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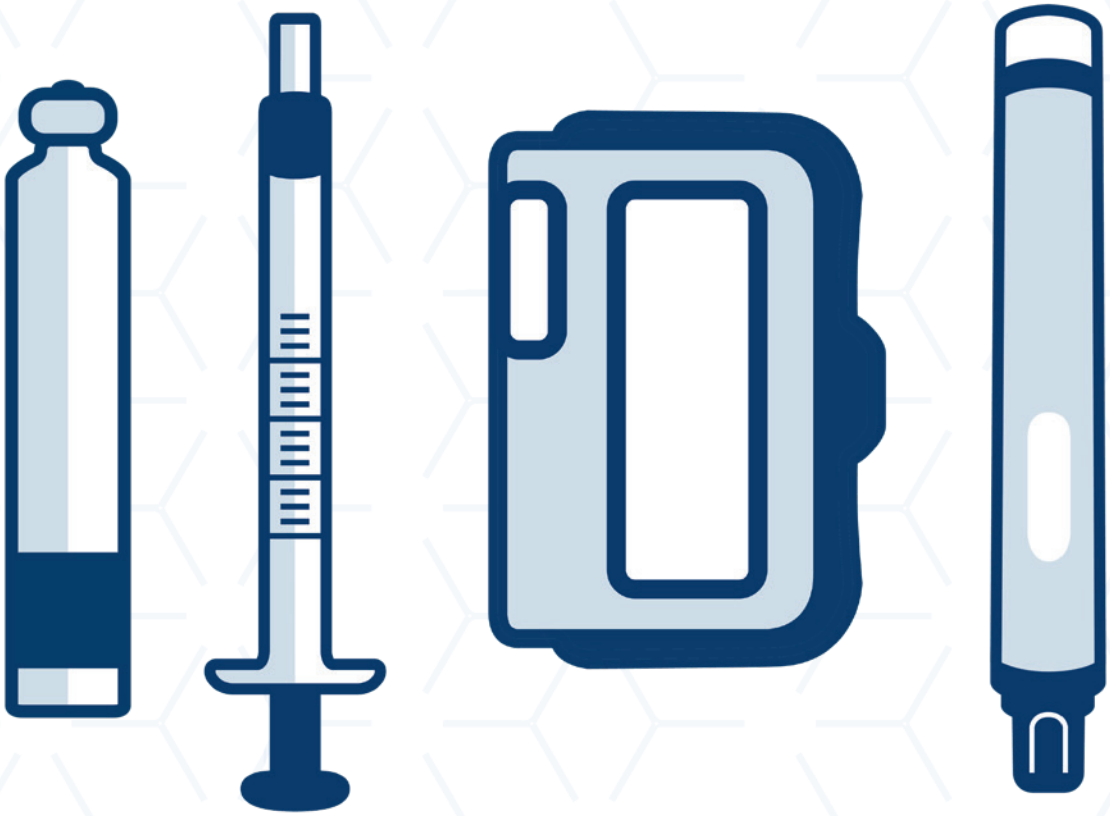

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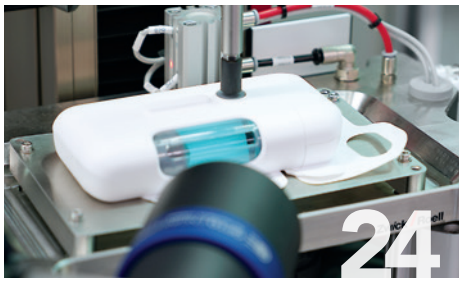

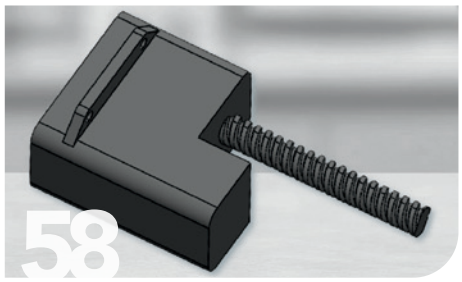

WEARABLE INJECTORS

ONdrugDelivery Issue N° 176, September 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.

Front cover image, "Patient wearing the YpsoDose injector", courtesy of Ypsomed AG. Reproduced with kind permission. (For more on YpsoDose, see this issue, Page 8.)

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Delivering Large Volumes:
The Current State of Wearable Injectors

Welcome back to ONdrugDelivery as we begin an exciting autumn and winter schedule of issue releases, which includes two brand new issue topics – "Dual Chamber Delivery Systems", out later this month, and "Delivering Gene & Cell Therapeutics", to be released in December. But first, to this issue of ONdrugDelivery, in which we focus in on the large-volume injection space and the current state of on-body delivery systems. With biologics having long faced challenges around volume and viscosity that make many of these critical therapies challenging to deliver via a conventional syringe or autoinjector, the promise of wearable delivery devices that can deliver subcutaneous injections in larger volumes over longer periods holds considerable appeal as a solution. However, wearable injectors are still a relatively young technology category, and different devices – many of which are featured within these pages – offer a variety of approaches.

Opening the issue, **Ypsomed** tackles the diverse nature of the wearable injector space (Page 8). Ypsomed's own wearable device, YpsoDose, takes a prefilled and preloaded approach, coming as a complete disposable unit, and this article discusses how the company's design priorities led to this solution.

Covering a variety of priorities and approaches, this issue also presents articles on **TxSphere**'s new Vista and how it compares with the company's existing Horizon III (Page 14); **BD**'s Libertas™ and the need to take a robust approach to risk management (Page 28); **Stevanato Group**'s Vertiva® with a look into how human factors and supply chain considerations play into design priorities (Page 36); **Enable**'s EnFuse® and the role it is playing in the UK NHS's cancer care services (Page 42); and **Nemera**'s Symbioze® with a deeper look into how specific design decisions are made to tackle the various challenges of wearable injector design (Page 48).

Oncology is a running theme throughout the issue, with cancer care proving to be a key target sector for many in the wearable injection space. Along with Enable's article, this issue features an Expert View from **LTS Device Technologies** (Page 54), discussing the results of a survey of attendees at the American Society of Clinical Oncology 2025 Global Meeting, which delved into their opinions on the current state of wearable injectors in oncological practice, as well as their potential future role in the sector.

Rounding out the issue, we feature articles digging into the technologies and services that support wearable injectors. **Herrmann Ultraschall** discusses the value of using ultrasonic welding technologies for manufacturing wearable devices (Page 20). