Rather than acting as an external consultant, Nolato embeds its engineers into its customers' teams from day one. These engineers support real-time design for manufacturing decisions, reducing late-stage changes and streamlining the transfer to production.

This collaborative model enables early alignment on key design features, supports sustainable and cost-efficient solutions, and reduces the risk of misalignment later in the process. Integrating mould flow simulation, tolerance analysis and virtual metrology from the start helps prevent downstream issues and supports faster decision making. By working side by side with customer teams, embedded engineers can gain deep contextual understanding that can be crucial in fast-paced development environments.

VIRTUAL FACTORY IN ACTION

In a recent project involving a multi-component drug delivery device, Nolato worked with a customer on 14 precision-moulded plastic components. The TDC team was fully integrated into the customer's development process, using virtual factory tools at every stage.

Using Moldex3D (CoreTech System Co, Zhubei City, Taiwan) for mould flow analysis and Zeiss Inspect (Zeiss, Oberkochen, Germany) for computed tomography (CT)-based metrology simulation (Figure 1), Nolato virtually analysed over 440 individual dimensions. This enabled the team to anticipate measurement outcomes and define a robust measurement strategy before pilot tools had been ordered. When physical parts were produced, all dimensions were within tolerance, with only four needing slight adjustments to approach the nominal target more closely. This was achieved without having an impact on the development timeline.

Figure 1: Nolato's virtual factory incorporates CT-based simulations as part of its toolset.

"THIS APPROACH ENSURES CONSISTENCY BETWEEN VIRTUAL VALIDATION AND PHYSICAL QUALIFICATION AND ENABLES FASTER CORRELATION BETWEEN PREDICTED AND ACTUAL OUTCOMES."

According to the customer, the project ran "easy and smooth", with specific praise for Nolato's simulation expertise and dimensional assurance. This outcome was achieved through early validation and data-driven decision making embedded in the development model. It reflects how systematic simulations and planning can replace costly iterations and uncertainty.

VIRTUAL PROTOTYPING AND DIMENSIONAL VALIDATION

The virtual factory methodology starts with simulation of component behaviour using a combination of:

- Mould flow analysis for evaluating material flow, cooling behaviour and warpage
- Tolerance stack-up simulations to ensure assembly fit and identify critical dimensions
- Finite element analysis for validating stress performance and structural reliability
- Virtual dimensional measurement planning for pre-validating inspection strategies
- CT scanning evaluation software for simulating and analysing measurement results.

Measurement programs are developed early using CT-based evaluation tools, simulating the inspection process as it will be carried out on physical parts (Figure 2). These programs are tested and verified in the virtual environment, allowing teams to apply the same measurement strategies to both simulation data and real-world samples. This approach ensures consistency between virtual validation and physical qualification and enables faster correlation between predicted and actual outcomes.

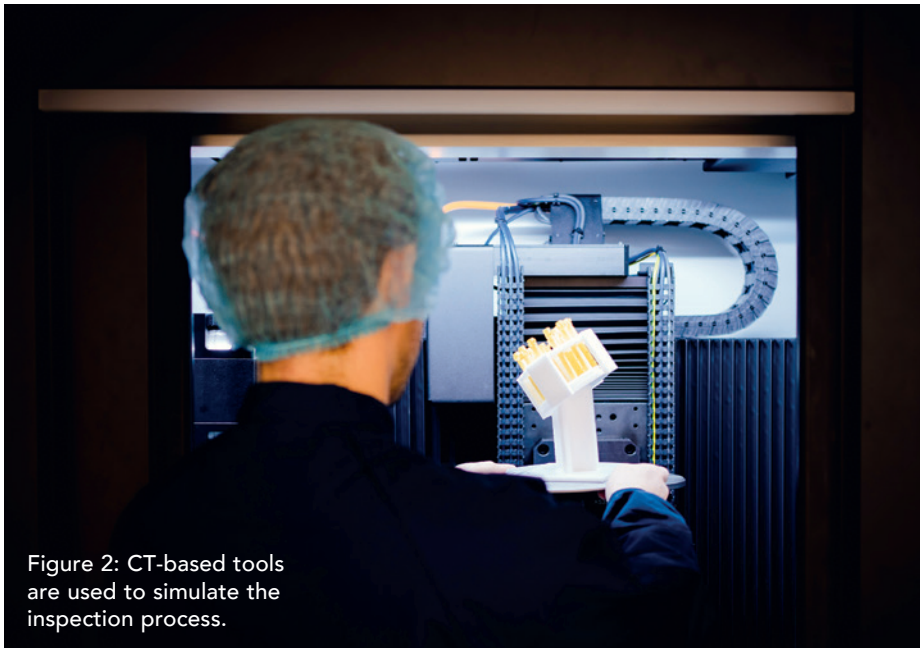


Figure 2: CT-based tools are used to simulate the inspection process.

These tools support detailed analysis of geometry, manufacturing feasibility and part-to-part fit before physical tools are created. Simulations also enable early identification of potential risks, such as sink marks, air entrapment or misalignment. The resulting metrology plans are then directly applicable when real parts are produced, saving time and reducing trial iterations.

This simulation-first approach ensures that the physical validation phase is faster and more predictable, reducing the time between design freeze and product launch. It also supports better communication between design and manufacturing stakeholders by providing a common reference based on quantifiable simulation results.

SCALABILITY: FROM PILOT TO HIGH-VOLUME MANUFACTURING

A key strength of Nolato's approach is its ability to scale. Starting from low-volume pilot production, the development path is designed to seamlessly support transfer into fully automated cleanroom manufacturing. This transition is supported by a phase-gated model involving design, tooling, automation and quality experts early in the project. As a result, virtual models evolve into validated processes with fewer surprises during scale-up. This structured collaboration ensures that automation strategies and quality control are already considered well before production reaches full scale.

FLEXIBLE INFRASTRUCTURE TO MATCH PRODUCT NEEDS

Nolato operates 17 certified medical manufacturing facilities worldwide, including ISO 13485-compliant and US FDA-registered sites. This allows its customers to localise production while maintaining high quality standards. Whether scaling a wearable injector or launching a high-volume pen injector, Nolato's global footprint and local decision making ensure responsiveness and alignment. Its recent expansions in Southeast Asia and Europe demonstrate the company's readiness to support dynamic project needs. This flexibility can help Nolato's customers navigate shifting regulatory environments and respond to market demand without compromising delivery timelines or quality.

FRONT-LOADED DEVELOPMENT FOR PREDICTABLE OUTCOMES

Nolato's virtual factory is not just a toolkit but a comprehensive methodology that connects simulation, measurement and manufacturing right from the start of product development. By embedding engineering expertise early and validating key performance indicators before steel is cut, Nolato helps development teams reduce uncertainty and accelerate delivery.

This model supports faster decision making, fewer tool iterations and more predictable manufacturing outcomes, resulting in more reliable product launches for demanding drug delivery devices. In a landscape where timelines are tight and compliance is non-negotiable, this kind of early integration provides a crucial advantage.

Patrik Ingvarsson

Patrik Ingvarsson is Technical Director at Nolato TDC EU, a centralised organisation supporting customers in developing new products with a focus on high-volume production and manufacturability. With over 25 years of experience in plastic part production and development, he holds an MSc in Mechanical Engineering specialising in polymer technology. Mr Ingvarsson's expertise spans part and mould design, injection moulding processes and material selection. He is highly experienced in using simulation technologies, including injection moulding and structural and thermal analysis, to optimise design and production efficiency.

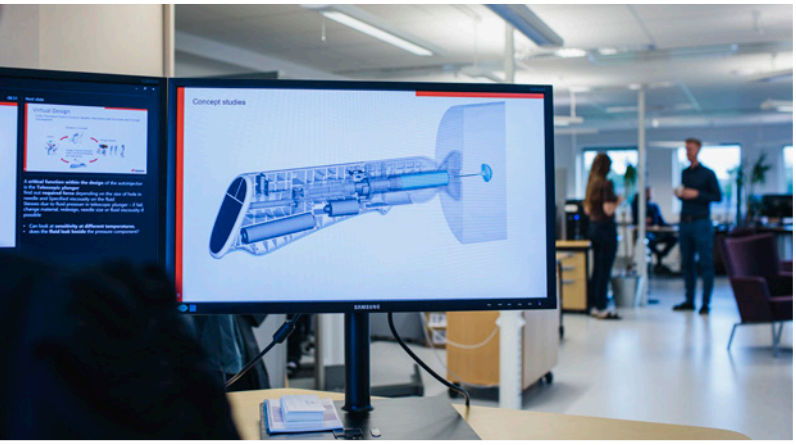
T: +46 76 888 0075
E: patrik.ingvarsson@nolato.com

Nolato MediTech AB
Medicingatan 4, Hörby 24293, Sweden
www.nolato.com

Innovative Drug Delivery Solutions from Concept to Market

At Nolato, we transform ideas into advanced drug delivery devices — from pen-injectors and auto-injectors to inhalers and wearable injectors. Backed with decades of expertise, we deliver end-to-end solutions, from R&D and prototyping to full-scale production and market launch.

With a global footprint spanning state-of-the-art, FDA-registered and ISO-certified facilities across Europe, Asia, and North America, we ensure local support and world-class manufacturing wherever you are. Our commitment to innovation, sustainability, and quality empowers patient-centric care and successful product launches worldwide.



Nolato | Medical Solutions | Box 93 | SE-242 21 Hörby | Sweden
Phone: +46 (0) 415 19 700 | E-mail: info.medicalsolutions@nolato.com | www.nolato.com

INFLUENCE OF MACHINE CONCEPTS ON OVERALL EQUIPMENT EFFECTIVENESS

Carsten Köhler of **BBS Automation** provides an overview of the key metrics that contribute to overall equipment effectiveness for manufacturing drug delivery devices, detailing some of the options available when considering large-scale, high-volume manufacture.

In today's competitive manufacturing landscape, achieving optimal operational efficiency, product quality and regulatory compliance is essential. Accurate calculation of production output plays a crucial role in assessing system performance, identifying bottlenecks and guiding continuous improvements. Different machine concepts – ranging from linear and rotary systems to continuous motion and cam-driven indexing – offer distinct advantages and challenges, influencing throughput, flexibility and suitability for specific applications like injection device production. Additionally, factors such as material supply and equipment accessibility significantly impact overall productivity and product quality. Understanding these elements and selecting appropriate production systems is essential for optimising operations, reducing waste and ensuring the consistent delivery of high-quality injection devices in demanding industries, such as pharmaceuticals and medical devices.

DEFINITION OF EQUIPMENT OUTPUT

A key topic in the planning phase for new production equipment is the required output of the product stream, identified by the overall equipment effectiveness (OEE). Under this metric, the elements of yield, availability, quality control samples and the count of acceptable parts are combined, as defined in

ISO 22400:2014 and illustrated in Figure 1:

- **Availability** measures the proportion of scheduled production time during which the equipment is operational and capable of producing. It accounts for planned downtime (e.g. maintenance) and unplanned downtime (e.g. breakdowns). It is crucial to reduce downtime and maximise productive periods, aligning with standards such as ASTM E2334-14.

- **Performance** evaluates how close the actual production rate is to the maximum possible rate, considering speed losses. In most systems, this rating is not looked at too closely, as most automation systems run at a fixed rate.

- **Quality** assesses the proportion of produced units that meet quality specifications without rework or rejection. The yield is part of this, as it accounts for the amount of waste produced. This metric is often the most important, as a reduction in bad parts carries more weight than some parts not being produced – especially in the final stages of production in injection systems where the drug wastage can be a major expense.

As this formula does not differentiate between losses induced by the production facility (e.g. meeting schedules, cleaning, batch changes) and machine-related downtime or bad parts, the term "machine OEE" is used. The aim is to consider only the losses that have been induced by the equipment for which the equipment manufacturer is responsible, especially during the buy-off and warranty period. The following sections highlight some important points to consider during evaluation of machine concepts to improve the performance and ease of handling of the equipment from the perspective of the production facility.

$$OEE = \frac{\text{Actual production time}}{\text{Possible production time}} \times \frac{\text{Actual output}}{\text{Possible output}} \times \frac{\text{Numbers of good product}}{\text{Actual output}} \times 100$$

Figure 1: OEE formula.

INFLUENCE OF CONCEPT SELECTION

Linear Versus Rotary Systems

Linear systems are flexible in both length and number of operating stations (Figure 2), supported by a wide variety of actuator designs, including robots, servo plug-and-play (PnP) and cam-driven. The layout of linear systems can be designed around material flow and operator access, meaning that the design can reflect the needs of production. Usually, the required investment is higher, as linear systems have a larger footprint.

The speed of these systems is determined either by the transport system of the work piece carriers or the process time of the integrated stations. Due to the length scalability of linear systems, the number of operations that can be conducted in parallel is high, which means that the output can be increased dramatically.

The opposing concept is the rotary system (Figure 3). In these systems, the consequences of the layout are not necessarily as obvious. These concepts are based around the philosophy that work piece carriers travel around a centre point in a fixed chain, mostly on a table or ring transport.

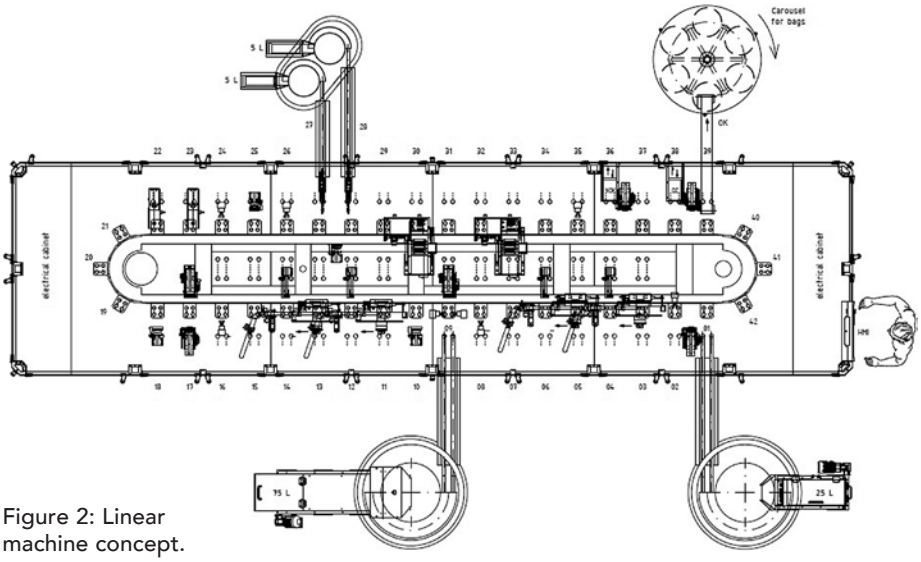


Figure 2: Linear machine concept.

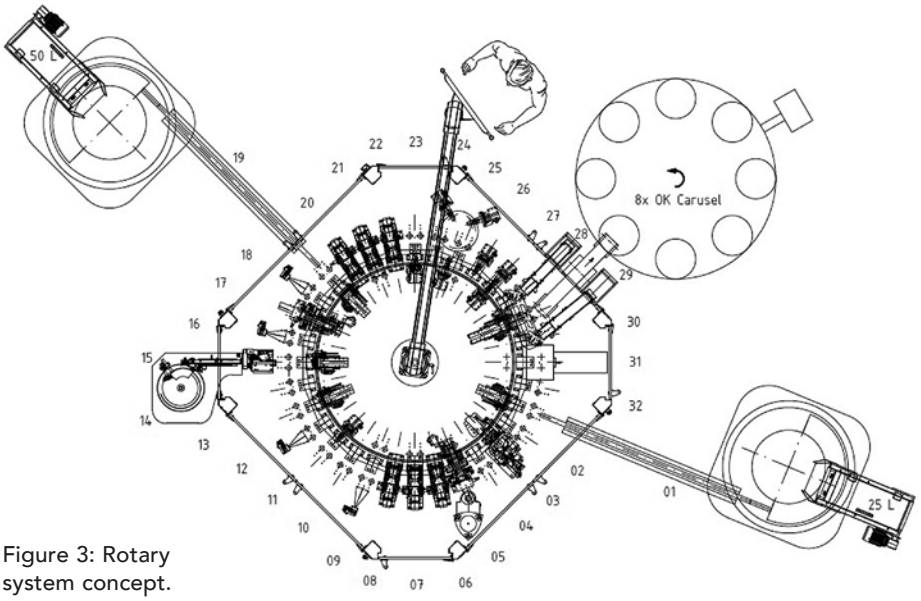


Figure 3: Rotary system concept.

"WHICH OF THE TWO BASIC DESIGN CONCEPTS – LINEAR OR ROTARY – IS SELECTED IS OFTEN DEPENDENT ON PREFERENCES, WITH POSSIBLE SOLUTIONS EXISTING ON BOTH PLATFORMS."

Due to this base concept, the size of these machines is limited. One reason for this limitation is that the unused space in the centre of the machine increases with size, making larger machines much less space efficient. The other factor is transport – if the machine is wider than a standard truck, the transport cost increases significantly. A single rotary system offers notable advantages for assembly steps with a limited number of parts, especially in facilities with smaller cleanroom facilities.

Which of the two basic design concepts – linear or rotary – is selected is often dependent on preferences, with possible solutions existing on both platforms. A limiting factor can be the output requirement – if the required number of parallel operations exceed the dimensions of the rotary system, it will be necessary to go with a linear system. Besides that, some supporting requirements may shift the balance to one or the other option.

Material Supply

Optimising material supply in a factory for automated production is essential for ensuring smooth operations, minimising downtime and reducing costs. The material supply to the equipment can be divided into two perspectives.

The first perspective is bringing materials to the production equipment. This influences the necessary layout from the viewpoint of the logistics path and storage areas around the production equipment. In larger production halls, dedicated material streams are essential for timed supplies. This requirement leans towards linear systems with dedicated feeding areas. In smaller facilities, the entry to the cleanroom is probably the end of the logistics chain. Here, the preferred option is often for the rotary system with the feeding spread around the equipment.

The second perspective is the equipment feeding components into the process stream. Depending on the geometry and flexibility requirements, a range of different designs exist. The most common feeding device is the feeder bowl, where the parts get transported by vibration (Figure 4). Other options are drum feeders, step feeders and so on. These variants are often focused on a specific geometry or feature of the components to be fed into the machine.

To achieve higher flexibility, some assemblies also use camera-guided robots. The components are dropped onto plates with clear lighting, after which a camera guides the robot to the pick-up position. As this option can accommodate various geometries, the speed is often slower than with other options.

The springs in injection devices – which can have a tendency to entangle – often define the feeding in drug delivery devices. This leads to concepts specifically accommodating the springs. Three distinct strategies are applied:

- **Drum Feeders:** This option is suitable for springs that have only a limited tendency to entangle and is the most common approach, sometimes with limitations in availability.
- **Tray Feeding:** This is suitable for any spring but, due to the logistics cost, is often only used as the last resort or in the case of springs with specially formed ends, such as hooks or loops.
- **Spring Winding at the Assembly Equipment:** Here it is important that the redundancy of the feeding system provides a continuous flow of springs towards the assembly process.

In general, the selection of the best feeding system is an essential part of achieving the highest OEE values. Without a continuous stable inflow of components, the best production equipment is unable to perform.

Accessibility

The accessibility of production equipment significantly influences the overall output and operational efficiency in a manufacturing environment. When equipment is easily accessible, maintenance, repairs and adjustments can be performed swiftly and effectively, minimising downtime and ensuring a continuous production flow. Prompt accessibility enables operators and maintenance personnel to quickly address issues, perform routine inspections and implement necessary changes without unnecessary delays, thereby maintaining optimal equipment performance and maximising throughput – crucial factors in high-volume injection device manufacturing where time is critical.

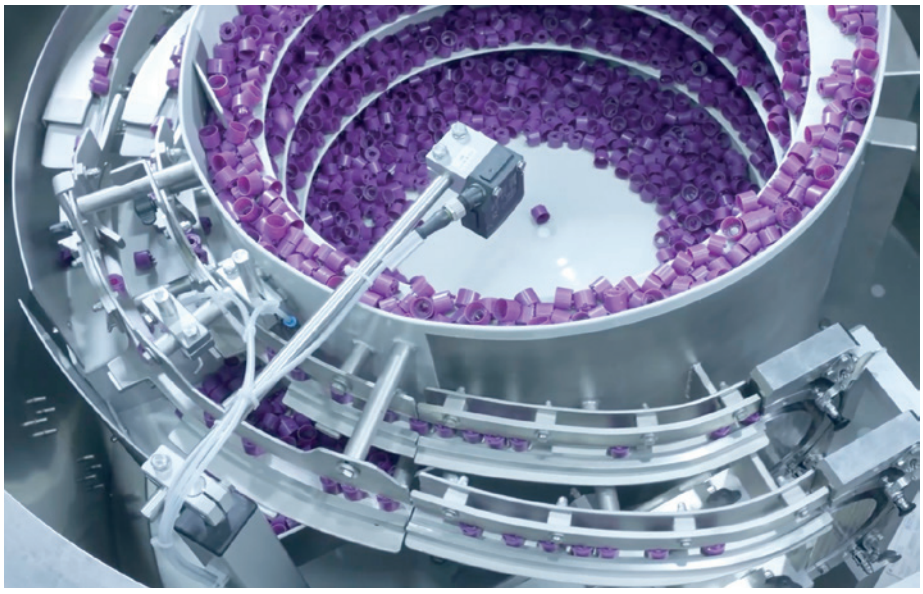


Figure 4: Vibratory feeder bowl.

When equipment used in injection device production – such as sterilisation chambers, assembly stations and filling lines – is hard to access, technicians may need to disassemble parts of the production line, resulting in longer repair times and interruptions in the manufacturing schedule. Therefore, designing production lines with accessibility in mind, such as incorporating sufficient space around machinery, modular layouts and ergonomic considerations, can substantially improve output levels and operational resilience. In summary, enhancing equipment accessibility is a key factor in optimising manufacturing performance and ensuring the consistent, high-quality output of injection devices.

DECISION ON PROCESS STATIONS

Pneumatic and Semi-Automatic Systems

Today, pneumatics are primarily used as secondary actuators rather than for primary movement. However, in semi-automatic systems designed for low-volume production, pneumatics remain a common choice due to their simplicity and cost-effectiveness. In high-volume production environments, however, servo-electric or cam-driven stations tend to dominate, offering greater precision and durability.

Pneumatic actuators benefit from straightforward integration and ease of maintenance, making them suitable for auxiliary functions such as clamping or positioning. Nonetheless, their operational lifespan is limited by the wear and tear of seals, which rely on pressure to function effectively; these seals typically require replacement after a certain number of cycles, often far below the lifespan of electric or mechanical systems. This limitation restricts their use for primary motion in high-speed, high-volume applications. Despite this, pneumatic systems remain widely available and cost-effective, especially in semi-automatic setups where their simplicity and rapid deployment outweigh longevity concerns.

Servo-Electric

In most production systems, multiple stations using servo-electric motion are used to enhance efficiency and precision (Figure 5). These systems range from semi-automatic tabletop setups to high-volume production lines featuring numerous parallel operations. The primary advantage of servo-electric solutions is their high degree of flexibility in motion control within the mechanical constraints of the axes used. When these stations are constructed with linear axes or robotic variants, the core feature becomes the programmable motion range, allowing for dynamic adjustments and customisation based on production needs. This adaptability significantly reduces downtime and tooling changes, enabling rapid setup for different product variants.

In the context of injection-moulding devices, this flexibility is particularly valuable, as it permits adjustments in dimensions within a single product group without extensive reconfiguration. Moreover, servo-electric systems facilitate the precise synchronisation of multiple axes, improving process consistency and quality. Their programmability also supports complex motion sequences, which can optimise cycle times and energy consumption, ultimately leading to increased productivity and reduced operational costs.

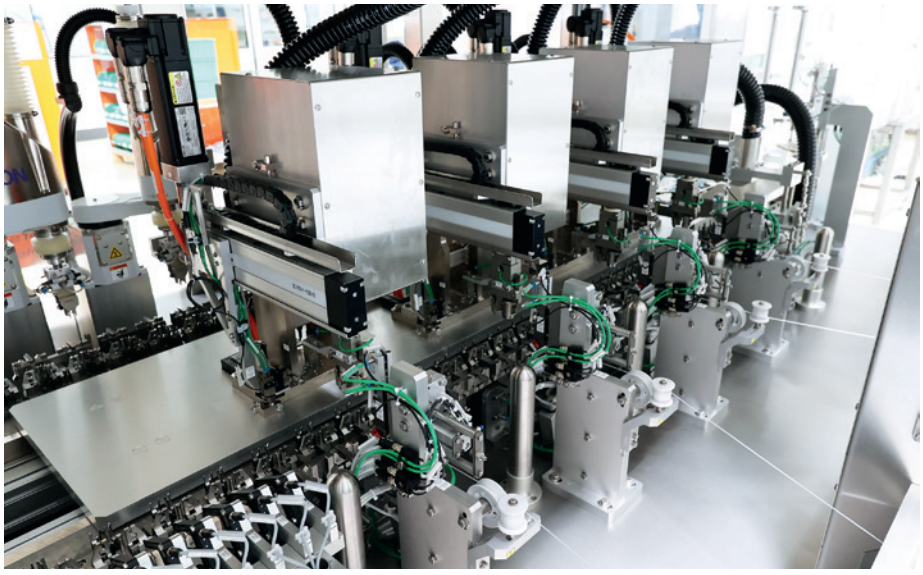


Figure 5: Servo-electric PnP.

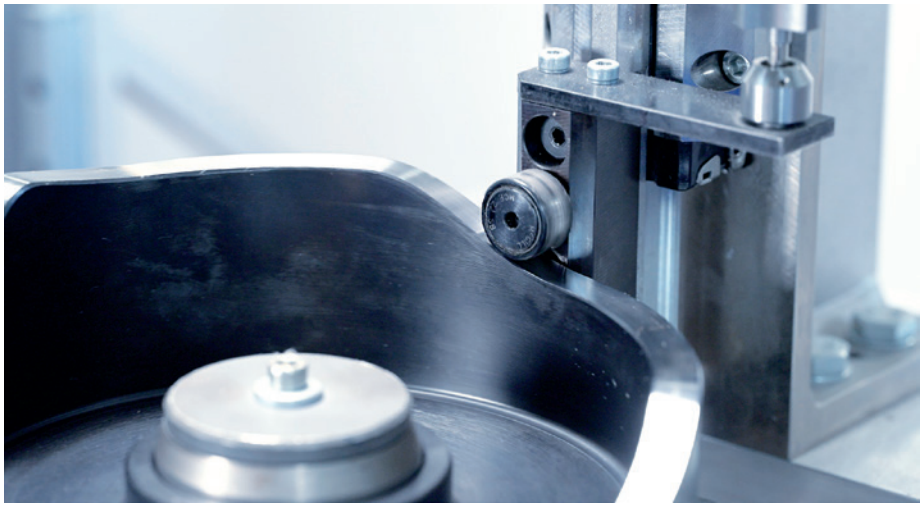


Figure 6: Detail of a cam drive.

Cam-Driven Indexing

The output features of a cam-driven indexing production system are characterised by precise, synchronised movement and high repeatability (Figure 6), making them

particularly suitable for the manufacturing of injection devices such as syringes, vials and safety caps. This type of system uses a cam mechanism to control the timing and positioning of workpieces, ensuring accurate indexing and transfer between processing stations critical for the assembly and sterilisation of injection devices.

One of the key features of these systems is their ability to perform rapid, consistent indexing movements, which significantly enhances cycle times and overall productivity. The cam profile determines the exact position, speed and timing of each indexing step, enabling precise control over the production process, which is essential for maintaining tight tolerances.

Another important feature of these systems is their reliability and robustness. Cam-driven systems are mechanically simple and durable and, therefore, capable of operating continuously with minimal maintenance over extended periods – often remaining operational for decades.

Their design also allows for simultaneous multi-station indexing, increasing throughput without sacrificing precision, which is important when producing large batches of standardised injection devices. And, while they are initially less flexible than programmable systems, a combined approach with servo-electric stations can help to eliminate this constraint.

Continuous Motion

The output features of a continuous motion production system are characterised by seamless, high-speed operation and consistent product flow (Figure 7), making them highly suitable for the manufacturing of injection devices. Unlike indexing or step-by-step systems, continuous motion systems maintain uninterrupted movement of injection devices along the production line, enabling rapid throughput and minimal cycle times.

Figure 7: Continuous motion setup.

"UNLIKE INDEXING OR STEP-BY-STEP SYSTEMS, CONTINUOUS MOTION SYSTEMS MAINTAIN UNINTERRUPTED MOVEMENT OF INJECTION DEVICES ALONG THE PRODUCTION LINE, ENABLING RAPID THROUGHPUT AND MINIMAL CYCLE TIMES."

SUMMARY

In the production of injection devices, achieving optimal efficiency begins with precise measurement of equipment performance through OEE. This standard metric, based on ISO 22400:2014, combines yield, availability and quality to determine the required production rate. Availability reflects operational uptime, performance gauges how closely actual output matches maximum capacity and quality assesses the percentage of acceptable parts, with particular emphasis on minimising waste – especially during critical final production stages.

The choice of equipment design – linear versus rotary systems – significantly impacts production flexibility, scalability and maintenance. Linear systems offer high adaptability, supporting varied layouts and parallel operations, but require larger footprints and higher investment.

Rotary systems are more compact and suitable for assembly steps with limited parts, making them ideal for smaller cleanroom environments, though their throughput capacity is constrained by size limitations.

Material supply strategies are equally vital; while dedicated feeders such as vibratory bowls are common, alternatives such as drum feeders, tray feeding and camera-guided robots can provide higher flexibility. Proper handling of components prone to entanglement, such as springs, through specialised feeding solutions can ensure high OEE by maintaining a steady inflow of components.

Accessibility of equipment also plays a crucial role in production efficiency. Designing machinery with sufficient space, ergonomic layouts and modularity can facilitate easy maintenance and reduce downtime, supporting higher throughputs. The actuators of process stations using pneumatics are cost-effective and simple for low-volume production, while servo-electric and cam-driven systems dominate high-volume manufacturing due to their precision, flexibility and durability. Meanwhile, continuous motion systems enable seamless, high-speed operations, maximising throughput for assembly and inspection tasks.

BBS Automation offers comprehensive solutions across all these areas, providing tailored equipment and automation systems designed to optimise performance, flexibility and reliability, ensuring high product quality and efficient manufacturing of injection devices.

Carsten Köhler

Carsten Köhler, DBA, is Vice-President Sales at BBS Automation, having specialised in automation solutions for medtech devices for over 15 years. Before joining BBS Autoamtion, Mr Köhler led specialised teams for medtech automation in various roles throughout the industry. His overall competence is comprehensive, including project planning, mechanical and electrical design, software, qualification and documentation.

T: +49 7141 7003 177
E: carsten.koehler@bbsautomation.com

BBS Automation Stuttgart GmbH
Planckstrasse 40, 71691 Freiburg (Neckar), Germany
www.bbsautomation.com

Expert View

AUTOINJECTORS VERSUS ON-BODY SYSTEMS: THE FUTURE OF LARGE-VOLUME DELIVERY

Dr Alex Vasiev and **Dr Ethan Miller**, both of Springboard, a Sanner Group Company, weigh up the benefits and costs of using on-body injectors versus autoinjectors, discussing delivery, design and patient population variability alongside recent advances in on-body injector development.

"AS DELIVERY TECHNOLOGIES ADVANCE, THE QUESTION IS NO LONGER WHETHER LARGE-VOLUME PARENTERAL THERAPIES CAN BE ADMINISTERED OUTSIDE THE CLINIC, BUT HOW TO DO SO MOST EFFECTIVELY. AUTOINJECTORS HAVE HISTORICALLY EMPOWERED PATIENTS TO SELF-ADMINISTER AT HOME, BUT THEIR PRACTICALITY DIMINISHES AS VOLUMES RISE BEYOND 2 ML."

With the continuing shift of healthcare from clinics to the home, more injectable therapies are moving from intravenous (IV) to subcutaneous (SC) administration, particularly in oncology and immunology. SC delivery of high-dose biologics offers clear advantages, including greater patient convenience and potential cost savings, but large-volume or high-viscosity formulations bring distinct challenges in formulation stability, device design and the route to commercialisation.

As delivery technologies advance, the question is no longer whether large-volume parenteral therapies can be administered outside the clinic, but how to do so most effectively. Autoinjectors have historically empowered patients to self-administer at home, but their practicality diminishes as volumes rise beyond 2 mL.

Debate continues across the industry on key considerations such as patient experience, cost and reimbursement, device complexity, regulatory uncertainty and the level of investment required for new infrastructure. A growing consensus suggests that large-volume delivery strategies may increasingly consolidate around wearable on-body injectors (OBIs) rather than oversized autoinjectors. As the adage goes: just because it can be done does not mean that it should.

THE HANDS-FREE ADVANTAGE

OBIs are inherently more complex and costly than autoinjectors. They often incorporate adhesive pads, multiple components and sometimes reusable elements, electronics and software. These features increase development costs, extend timelines and place higher demands on both supply chains and users. Autoinjectors, in contrast, are simpler and more cost-efficient. However, when used for volumes exceeding 2 mL, they require greater power and enhanced user interfaces to accommodate longer injection times, as well as larger, heavier form-factors that erode their perceived advantages.

Figure 1: Large-volume autoinjectors require increased power, posing a technical challenge; however, the primary barriers remain usability issues and the pain associated with rapid delivery of large volumes.

Both device types also raise reliability considerations. OBIs must address risks such as occlusion, leakage and incomplete dosing during extended wear, whereas large-volume autoinjectors must ensure the long-term stability of their high-power mechanisms and maintain the integrity of novel container closures.

The primary limitations of large-volume injections stem from human physiology. Autoinjectors are generally well tolerated for small volumes (<2 mL),[1,2] but rapid administration of larger volumes can strain SC tissue, elevate interstitial pressure and increase discomfort. Attempts to reduce injection volumes by concentrating formulations can introduce additional challenges – higher viscosity solutions require more power to deliver effectively (Figure 1).

OBIs overcome many of these limitations by enabling hands-free, extended delivery over minutes to hours, which significantly reduces power requirements (Figure 2). Slower, controlled administration decreases tissue stress and interstitial pressure, improving overall tolerability. Studies, including that by Doughty *et al* (2016),[3] demonstrate that extended delivery can substantially reduce perceived pain. This extended delivery time therefore not only enhances patient comfort but also provides greater dosing flexibility and a broader operational envelope, which is a benefit in early clinical evaluation.

DEVICE AND CLINICAL STRATEGY

SC absorption is influenced by injection volume, viscosity and administration site, making device selection critical to clinical success. Early-phase studies (Phase I/Ib) evaluate a range of injection volumes, formulation concentrations and delivery rates to characterise pharmacokinetics, systemic exposure and tolerability. To accommodate this, delivery devices need to be easily configurable.[4]

While OBIs often involve longer development timelines than standard autoinjectors, they offer significant advantages once established, including the ability to handle a broad range of formulations and easier configuration across different dosing regimens. By contrast, large-volume autoinjectors have more limited formulation flexibility and may require substantial modifications to support changes in injected volume, which is especially true of spring-powered systems.

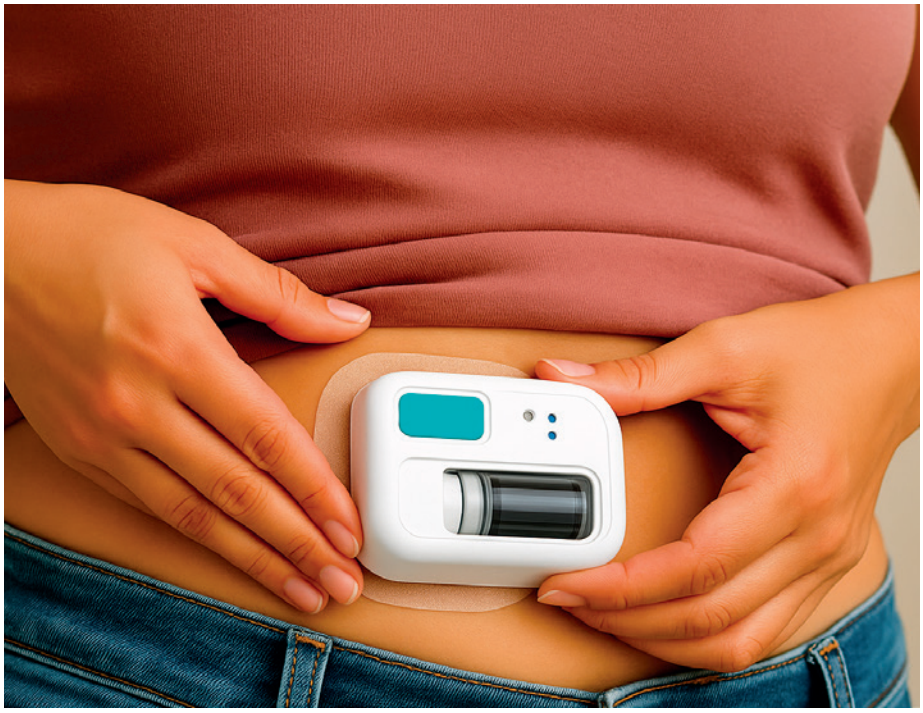


Figure 2: Wearable technologies are becoming the established solution for the delivery of high-dose (large-volume or high-viscosity) formulations.

One key opportunity identified by The Subcutaneous Drug Development and Delivery Consortium is the use of bridging strategies informed by pharmacokinetics and pharmacodynamics to guide the transition from IV to SC formulations.[4] In this context, *in silico* device and tissue modelling plays a pivotal role in optimising device selection and predicting performance for a given therapeutic profile, supporting early, informed decision-making ahead of clinical development.

OPTIMISING INJECTION PARAMETERS

For both device types, identifying the optimal balance between injection speed, volume and formulation properties remains a significant challenge. The interplay of device, tissue mechanics and formulation creates a highly complex, multi-dimensional parameter space, while limited clinical data further complicates predictions. Even sophisticated modelling approaches can only partially capture this complexity. Nevertheless, several groups have developed sophisticated models to better understand the mechanics and pharmacokinetics of large-volume SC (LVSC) injections:

- **Hou *et al*** (2021)[5] used a multiphysics finite-element model treating SC tissue as a poroelastic medium, coupling tissue deformation, interstitial fluid dynamics and lymphatic uptake. Their simulations captured steep local pressures and slow clearance but relied on assumptions of tissue homogeneity and ignored vascular heterogeneity.

- **Pepin *et al*** (2023)[6] introduced SubQ-Sim, a physiologically based biopharmaceutics model integrating device parameters, depot formation and variability from disease states and "life events", revealing dynamic links between back-pressure, depot geometry and formulation losses.

- **Li *et al*** (2024)[7] advanced multi-scale modelling by coupling macroscale skin transport with mesoscale lymphatic uptake, highlighting non-uniform drug distribution, the dominant role of initial lymphatics and the critical influence of binding interactions.

Despite these advances, variability between patients in tissue permeability, extracellular matrix properties and lymphatic function complicates defining universal injection parameters.

ACCOUNTING FOR POPULATION HETEROGENEITY

Predictive modelling can help anticipate thresholds where tissue stress, pain, or suboptimal drug distribution may occur. Computational models and practical testing strategies can be used to bring clarity to the complex problem of tissue response during large-volume injections. By simulating tissue deformation, interstitial fluid dynamics and lymphatic uptake, these models identify regions of elevated pressure, potential depot formation and back-pressure that influence patient tolerability and pharmacokinetics.

However, models alone cannot capture tissue heterogeneity or individual variability. Experimental validation using *ex vivo* tissue analogues, synthetic gels, or animal models can provide real-world insight under varying injection volumes, viscosities, needle geometries and flow rates. Integrating models with experimental data creates an iterative feedback loop in which simulations inform experimental design and experimental results refine the models. This approach can guide needle and delivery mechanism specifications and define appropriate windows for injection rates, optimising devices to be robust, physiologically appropriate and capable of delivering large-volume SC injections safely and effectively.

"INTEGRATING MODELS WITH EXPERIMENTAL DATA CREATES AN ITERATIVE FEEDBACK LOOP IN WHICH SIMULATIONS INFORM EXPERIMENTAL DESIGN AND EXPERIMENTAL RESULTS REFINE THE MODELS."

Figure 3: The effect of hyaluronidase adjuvant on the tissue back-pressure experienced during a 10 mL, 7 cP injection over several minutes. Note that the effect becomes apparent after a certain timescale during delivery and that a plateau is reached during the delivery. Reproduced from Pepin *et al* (2023).

RISK

Risk considerations differ between OBIs and large-volume autoinjectors. OBIs involve slow, prolonged deliveries, which introduce the potential for adhesive failure and incomplete dosing. Electronic or connected OBIs can help mitigate these risks through adherence monitoring, guided setup and automated alerts, but these features also add complexity for the user and extend the path to regulatory compliance, lengthening development timelines.

Large-volume autoinjectors rely on high-power mechanisms to deliver the formulation within an appropriate timeframe. Rapid activation of these mechanisms can cause component or container failure, while sustained mechanical stress may result in creep, potentially triggering premature activation. As described previously, they also require longer delivery times. Coupled with often larger and heavier form-factors, this can create additional challenges related to user dexterity and comfort.

Overall, selecting a delivery device for large-volume formulations requires careful balancing of multiple factors. OBIs provide slow, controlled delivery with reduced tissue stress but come with added device complexity, while high-powered autoinjectors offer rapid delivery but introduce mechanical risks and physical limitations. Collaborating with partners who possess in-depth expertise in human factors, device physics and development can help address these challenges early in the development programme, improving both device performance and patient outcomes.

ENABLING ADVANCES IN TECHNOLOGY

Advances in materials, adjuvants and digital technologies are critical enablers for large-volume SC delivery. Adjuvants such as hyaluronidase are being explored to improve tissue permeability, though their effectiveness for pain reduction and effectiveness for the delivery of extremely viscous formulations maybe limited (Figure 3).[4]

Adhesive systems have evolved rapidly, with sweat-adaptive, light, hydrogel films providing strong, conformal adhesion while maintaining comfort and breathability.[8,9] These hydrogels dynamically respond to moisture, reducing skin irritation during extended wear and ensuring secure device placement.

Connected OBIs integrate companion apps and cloud connectivity for remote monitoring, guided setup and automated alerts. While supporting adherence, patient safety and clinical oversight, these systems introduce regulatory considerations for Software as a Medical Device, including clinical validation, cybersecurity safeguards and lifecycle management.

Device performance is influenced by drive mechanisms, needle geometry and material selection, which interact with formulation viscosity and injection volume. Optimising these parameters is essential to maintain reliable delivery. Predictive modelling and bench testing can help guide adhesive selection, device ergonomics and flow control, ensuring safe and effective administration.

As patient populations become increasingly tech-savvy, adoption of connected OBIs is expected to accelerate, offering both clinical advantages and practical feasibility for large-volume SC therapies (Figure 4).

ADOPTION IN LARGE-VOLUME APPLICATIONS

Current adoption trends illustrate the impact of these considerations on the device market. OBIs have been on the market longer and benefit from an early adoption advantage, whereas truly large-volume autoinjectors (≥5 mL) are more recent innovations and have only just begun to see extensive development. The technological advantages of OBIs, combined with growing industry and patient acceptance, position them as the likely dominant platform for large-volume SC therapies.

Autoinjectors: Large-Volume Devices in Development

The following are the current key players in the large-volume autoinjector field:

- **Maggie® 5.0 mL (syringe-based):** SHL Medical (Zug, Switzerland) has partnered with Grand River Aseptic Manufacturing (Grand Rapids, MI, United States) to offer fill-finish services for this ready-to-use cartriQ 5 mL cartridge, co-developed with SCHOTT Pharma (Mainz, Germany).

"AS PATIENT POPULATIONS BECOME INCREASINGLY TECH-SAVVY, ADOPTION OF CONNECTED OBIs IS EXPECTED TO ACCELERATE, OFFERING BOTH CLINICAL ADVANTAGES AND PRACTICAL FEASIBILITY FOR LARGE-VOLUME SC THERAPIES."

- **YpsoMate 5.5 mL (syringe-based):** This device from Ypsomed (Burgdorf, Switzerland) features an integrated prefilled syringe developed in collaboration with SCHOTT Pharma.
- **Bios platform (syringe-based):** SMC Ltd (Somerset, WI, US) is among the few vendors to report a development agreement (October 2024) with a biopharma partner specialising in genetic rare diseases. The device is capable of delivering up to 5 mL of extremely high-viscosity fluids. The only other comparable device in this list is the Kaléo Aerio, although information is more limited.
- **Aerio™ platform (cartridge-based):** A platform by Kaléo (Richmond, VI, US), the maturity of the large-volume variant is unclear; the AerioDuo (up to 20 mL) is currently in preclinical development with an undisclosed pharmaceutical partner. Kaléo also holds approvals for emergency delivery of epinephrine and naloxone via the AerioUno (AUVI-Q). The device is gas-powered and designed for delivering large volumes of highly viscous fluids.
- **Windgap Medical's LVDC platform (cartridge-based):** Another gas-powered large-volume, high-viscosity device, Windgap (Watertown, MA, US) claims delivery of viscosities over 5,000 cP and is conducting feasibility assessments with several pharmaceutical companies.

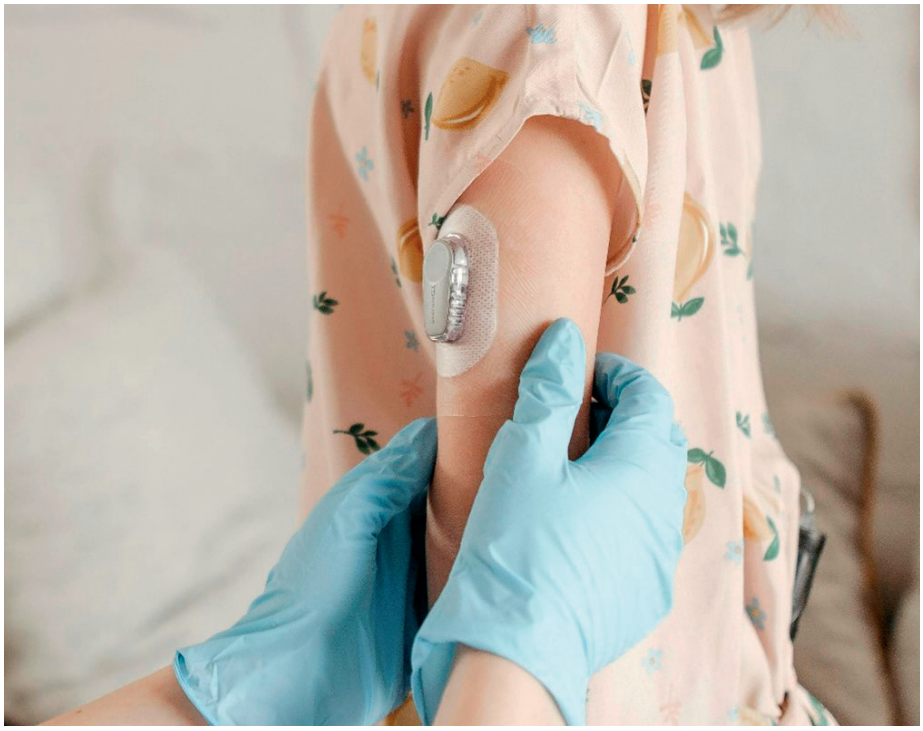


Figure 4: The growing adoption of wearables in both consumer and diabetes care is driving advancements in connectivity and adhesive technologies, enhancing usability, comfort and extending wear time.

On-Body Device (OBD) Approvals

While not large-volume, these devices are relevant to the wearables market and represent a milestone in wearable adoption, reflecting growing understanding of usability and validation of core technologies.

- **Onpro**: Derived from Omnipod technology by Insulet (Acton, MA, US), this OBI delivers Amgen's Neulasta (pegfilgrastim).
- **Coherus (Redwood City, CA, US) UDENYCA OBI**: Based on the LTS/Sorrel (Andernach, Germany) platform, this biosimilar to Neulasta was FDA-approved in 2024 for same-day wearable delivery of pegfilgrastim-cbqv.
- **SQ Innovation (Zug, Switzerland) Lasix ONYU**: Uses a Gerresheimer (Düsseldorf, Germany) OBI (up to 3 mL) and received tentative FDA approval in 2024. Commercial availability is expected once an existing product's exclusivity expires later in the year.

Large-Volume OBI Approvals

Several devices delivering higher volumes have achieved regulatory success:

- **Enable Injections' (Cincinnati, OH, US) enFuse®**: Received its first US combination product approval in 2023 for Apellis' (Waltham, MA, US) EMPAVELI (pegcetacoplan), a twice-weekly 20 mL injection. Regulatory approvals expanded in 2025 in the EU, UK and Brazil, with ongoing clinical studies involving Roche (Basel, Switzerland), Sanofi (Paris, France), Apellis Pharma, UCB (Brussels, Belgium), Viridian (Waltham, MA, US), Serina Therapeutics (Huntsville, AL, US) and Sobi (Stockholm, Sweden).
- **West (Exton, PA, US) SmartDose**: First combination product approval came in 2016 with Amgen's Pushtronex system for Repatha (evolocumab). After withdrawal, West entered a development agreement in 2019 with scPharmaceuticals (Burlington, MA, US) for SmartDose 10 mL delivery of FUROSCIX, gaining FDA approval in 2022.

Large-Volume OBI Clinical Programmes

OBIs are increasingly explored for high-dose monoclonal antibody delivery:

- **Sanofi's isatuximab (Sarclisa)**: SC program using Enable Injections' enFuse® reported Phase 3 IRAKLIA results in 2025, demonstrating non-inferiority versus IV delivery.[4]
- **BD Libertas system**: Available in 2–5 mL and 5–10 mL configurations; entered its first pharma-sponsored clinical trial in 2025.
- **Stevanato Group's (Padua, Italy) Vertiva**: Available in 3 mL and 10 mL formats, with new human-factors and sustainability data recently presented.
- **Ypsomed's YpsoDose**: Supports injections up to 10 mL for high-viscosity formulations; collaborations with SCHOTT (RTU FIOLAX cartridges) and CDMO ten23 health support fill-finish and assembly.
- **LTS (Sorrel) OBIs**: Following LTS's 2023 acquisition of Sorrel, the low-volume UDENYCA OBI received FDA approval at the end of 2024; the 5–20+ mL device is in development with multiple pharmaceutical partners.
- **Gerresheimer Gx SensAir OBI concept**: Integrates digital health features by Aptar (Crystal Lake, IL, US) for adherence monitoring; expanded ready-to-fill syringe and cartridge production which supports SensAir and related programs. Regulators are cautiously supportive, closely monitoring safety and usability.

WHAT IS THE PROGNOSIS?

The evolution of large-volume SC drug delivery reflects a complex interplay between device performance, biological constraints and patient preference. Traditional autoinjectors remain simple and familiar, but their advantages diminish as injection volumes and viscosities increase. High-power requirements introduce mechanical risks and rapid injections can cause pain.

OBIs, increasingly familiar to both industry and users, along with advances in adhesive and sensing technologies, offer a practical solution for delivering high-volume biologics safely and consistently. Extended-duration, hands-free administration reduces tissue stress and interstitial pressure, improving tolerability.

Looking ahead, OBIs are well positioned to play a leading role in the delivery of large-volume biologics, but the choice between autoinjectors and OBIs is not straightforward. Patient preferences vary – some prioritise the speed and discretion of autoinjectors, while others accept

"THE FUTURE OF DELIVERY LIES IN TAILORED DEVICE STRATEGIES OPTIMISED FOR SPECIFIC THERAPIES, CLINICAL CONTEXTS AND PATIENT NEEDS."

longer wear times for greater comfort and dosing flexibility. Safety, cost, regulatory requirements and development timelines also influence adoption, with each stakeholder group bringing distinct priorities. The future of delivery lies in tailored device strategies optimised for specific therapies, clinical contexts and patient needs.

Engaging a multidisciplinary CDMO early in development can reduce costs, de-risk technical challenges and strengthen supply chains. With expertise in device design, human factors, risk management and design-for-manufacture-and-assembly for later scale-up.

ABOUT THE COMPANY

Springboard is a technology and design consultancy, which creates and develops new products and technology, including products in the field of medtech and drug delivery devices, assisting companies in resolving technical challenges and decreasing time to market. Springboard is part of the Sanner Group, which provides high quality, agile and cost-effective manufacturing for medical devices, including drug delivery devices.

REFERENCES

1. *Ziklstra E et al, "Impact of Injection Speed, Volume, and Site on Pain Sensation". J Diabetes Sci Technol, 2017, 12(1), pp 163–168.*
2. *Schwarzenbach F et al, "Evaluation of the impact of viscosity, injection volume, and injection flow rate on subcutaneous injection tolerance". Med Devices (Auckl), 2015, p 473.*
3. *Doughty DV et al, "Understanding subcutaneous tissue pressure for engineering injection devices for Large-Volume protein Delivery". J Pharm Sci. 2016, 105(7), pp 2105–2113.*
4. *Bruin G et al, "An industry perspective on clinical development and regulatory strategies for subcutaneously administered high-dose biologics". J Control Release, 2025, 386, p 114156.*
5. *Hou P et al, "Multiphysics modelling and simulation of subcutaneous injection and absorption of biotherapeutics: sensitivity analysis". Pharm Res, 2021, 8(6), pp 1011–1030.*
6. *Pepin XJH et al, "SubQ-Sim: A Subcutaneous Physiologically Based Biopharmaceutics Model. Part 1: The Injection and System Parameters". Pharm Res, 2023, 40(9), pp 2195–2214.*
7. *Li C et al, "A multi-scale numerical study of monoclonal antibodies uptake by initial lymphatics after subcutaneous injection". Int J Pharm, 2024, 661, art 124419.*
8. *Wang G et al, "Biomimetic breathable nanofiber electronic skins with temperature-controlled self-adhesive and directional moisture-wicking properties for bifunctional pressure and non-contact sensing". Nano Energy, 128, art 109779.*
9. *Zhang et al, "Sweat-enhanced adhesive hydrogel enables interfacial exchange coupling for wearable strain sensor". Chemical Engineering Journal, 2024, 495, art 153385.*

Dr Alex Vasiev

Alex Vasiev, PhD, Head of Drug-Device Integration at Springboard, is a multidisciplinary engineer with extensive R&D experience in both academia and consultancy. His primary focus is on the intersection of engineering, physics and biological systems. Before joining Springboard, Dr Vasiev managed front-end design and development at Oval (now SMC). In the field of drug delivery, Dr Vasiev has developed a range of innovations, including smart hydrogel microcarriers, patch pumps, soft mist inhalers and several high-viscosity autoinjectors. He holds an MEng in Mechanical Engineering with Aeronautics and a PhD in Biomedical Engineering from the University of Glasgow (UK).

T: +44 1223 856136
E: alex.vasiev@springboard.pro

Dr Ethan Miller

Ethan Miller, PhD, Senior Biophysicist at Springboard, is an experimental biophysicist with a background in developing synthetic biological systems and high-resolution imaging. He can quickly grasp new concepts and break down complicated problems allowing him to discover creative solutions. His experience includes medical device development, manipulation of synthetic biomembranes with microfluidics and nanoscale surface characterisation.

T: +44 1223 856463
E: ethan.miller@springboard.pro

Springboard Ltd – a Sanner Group Company
St John's Innovation Centre, Cowley Road, Cambridge, CB4 0WS, United Kingdom
www.sanner-group.com

Interview: Delivering the Future – Inside the World of Autoinjector Innovation

In this exclusive interview, **Steven Kaufman** of **Portal Instruments** talks with ONdrugDelivery's Guy Furness about the world of autoinjectors, looking at the current status quo in the industry, using Portal's PRIME Nexus™ smart reusable electromechanical autoinjector as a lens to bring into focus how things have changed and where they might be going.

Q How have you seen drug delivery devices evolve over the course of your career and where do you believe things are heading in the next decade?

A Across my career, I've worked with several great companies and witnessed the growth of the industry firsthand. From my perspective, two of the most significant changes are, first, people are more knowledgeable across the industry when pairing their primary container with the right device and final assembly solution and, second, pharma evaluates device technologies much earlier today than they did a decade ago and are willing to invest when it makes sense to do so.

The latter is a profound shift. Historically, pharma companies would wait until the end of Phase II or early Phase III trials, or even until after launching in a prefilled syringe (PFS) before thinking about a device solution. Today, both pharma and biotech, large and small, select device platforms much earlier in their development cycle and hire staff or use consultants that are from the device space and integrate them into their teams – which I think is a positive move.

Another shift I'm seeing is that people are starting to focus more on device differentiation. For example, as interim CCO at Portal, I introduce the PRIME Nexus™ smart reusable autoinjector regularly to potential customers and get to hear feedback firsthand (Figure 1). There is a strong attraction to sustainability and flexibility in terms of delivery envelope, as well as having device solutions that are economical. These are all common themes in many of my discussions.

I believe that we are at a tipping point where the industry is starting to look at new devices differently and to be open to changes. So far, we've seen incredible success from the major platform

"I BELIEVE THAT WE ARE AT A TIPPING POINT WHERE THE INDUSTRY IS STARTING TO LOOK AT NEW DEVICES DIFFERENTLY AND TO BE OPEN TO CHANGES."

Steven Kaufman

Chief Commercial Officer

E: steven.kaufman@portalinstruments.com

Steven Kaufman is a distinguished executive in the drug delivery industry with more than 21 years of experience delivering innovative solutions to pharmaceutical and biotechnology companies. As Portal Instruments' Chief Commercial Officer, he brings extensive expertise in combination products and self-injection technologies. Prior to joining Portal Instruments in November 2024, Mr Kaufman held executive leadership positions in strategy, marketing and business development at several industry-recognised organisations, including Stevanato Group, Bespak and SHL Medical.

Throughout his career, he has successfully led international teams and driven business growth through strategic partnerships, intellectual property development and competitive positioning. His subject matter expertise spans the full spectrum of drug delivery systems, including autoinjectors, pen injectors, wearable devices, inhalers and other combination products. In addition, he has a comprehensive understanding of fill-finish, primary containers, training devices, tooling, equipment and final assembly.

Mr Kaufman completed his International Master of Business Administration studies with an emphasis on marketing and international business at the National Chengchi University in Taiwan (2003–2006) and completed his undergraduate studies at Western University in Canada (1987–1991).

Figure 1: Portal's PRIME Nexus™ reusable autoinjector.

autoinjector devices like Molly (SHL, Zug, Switzerland) and YpsoMate (Ypsomed, Burgdorf, Switzerland), which have replaced a lot of the time-consuming bespoke customised device solutions. They are great devices, and I have a lot of respect for both companies. And now we're starting to see some of the other disposable autoinjector platforms – and reusable autoinjectors – garnering attention. I think that's pointing to where the industry could be heading in the future.

In the very near term, we're probably going to be staying with a lot of the same types of traditional devices – more platforms, more single-use disposable – but with the issues of higher viscosity and different fill volumes, and different primary containers, it is very difficult for one device to suit all those needs. At the same time, sustainability continues to be a very significant topic, particularly in Europe and in the context of glucagon-like peptide-1 agonists (GLP-1s), for example. Now, globally, so many devices are used daily for GLP-1 treatment and that number continues to grow.

Q You touched upon sustainability. Considering current industry trends, how can drug delivery device companies help minimise waste and reduce overall treatment costs as well?

A One of the big things is that, as an industry, we've gone from making millions and tens of millions of autoinjectors a year, to over a billion a year. When this many autoinjectors, and drug delivery devices in general, are being disposed of, a lot of people start to wonder "Is this the right approach?" – both from a sustainability and a cost perspective.

PRIME Nexus™ and other reusable autoinjectors could have a unique opportunity to help pharma companies to find a cost model that works much better than the current disposable paradigm. For example, if you're on a GLP-1, you're going to be using roughly 156 autoinjectors over three years, all of which are disposed of in a sharps container. Think about all the waste and cost that generates.

Compare that with a reusable device where, at least in PRIME Nexus™' case, we have a single device that is good for around three years of use. It sits in your home, very much like an electric toothbrush on a docking station, charged and ready to go. The disposable part is a relatively small cassette that inserts in the reusable device. These cassettes are designed for 1 and 2.25 mL PFSs (with 5.5 and 10 mL PFSs under development), which brings huge advantages from a flexibility perspective – but also radically reduces the environmental impact.

The key, though, is that the price point for the reusable has to be at an affordable level. At Portal, we believe that with the current device and the cost structure, you're paying back the cost of the device within six months from the per-dose savings. Then you still have it for another two and a half years.

I'm not saying that price is the only consideration – sustainability is important, flexibility is important – but achieving that balanced approach to the cost makes it easier for companies to convert from the standard disposable platform autoinjector model.

"PRIME NEXUS™ AND OTHER REUSABLE AUTOINJECTORS COULD HAVE A UNIQUE OPPORTUNITY TO HELP PHARMA COMPANIES TO FIND A COST MODEL THAT WORKS MUCH BETTER THAN THE CURRENT DISPOSABLE PARADIGM."

Q Looking to the future, what key features should every autoinjector have – both in terms of entry level requirements and, further than that, what separates the very best from the rest?

A To answer the second part first, I think what differentiates the best from the rest is the ability to think through the entire value chain – to understand the fill-finish side, the primary container side, the device side, the manufacturing side and the final assembly, labelling and release. The most successful companies are ones that understand the full value chain and can support decisions throughout the entire journey. There are plenty of companies that can assist with connectivity, human factors, small- to large-scale final assembly, primary container verification or feasibility studies – but ultimately you need

Figure 2: The PRIME Nexus™ reusable smart autoinjector is suitable for 1 mL and 2.25 mL PFSs (using the same cassette) and the 5 mL and 10 mL PFS versions are under development.

the knowledge and experience to bring that all together. At Portal, we pride ourselves with having a strong team with a supportive partner structure. We are proud of our relationship with Gerresheimer (Düsseldorf, Germany) as our strategic partner for the commercialisation of the PRIME Nexus™ device, which was recently made public (Figure 2).

Going back to the first part of the question, I think – at a bare minimum – devices need to be what I often call a "hybrid" design. I may be biased, but I like the Aidaptus device (Owen Mumford, Woodstock, UK, in partnership with Stevanato Group, Padua, Italy), which accommodates both 1 and 2.25 mL PFSs in one form factor, another example is Eco-inject (London, UK) a company that has also has a hybrid autoinjector using sustainable materials for both 1 and 2.25 mL PFSs. PRIME Nexus™ is the same in principle, using hybrid cassette designs with no metal parts and a low component count that can hold 1, 2.25, 5.5 and 10 mL PFSs, but the main device itself is reusable, and I think that such devices have other distinct advantages.

Beyond having the flexibility to facilitate different primary containers, I would say that autoinjectors need to be able to deal

with high variance in viscosity and changes in fill volume. For PRIME Nexus™, we were originally scoped out handling up to 50 cP, but we've performed studies where we effectively delivered in the hundreds of centipoise. I think it's important to expand the performance envelope of new devices beyond what we have currently in the market, and I can see that biotech and pharma companies are starting to expect that device companies can do this.

Q How important are connectivity and digital health for developing combination products for the delivery of novel biologics?

A The core appeal of digital health is its potential to help address human factors and patient adherence concerns. There's a significant opportunity to improve onboarding and the general patient experience here, which may be critical to tackling the industry's long-standing challenges with adherence. Another factor that comes to mind is that digital health can also be a source of data for patients and biopharmaceutical companies, which can give them a better chance of getting their products to market, so there's a lot of value there as well. At Portal, our current focus is to just keep carrying out feasibility studies to keep demonstrating the connectivity technology to potential partners. And if a customer would like to implement the technology, we can easily add that to the device with the support of our partners like Gerresheimer.

Q How does Portal employ its extensive experience in combination product development across regulatory, industrialisation and commercialisation to help pharma and biopharma companies de-risk and accelerate their drug device combination programme?

A It's true that across our team at Portal – the executives, the board and all the people that are working to make the device and performing the studies – we have the required device development knowledge from working with electromechanical solutions for more than a decade and there's a lot of expertise within our teams and from our partners. We pride ourselves on being extremely flexible and nimble, which is possible because we're a relatively small company. That flexibility helps us really use our collective experience to try and ensure that patients are properly considered when our partner pharma companies are looking at different options. We have that institutional knowledge across quality, regulatory, commercial and R&D.

"WHAT IS PARTICULARLY EXCITING IS WHEN WE CAN SHOW THAT THINGS THAT HAVE BEEN CONSIDERED CHALLENGING ARE NOW POSSIBLE WITH NEXT-GENERATION DEVICES, SUCH AS DELIVERING FORMULATIONS OVER 100 CP."

What is particularly exciting is when we can show that things that have been considered challenging are now possible with next-generation devices, such as delivering formulations over 100 cP, as I mentioned earlier. Working with pharma companies, we can use our experience to guide them and recommend certain primary containers, or we can give them feedback from what we've seen from our human factors studies. On that front, we've started to work with Interface Analysis Associates (Saratoga, CA, US), Kymanox (Morrisville, NC, US) and others, and we have been running several usability studies to do more in that area ourselves in-house.

Our experience has also allowed us to apply consistent underlying principles to the design of PRIME Nexus™. We've made sure that it's flexible but cost effective at the same time. To reiterate a couple of the key points, it's about the ability to deal with multiple fill volumes and different viscosities within the same platform and being able to maintain almost the same injection time regardless. Injection time has come up a lot in our conversations recently. We can fine tune the delivery parameters based on the needs of the formulation. And then, we can lean on our experience again to help with clinical studies or during drug development where it's still unknown what the final fill volume will be.

With automatic needle insertion and retraction and the versatility of the platform, PRIME Nexus™ has unprecedented flexibility. You don't have to make any changes to the hardware because the software can easily be updated and changed, which is possible due to PRIME Nexus™ being an electromechanical device. And, if I may say so, the device is designed to look elegant as well, which I'm a big advocate of.

I've been asthmatic since I was 10, and when I was a kid I used to feel the need to hide my inhaler because I didn't want the other kids knowing I had an issue. So, over the course of my career, I've tried to work with companies that want to make devices that are not only effective and great for patients but that are also designed to not look so distinctively medical, and that by doing so we can help to remove the stigma associated with taking medication.

I think one mistake that people make with electromechanical devices, be they on-body injector or autoinjector, is to try to make them too complex and include too many bells and whistles. We have to provide options, but at the same time, we need to keep them simple.

If we can achieve that simplicity, cover the whole value chain with our partners, help the environment and find a cost-effective balance, I think that devices like PRIME Nexus™ have a real opportunity to influence the market and provide significant benefit to pharma companies and patients alike.

Portal Instruments
190 5th Street
Cambridge
MA 02141
United States
www.portalinstruments.com

USING OXYCAPT™ MULTILAYER PLASTIC VIAL FOR GENE AND CELL THERAPIES STORED IN DRY ICE AND LIQUID NITROGEN

MITSUBISHI GAS CHEMICAL

Hiroki Hasegawa and **Tomohiro Suzuki** of **Mitsubishi Gas Chemical** consider the various challenges presented by cold-chain logistics to both traditional glass vials and many cyclo-olefin polymer alternatives, and how the company's OXYCAPT™ vials offer significant advantages for maintaining container closure integrity compared with other materials on the market.

OXYCAPT OVERVIEW

OXYCAPT™ is a multilayer plastic vial and syringe developed by Mitsubishi Gas Chemical (MGC), offering a number of advantageous qualities as a primary drug container, including:

- Excellent oxygen and ultraviolet (UV) light barrier
- Strong water vapour barrier
- Very low extractables
- High pH stability
- Low protein adsorption and aggregation
- High transparency
- High break resistance
- Easy disposability
- Lightweight material.

MGC continuously conducts studies to confirm these properties. The latest results of these are shared in the later part of the article. Before that, the first half of this article provides an overview of the OXYCAPT multilayer plastic vial (Figure 1). The material consists of three layers – the drug contact layer and the outer layer are made of cyclo-olefin polymer (COP) and the oxygen barrier layer is made of MGC's novel polyester (Figure 2).

MGC recently obtained a report on the environmental impact of glass and plastic containers for medical use from a Japanese research company. The report shows that plastic containers for medical use are much more environmentally friendly compared with glass containers. For example, the carbon footprint, nitrogen oxide emissions,


Figure 1: OXYCAPT multilayer plastic vial.

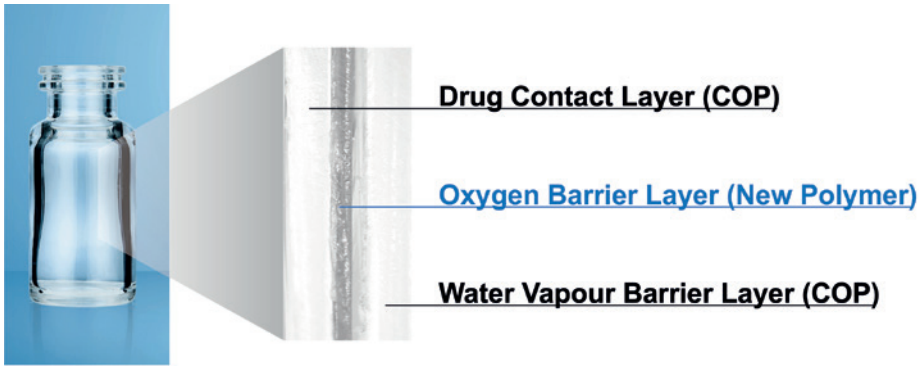


Figure 2: Multilayer structure of OXYCAPT.

"OXYCAPT PROVIDES AN EXCELLENT OXYGEN BARRIER – FOR EXAMPLE, THE OXYGEN BARRIER OF AN OXYCAPT VIAL IS ABOUT 20 TIMES BETTER THAN THAT OF A COP MONOLAYER VIAL."

sulphur oxide emissions and water consumption associated with plastic containers for medical use are several times smaller than those of their glass equivalents.

OXYCAPT provides an excellent oxygen barrier – for example, the oxygen barrier of an OXYCAPT vial is about 20 times better than that of a COP monolayer vial. Furthermore, OXYCAPT provides an excellent UV barrier. While about 70% of 300 nm UV light transmits through glass and COP, only 1.7% transmits through OXYCAPT. MGC has confirmed that this feature contributes to the stability of biologics.

While OXYCAPT cannot reach the performance of glass with respect to acting as a water vapour barrier, its properties are similar to those of COP, which has been used for injectable drugs for a long time. This means that OXYCAPT easily meets the requirements of a water vapour barrier set out by the ICH guidelines.

Studies have shown an extremely low level of extractables from OXYCAPT. One study was conducted to confirm the levels of volatile, semi-volatile and non-volatile impurities from OXYCAPT. Water and four solutions (50% ethanol, sodium chloride, sodium hydroxide and phosphoric acid) were selected, and impurities were measured by gas chromatography mass spectrometry (GC-MS) and liquid chromatography-UV spectroscopy-mass spectrometry (LC-UV-MS) after 70 days at 40°C. Compared with the control, impurities were not detected in the OXYCAPT containers. A second study confirmed that inorganic extractables levels from OXYCAPT were similar to those from COP, which is well known for being an extremely pure polymer with a better extractables profile than Type 1 glass. Lower levels of inorganic extractables are known to contribute to better pH stability in drug products.

The OXYCAPT vial is produced by co-injection blow-moulding technology. MGC has also developed inspection methods for testing the oxygen barrier layer. All the containers are fully inspected by state-of-the-art inspection machinery.

MGC can offer bulk vials and ready-to-use (RTU) vials, with its RTU products provided in standard nest-and-tub or tray formats. The nest and tub are mainly sterilised using gamma rays. There are 2, 6, 10 and 20 mL variants for vials. MGC is willing to provide samples for initial testing free of charge.

Each polymer meets the requirements of US Pharmacopeia (USP) regulations USP <661>, USP <87> and USP <88>, as well as those of the European Pharmacopoeia, and has been filed in the US FDA's drug master file (DMF). The vials are also compliant with each pharmacopoeia and have been filed in the DMF.

The primary target market for OXYCAPT is the therapeutic application of biologics. As mentioned in ICH Q5C (Stability of Biotechnological/Biological Products), oxidation is one of the causes of protein instability. As such, the oxygen and UV barrier properties of OXYCAPT contribute to the stability of biologics stored within. Furthermore, some drug developers have recently started evaluating OXYCAPT vials for their gene and cell therapies; the RTU vial is sterilised by gamma radiation, making it ideal for protein-based drugs.

OXYCAPT AT ULTRA-LOW TEMPERATURES

Plastic vials generally exhibit greater toughness at ultra-low temperatures compared with glass, markedly mitigating the risk of breakage during transportation and under thermal stress. For example,

Vial	Total Number of Breakages					Total Number of Layer-Separations				
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
OXYCAPT™-P V10 RT	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20
Competitor's Glass Vial(10R)	5/20	10/20	14/20	20/20	–	N/A				

Table 1: Heat cycling stress test performed with mannitol aqueous solution.

OXYCAPT vials demonstrated excellent performance in a heat cycling test designed to evaluate resistance to physical stresses such as material contraction and expansion, as well as the volumetric expansion of aqueous drug formulations. In this study, 8 mL of a 10 w/v% mannitol aqueous solution was filled into 20 10R OXYCAPT vials and 20 conventional glass vials, which were then sealed with rubber stoppers. The vials were alternately placed in constant-temperature chambers set at -80°C and 40°C, with each cycle consisting of storage at both temperatures for three to four consecutive days. This alternating process was repeated for a total of five cycles. By the end of the fifth cycle, all 20 glass vials were broken, whereas none of the 20 OXYCAPT™ vials exhibited any visible defects, such as cracks or layer separation (Table 1).

"OXYCAPT VIALS DEMONSTRATED EXCELLENT PERFORMANCE IN A HEAT CYCLING TEST DESIGNED TO EVALUATE RESISTANCE TO PHYSICAL STRESSES SUCH AS MATERIAL CONTRACTION AND EXPANSION, AS WELL AS THE VOLUMETRIC EXPANSION OF AQUEOUS DRUG FORMULATIONS."

Container Closure Integrity

State-of-the-art drug products, including messenger RNA (mRNA)-based drugs and gene and cell therapies, are typically transported and stored at ultra-low temperature conditions (-78°C) using dry ice or at cryogenic temperature (-180°C) in the vapour phase of liquid nitrogen. Under these circumstances, there is a risk of losing container closure integrity (CCI), particularly for glass vials. This risk arises from the remarkable difference in the coefficients of thermal expansion between the vial's glass flange and the elastomeric closure.

To simulate the conditions under which gene and cell therapy products are transported and stored, MGC conducted a CCI study using OXYCAPT vials. In this study, OXYCAPT vials and conventional glass vials were prepared, sealed under ambient air with non-laminated bromobutyl rubber stoppers and aluminium caps, after which their initial oxygen concentration was measured using an FMS-760, a headspace oxygen analyser (LIGHTHOUSE Instruments, Charlottesville, VA, US).

The vials were then stored in the vapour phase of liquid nitrogen within a dry shipper for up to three months. During storage, the oxygen concentration inside the vials was periodically measured to verify whether or not it remained at approximately 20.9%. The results showed that all of the conventional glass vials lost CCI within seven days, whereas the OXYCAPT vials maintained CCI even after three months (Figure 3). These findings demonstrate that OXYCAPT vials effectively prevent the ingress of air, moisture and contaminants, even under cryogenic conditions.

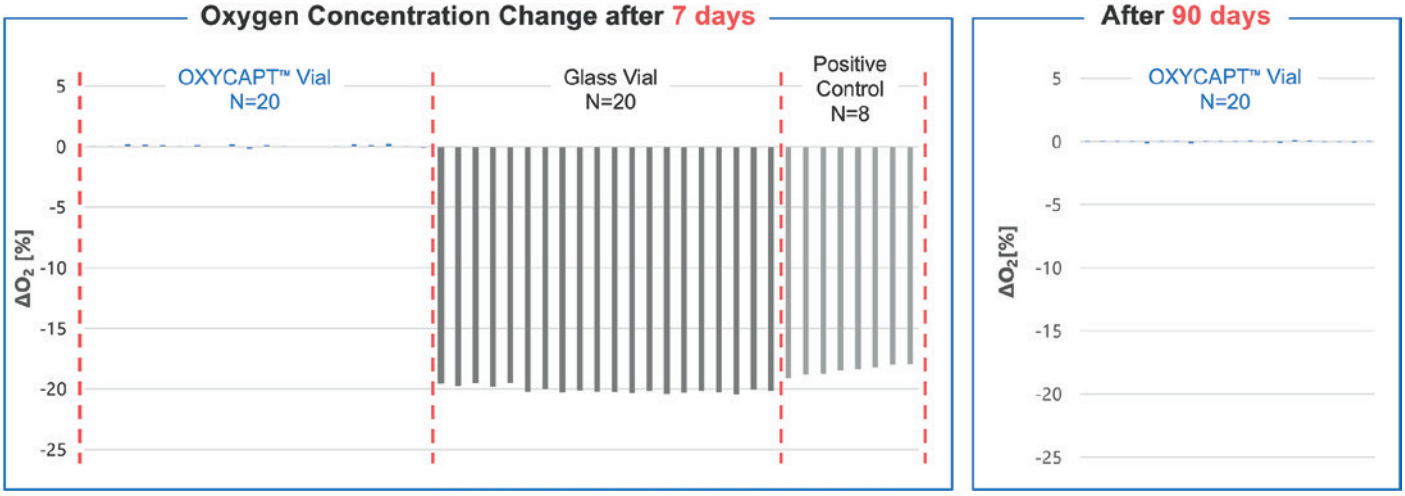


Figure 3: CCI test results in vapour phase of liquid nitrogen.

Risk of Carbon Dioxide Ingress

While plastic vials are capable of markedly mitigating the risk of loss of CCI, conventional plastic vials present an alternative inherent risk under conditions of coexisting dry ice – the permeation of carbon dioxide (CO_2). To elucidate this latent risk, a simulated study was conducted using dry ice, as illustrated in Figure 4.

Five 10R OXYCAPT vials and five conventional COP vials were used as test samples. The vials were sealed with commercially available bromobutyl rubber closures and aluminium caps under a 100% nitrogen atmosphere. The vials were placed in an insulated container filled with dry ice and stored for seven days. Immediately upon removal (T_0), the CO_2 partial pressure in the vial headspaces was measured using FMS-CO_2 (LIGHTHOUSE Instruments). The vials were then stored under ambient conditions at either 5°C or 23°C, and the CO_2 partial pressure was measured again after one day, with subsequent periodic measurements performed over time.

As shown in Figure 5, no CO_2 was detected in the headspaces of either the COP or OXYCAPT vials at T_0, demonstrating excellent CCI at -78°C. However, when subsequently stored at 23°C for one day, the COP vials exhibited a CO_2 partial pressure of approximately 1.5 Torr (Figure 6). This phenomenon was also observed when the COP vials were stored at 5°C. In contrast, the OXYCAPT vials maintained a CO_2 concentration of 0% over a period of 70 days, even under continuous storage at 23°C (Figure 7).

This time-dependent permeation phenomenon of CO_2 can be attributed to the inherent physical properties of CO_2, which exhibits relatively high solubility coefficients at ultra-low temperatures and is readily soluble even in plastics. During cold storage, the CO_2 generated through the sublimation of dry ice dissolves into the near-surface region of the polymer layer. Under ultra-low temperature conditions, gas molecules scarcely diffuse through the polymer layer, meaning that, even when the headspace CO_2 partial pressure was measured immediately after removal from cold storage, no detection was observed (Figure 8). In contrast, upon subsequent storage under comparatively mild conditions, such as room temperature or

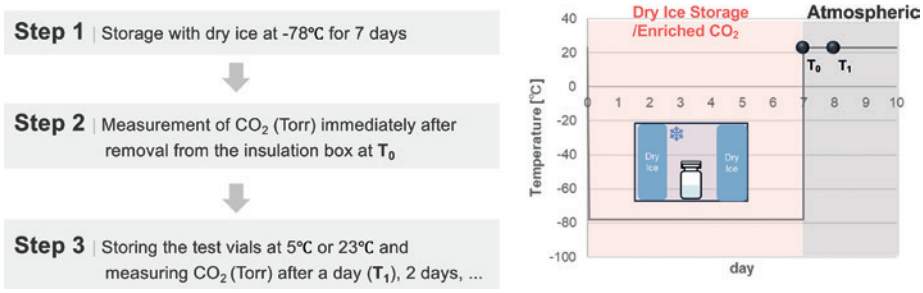


Figure 4: Environmental profile during CCI test with dry ice.

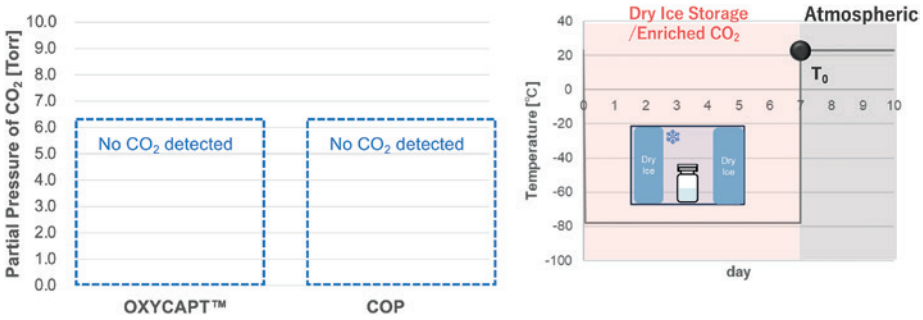


Figure 5: CO_2 measurements in vial headspace immediately after removal.

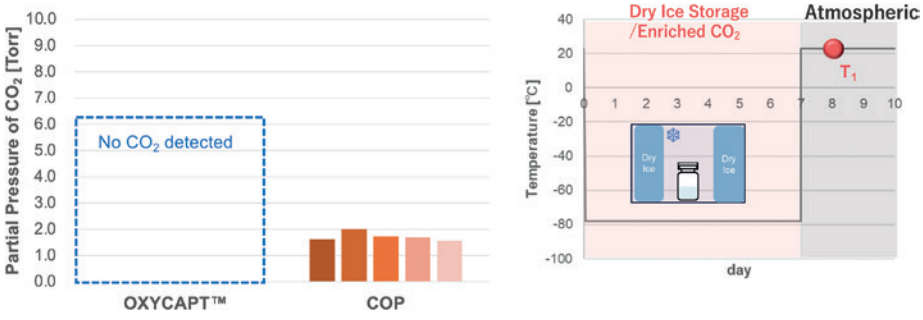


Figure 6: CO_2 measurements in vial headspace one day after removal.

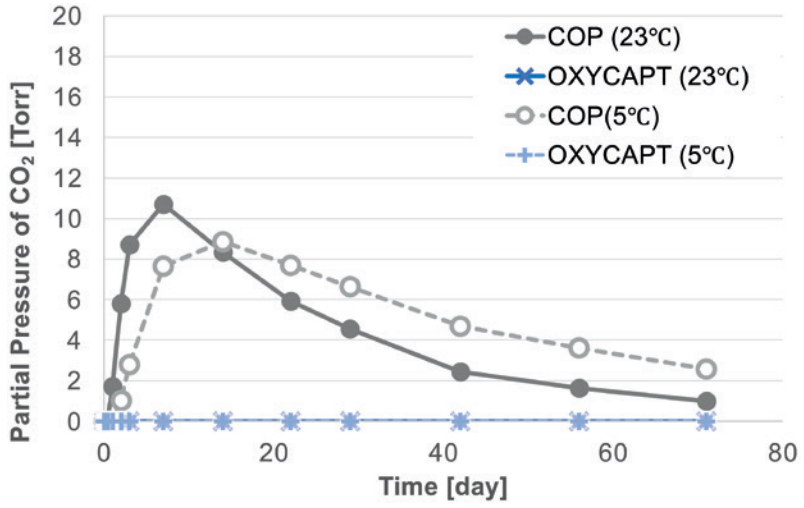


Figure 7: Changes in CO_2 partial pressure in vial headspaces after removal from insulated chamber.

2–8°C, the dissolved CO_2 rapidly diffuses through the polymer and reaches the vial headspace (Figure 9).

An additional verification study was conducted using vials filled with distilled water, in which the pH was measured following storage with dry ice. Thirty samples were prepared for each vial type – 10R OXYCAPT, COP and glass. The vials were filled with distilled water under a nitrogen atmosphere and the initial pH value was measured at T_0 before sealing the vials with commercially available bromobutyl rubber stoppers (non-laminate). The samples were then divided into two groups – 15 vials were stored for seven days in the presence of dry ice and 15 vials were stored in a -80°C deep freezer. After storage, five vials from each group were thawed at 23°C for eight hours, after which the pH was measured again (T_7). Additional destructive testing was performed on independent sets of five vials each at one day (T_{7+1}) and four days (T_{7+4}) after thawing, with each vial discarded following measurement. The results showed that, in the COP vials stored with dry ice, the pH decreased beginning at T_{7+1}. In contrast, the OXYCAPT vials maintained their initial pH even at T_{7+4} (Figure 10).

In practice, upon delivery, pharmaceuticals transported with dry ice may be thawed or temporarily refrigerated at 2–8°C prior to administration. Under such conditions, exposure to ambient or refrigerated temperatures can result in the permeation of dissolved CO_2. Once present, CO_2 dissolves in aqueous drug formulations, generating protons and therefore posing a latent risk of detrimental pH shift in drug formulation.

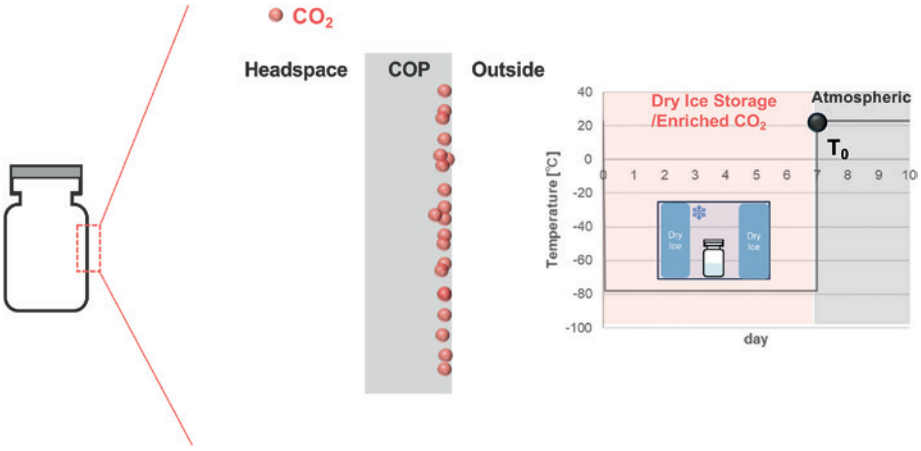


Figure 8: Schematic illustration of CO_2 dissolution in COP vials immediately after removal from dry ice.

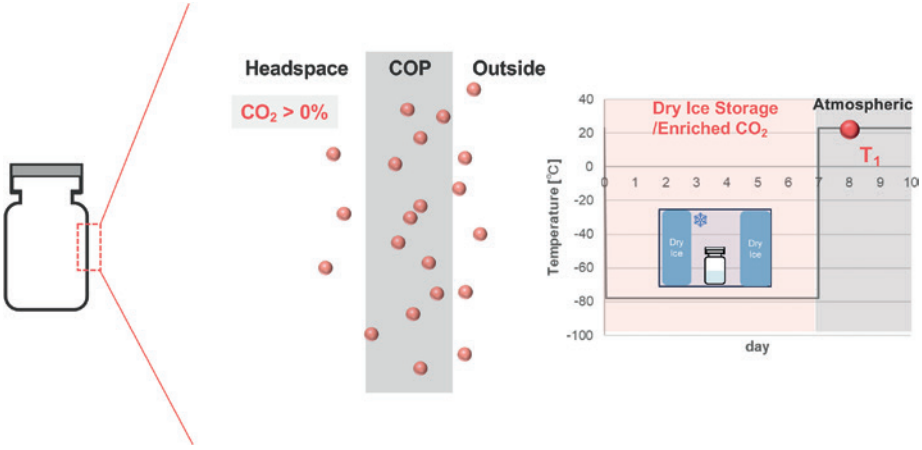


Figure 9: Schematic illustration of CO_2 diffusion through COP vials one day after removal.

To mitigate this "time-delayed" CO_2 permeation phenomenon, secondary packaging is sometimes used. However, secondary packaging introduces additional concerns, including the risk of physical damage, increased material and logistical costs and the necessity for packaging validation. In view of these challenges, OXYCAPT, which provides inherent gas-barrier properties at the level of the primary container, represents an optimal solution by ensuring CCI while simultaneously offering advantages in cost efficiency and environmental sustainability.

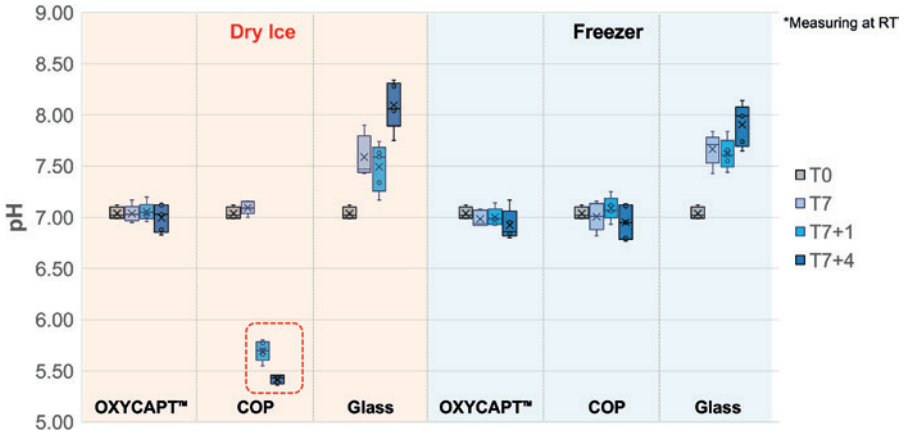


Figure 10: pH variation of distilled water after dry ice storage.

"OXYCAPT REPRESENTS AN OPTIMAL SOLUTION BY ENSURING CCI WHILE SIMULTANEOUSLY OFFERING ADVANTAGES IN COST EFFICIENCY AND ENVIRONMENTAL SUSTAINABILITY."

Hiroki Hasegawa

Hiroki Hasegawa is an Assistant Research Manager in Mitsubishi Gas Chemical's Advanced Business Development division. He earned a Diploma in Science in 2013 and a Master of Science degree in 2015 from Osaka University (Japan). He has worked for MGC since April 2015, in charge of macromolecular science, especially in composition development of thermosetting resin. In 2018, he joined the development team for OXYCAPT.

T: +81 463 21 8627
E: hiroki-hasegawa@mgc.co.jp

Tomohiro Suzuki

Tomohiro Suzuki, Associate General Manager at Mitsubishi Gas Chemical (MGC), graduated from Waseda University (Japan) in 1997 and joined MGC in 1998. He belonged to the Oxygen Absorbers Division until 2011, after which he was transferred to the Advanced Business Development Division in 2012 to be a member of the OXYCAPT development team. Since then, he has been in charge of marketing for the OXYCAPT vial and syringe.

T: +81 3 3283 4913
E: tomohiro-suzuki@mgc.co.jp

Mitsubishi Gas Chemical Company, Inc
Mitsubishi Building, 5-2 Marunouchi 2, Chiyoda-ku, Tokyo 100-8324, Japan
www.mgc.co.jp/eng

2025/26 Editorial Calendar

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

OCT/NOV Sustainability in Drug Delivery DEADLINE PASSED	**NOV** Pulmonary & Nasal Drug Delivery DEADLINE PASSED	**DEC** NEW ISSUE TOPIC Delivering Gene & Cell Therapeutics DEADLINE: **Nov 6, 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**
MAY/JUN Oral Drug Delivery DEADLINE: **Apr 16, 2026**	**JUN** Connectivity in Drug Delivery DEADLINE: **May 7, 2026**	**JUL** Industrialising Drug Delivery DEADLINE: **May 21, 2026**
SEP Wearable Injectors DEADLINE: **Aug 6, 2026**	**SEP/OCT** Dual-Chamber Delivery Systems DEADLINE: **Aug 20, 2026**	**OCT** Prefilled Syringes & Injection Devices DEADLINE: **Sep 3, 2026**
OCT/NOV Sustainability in Drug Delivery DEADLINE: **Sep 17, 2026**	**NOV** Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 1, 2026**	**DEC** Delivering Gene & Cell Therapeutics DEADLINE: **Nov 5, 2026**

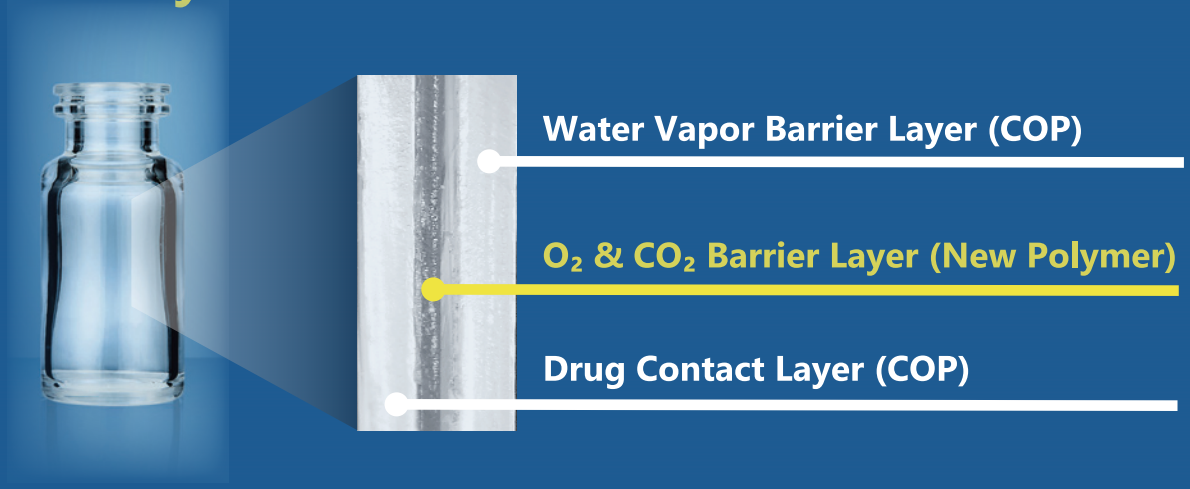
ondrugdelivery.com/subscribe

20 YEARS ON drugDELIVERY

OXYCAPT™ Multilayer Plastic Vial

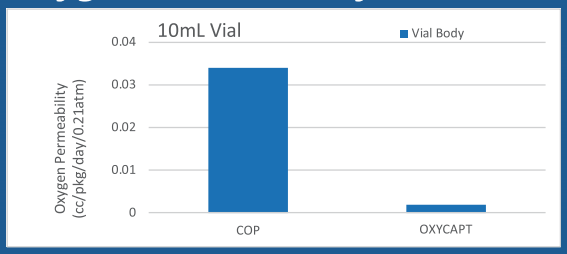
for Biologics & Cell/Gene Therapy Products

Multilayer Structure

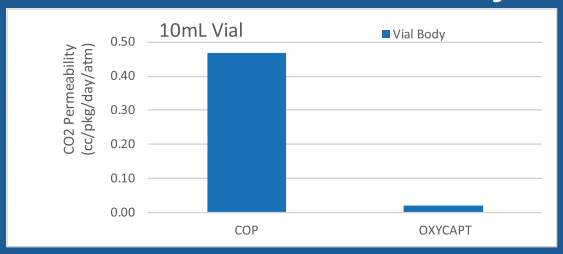


- **Excellent O_2 & CO_2 Barrier**
- **Excellent UV Barrier**
- **Very Low Extractables**
- **Very Low Protein Adsorption**
- **High Compatibility with High & Low pH Drugs**
- **Excellent Break Resistance at Deep Cold Temp.**
- **Excellent CCI at Deep Cold Temp. with Dry Ice**
- **Maintain Excellent CCI after Freezing & Thawing Process**

Oxygen Permeability



Carbon Dioxide Permeability



MITSUBISHI GAS CHEMICAL

Mitsubishi Gas Chemical Company, Inc.
https://www.mgc.co.jp/eng/products/abd/oxycapt.html
Mitsubishi Gas Chemical America, Inc.
http://www.mgc-a.com
Mitsubishi Gas Chemical Europe GmbH
https://www.mgc-europe.de

Martin Høier Thomsen
martin.thomsen@technolution.dk
www.mgsmfg.com

MGS is a global healthcare CDMO dedicated to transforming its clients' challenges into innovations that improve lives. With deep expertise and vertically integrated global capabilities, MGS accelerates innovation for leading pharma, diagnostic and medtech innovators, bridging the gap between imagination and realisation with precision, quality and efficiency.

See **Page 26**

Christoph Grinda
christoph.grinda@nipro-group.com
www.nipro-group.com

Nipro Pharma Packaging specialises in developing and manufacturing advanced pharma packaging products and complete packaging solutions for early development drugs or the enhancement of packaging solutions for existing drugs.

See **Page 16**

Tomohiro Suzuki
tomohiro-suzuki@mgc.co.jp
www.mgc.co.jp/eng

Mitsubishi Gas Chemical (MGC) is a major chemical products manufacturer, operating across a wide range of fields, from basic chemicals to fine chemicals and functional materials. In 2012, MGC established a new division as a centre for continually creating new businesses. In the field of drug delivery, the company has developed the OXYCAPT plastic vial and syringe as an alternative to glass containers.

To learn more, see **Page 134**

Patrik Ingvarsson
patrik.ingvarsson@nolato.com
www.nolato.com

Nolato delivers industrialised drug delivery solutions with decades of experience and over 250 engineers worldwide, including full-service development – from R&D to scalable, US FDA-registered production – ensuring a smooth transition from prototype to high-volume manufacturing. With global, ISO-certified facilities, Nolato empowers pharmaceutical partners to bring sustainable, high-quality devices to market efficiently.

To learn more, see **Page 114**

Tim Holden
pharmaservices@owenmumford.com
www.owenmumford.com

Owen Mumford is a medical device manufacturer that develops products for its own brand and custom device solutions for pharmaceutical and diagnostic companies. Owen Mumford provides research, design and manufacturing capabilities for device production.

To learn more, see **Page 36**

Charlie Bowen
charlie.bowen@pfizer.com
www.pfizer.co.uk

Pfizer is a global pharmaceutical corporation headquartered in New York (NY, US), with its research headquarters in Groton (CT, US). It is among the world's largest pharma companies. It is listed on the New York Stock Exchange, and its shares have been a component of the Dow Jones Industrial Average since 2004.

To learn more, see **Page 60**

info@portalinstruments.com
www.portalinstruments.com

Portal Instruments develops an innovative drug delivery injector aiming to transform the delivery of biologics. Portal's connected, reusable electromechanical platform is designed to reduce environmental waste, lower long-term treatment costs and enhance the patient experience through a more comfortable administration process.

To learn more, see **Page 130**

Iker Ibisate
i.ibisate@rpk.es
www.rpk-medical.com

RPK Medical, part of RPK Group, specialises in creating custom solutions in springs, stamping bending and assemblies, operating six factories across Europe, North America and Asia, and employing more than 800 people. The company ensures quality through tailored cleaning and packaging in cleanrooms worldwide.

To learn more, see **Page 72**

SANNER GROUP
Protecting Health.

Heike Lang
h.lang@sanner-group.com
www.sanner-group.com

Since 1894, **Sanner** has successively developed from a market leader for desiccant closures and effervescent tablet packaging into a sought-after provider of CDMO services for medical devices and diagnostics, pharmaceuticals and consumer healthcare. More than 820 employees and facilities across Germany, France, Hungary, China, and the US supply products globally.

To learn more, see **Page 60**

SCHOTT PHARMA

Isabelle Jeangoudoux
isabelle.jeangoudoux@schott.com
www.schott.com

SCHOTT Pharma is a provider of drug containment and delivery solutions for injectables, ranging from prefillable syringes, to cartridges, vials, and ampoules. It manufactures syriQ BioPure® glass prefillable syringes for biologics, and SCHOTT TOPPAC prefillable syringes, made of COP.

To learn more, see **Page 92**

SHAILY

Rajesh Sharma
sales.pharma@shaily.com
www.shaily.com

Shaily specialises in the design and manufacturing of high-quality pen injectors, autoinjectors and drug delivery devices for the pharmaceutical and medical device sectors. With a commitment to innovation and precision, Shaily provides advanced drug delivery solutions that enhance patient care and meet the stringent requirements of the global healthcare industry.

See **Page 146**

SMC® Ltd.

Asmita Khanolkar
asmita.khanolkar@smcltd.com
www.smcltd.com

SMC Ltd is a global contract manufacturer for the pharmaceutical, medical device and diagnostics industries. With over 35 years of experience, SMC specialises in "end-to-end" integrated solutions for clinical and commercial manufacturing of drug delivery combination products. SMC's services include device development, manufacturing, automation, fill-finish and more.

To learn more, see **Page 42**

TERUMO
MEDICAL CARE SOLUTIONS

Michele Guasti
michele.guasti@terumo-europe.com
www.terumopharmaceuticalsolutions.com

As Part of **Terumo Medical Care Solutions**, the Pharmaceutical Solutions Division develops patient-oriented parenteral delivery solutions for therapeutic performance and safety. Terumo's expert teams lead the industry in developing and manufacturing advanced, high-performing infusion and injection technologies, including contract development and manufacturing organisation services for all parenteral applications.

To learn more, see **Page 50**

tip-top.com

Barry Liversidge
barry@tip-top.com
www.tip-top.com

tip-top specialise in the design and development of Proprietary sharps protection technology for out-licensing to the medical and pharmaceutical sectors and has amassed a large portfolio of patents relating to standalone safety needles and integrated needlestick protection systems for prefillable syringes.

See **Page 03**

West®

Dr Bettine Boltres
bettine.boltres@westpharma.com
www.westpharma.com

West Pharmaceutical Services is a provider of innovative, high-quality injectable solutions and services. As a trusted partner to established and emerging drug developers, West helps ensure the safe, effective containment and delivery of life-saving and life-enhancing medicines. With over 10,000 team members across 50 sites worldwide, West helps support its customers by delivering approximately 43 billion components and devices each year.

To learn more, see **Page 56**

WIRTHWEIN

Tom Van Ginneken
tom.van-ginneken@wirthwein-medical.com
www.wirthwein-medical.com

Wirthwein Medical is a high-performance system supplier and development partner for customer-specific plastic solutions in diagnostics, medical technology and pharmaceuticals. The company operates two sites in Germany with ISO 14644-1 Class 7 cleanrooms. Its services cover the entire value chain, including development, design, mould making, injection moulding, extrusion blow moulding, assembly, finishing and logistics.

To learn more, see **Page 78**

More Spotlights overleaf

SHL MEDICAL

OUTSTANDING SPONSOR

SHL Medical designs, develops and manufactures self-injection solutions, such as autoinjectors, pen injectors and specialty delivery systems for large-volume and high-viscosity formulations. By partnering with leading pharma and biotech companies, SHL Medical will continue to develop and supply products and services to support, engage and oversee patients whose quality of life relies on innovative self-treatment therapies.

Courtney Nicholas Sutton
courtney.sutton@shl-medical.com
www.shl-medical.com

To learn more, see **Page 10 & 65**

Stevanato Group

KEY SPONSOR

Stevanato Group is a global provider of drug containment, drug delivery and diagnostic solutions to the pharmaceutical, biotechnology and life sciences industries, 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.

Enrico Barichello
enrico.barichello@stevanatogroup.com
www.stevanatogroup.com

To learn more, see **Page 10**

YPSOMED SELFCARE SOLUTIONS

KEY SPONSOR

With over 40 years of experience, **Ypsomed**'s comprehensive drug delivery device platforms consist of autoinjectors for prefilled syringes, disposable pens, reusable pen injectors, ready to-use prefilled wearable patch injectors and injection devices for drugs in dual chamber cartridges. Ypsomed is well equipped to tackle digital healthcare challenges and has strategically invested in the development of connected solutions and therapy-agnostic digital device management services.

info@ypsomed.com
www.ypsomed.com

To learn more, see **Page 18**

Aptar pharma

Sébastien Cordier
sebastien.cordier@aptar.com
www.aptar.com/pharma

Aptar Pharma offers proven drug delivery solutions and services that support pharmaceutical companies worldwide to develop safe, efficient and compliant medicines. Aptar Pharma's drug delivery systems, components and active material solutions serve the widest range of delivery routes, Aptar's digital healthcare solutions help improve patient adherence and Aptar Pharma Services helps accelerate and derisk development.

To learn more, see **Page 65**

BAUMANN MEDICAL

David Pircher
medical@baumann-group.com
www.baumann-group.com

BAUMANN Group, headquartered in Switzerland and employing around 1,400 people across nine countries, manufactures over 4.8 billion springs, stampings and bendings annually – approximately 152 per second. Baumann Medical, an independent division within the group, provides tailor-made solutions and services in medical devices at ISO 13485 certified sites, addressing the specific needs of the medical and pharmaceutical industries.

To learn more, see **Page 84**

BBS AUTOMATION

Carsten Köhler
carsten.koehler@bbsautomation.com
www.bbsautomation.com

BBS Automation is an automation provider with 2,500 employees in 20 sites worldwide, offering a broad range of solutions, including assembly, testing, winding, insertion and take-out technology, feeder and palletising systems. Serving the mobility, medtech, consumer goods, new energy and electronics industries, BBS delivers solutions from a single source, at sites across Europe, North America and Asia. BBS is part of the Dürr Group.

To learn more, see **Page 118**

CONTEXO automation

Matthias Müller
info@contexo-gmbh.de
www.contexo-automation.de

Contexo is a family-run mechanical engineering company based in Germany that specialises in building high-performance assembly machines. Most of Contexo´s machines process plastic parts with sizes of up to 500 cm³ and can handle over 80 production processes. In the medical device sector, Contexo focuses on primary packaging and diagnostic products, as well as contract manufacturing services.

To learn more, see **Page 102**

More Spotlights overleaf

John Merhige
jmerhige@credencemed.com
www.credencemed.com

Credence MedSystems solves challenges in parenteral drug delivery. Its philosophy of Innovation Without Change preserves existing processes and primary package components. Companion includes needle-retraction, reuse prevention and usability features. The Dual Chamber platform simplifies delivery requiring reconstitution or sequential delivery. The Metered Dosing lineup enables precise microdosing in ophthalmics and aesthetics.

See **Page 04**

Sarah Horton
medical@dca-design.com
www.dca-design.com

DCA is a product design consultancy with a wealth of experience developing leading drug delivery devices for global markets, including all types of injection, infusion, inhalation, intranasal, oral and topical devices. DCA provides comprehensive, expert support for device design and development, including strategy, usability, connectivity, engineering, electronics, medical device software and industrialisation.

See **Page 02**

Bernd Zeiss
bernd.zeiss@
gerresheimer.com
www.gerresheimer.com

Gerresheimer is an innovative system and solution provider and global partner for the pharma, biotech and cosmetics industries. The company offers a comprehensive portfolio of pharmaceutical packaging, drug delivery systems, medical devices and digital solutions. With around 13,400 employees and over 40 production sites in 16 countries, Gerresheimer has a global presence and produces locally for regional markets.

To learn more, see **Page 66**

Nicole Miller
nicmille@wlgore.com
www.gore.com

W. L. Gore & Associates is a global materials science company that solves complex technical challenges in demanding environments – from space to the human body. Founded in 1958, Gore fosters a team-oriented culture with about 13,000 Associates and generates US$5.3 billion (£4 billion) in annual revenue.

See **Page 17**

Chelsea Keeton
ckeeton@
grandriveraspecticmfg.com
www.grandriveraspecticmfg.com

Grand River Aseptic Manufacturing (GRAM) is a pharmaceutical contract development and manufacturing organisation providing fill-finish services for liquid and lyophilised vials, syringes and cartridges. GRAM's syringe and cartridge technology and drug delivery partnerships place it at the forefront of client value delivery and pharmaceutical manufacturing services.

To learn more, see **Page 108**

Ana Isabel Gutierrez
ana_isabel.gutierrez@
presspart.com
www.presspart.com

H&T Presspart is a manufacturer of drug delivery devices and components with more than 50 years' experience and enjoys a worldwide reputation for competence, quality and innovation in the pharmaceutical market. H&T Presspart's Technology Center supports its customers' new product developments and strategic initiatives. H&T Presspart has four European manufacturing sites in Germany, Spain, Switzerland and the UK and also has sales representation in China, India, the US and Uruguay.

See **Page 35**

Twan Mertens
twan.mertens@
igsgebojagema.nl
www.igsgebojagema.nl

IGS GeboJagema is a high-precision mould maker that designs, manufactures, validates and maintains moulds for products where extreme precision is vital, from glasses and contact lenses to asthma inhalers, insulin pens and blood diagnostic devices. IGS GeboJagema specialises in collaborating with medical original equipment manufacturers early in the product lifecycle, allowing its exceptional engineering team to develop innovative moulding solutions.

To learn more, see **Page 96**

info@lifecore.com
www.lifecore.com/contact/

Lifecore is a CDMO specialising in the development, fill/finish, and commercialisation of sterile injectables, biologics, medical devices, and combination products. With a >40-year regulatory track record and >20 commercial products, Lifecore offers end-to-end services including formulation process development, aseptic fill/finish, analytical, packaging, and stability studies. Capabilities include expertise with highly viscous products.

See **Page 05**

Smart, Scalable Self-medication Solutions

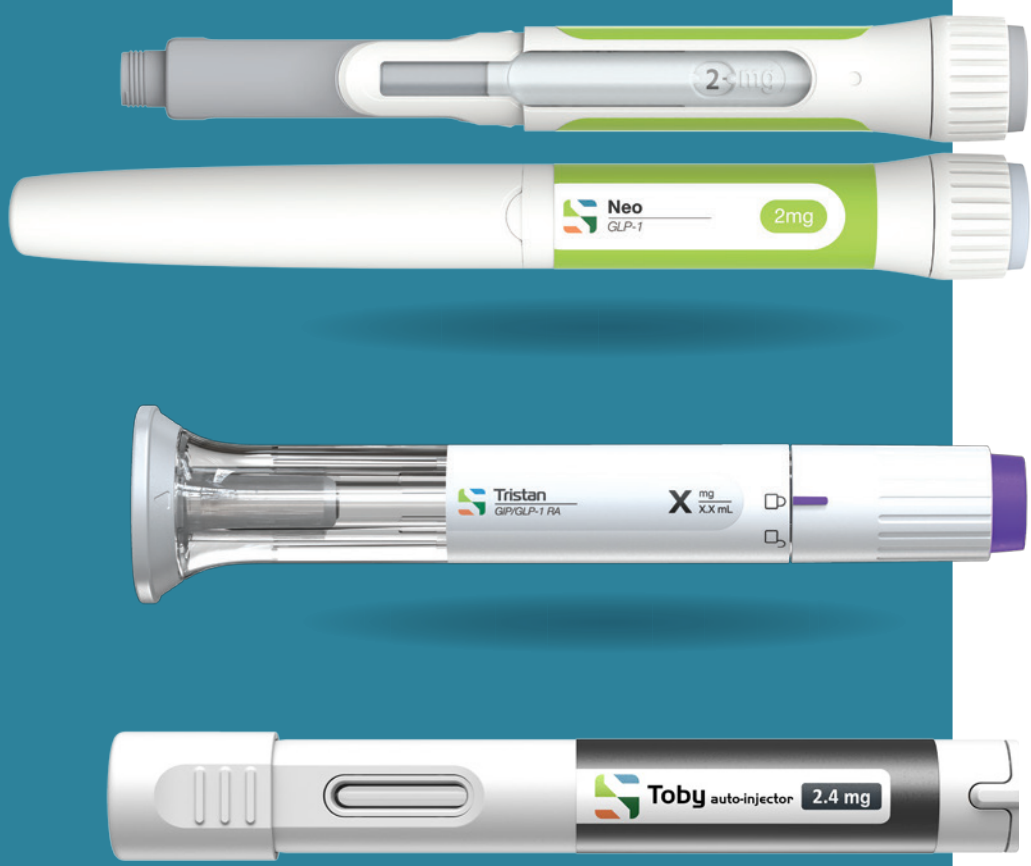
Shaily Pen Neo, Shaily AI Tristan and Shaily AI Toby are key offerings from our comprehensive range of drug delivery systems. They are designed, engineered and manufactured for patient comfort, medication compliance and in-line with regulatory compliance and performance.

Visit shaily.com/healthcare, or scan the QR code, to discover all of our platforms.

Shaily Pen Neo is an innovative spring driven pen injector, intended for use with 1.5mL and 3mL cartridges.

Shaily AI Tristan supports 1.0–3.0 ml pre-filled syringes and cartridge-based auto-injectors with ¼–1 inch needles for subcutaneous or intramuscular use. It features automatic needle insertion and a robust, high-performance torsion spring design.

Shaily AI Toby is a two step auto-injector designed with focus on reliability of function and mass manufacturing. Robustness is integrated in the design aspects for manufacturing and assembly.



Creating innovative designs for cost-effective drug delivery systems resulting in a better patient experience and supporting sustainable global health.

E sales.pharma@shaily.com **T** +91 9820-900231 **W** shaily.com/healthcare

SHAILY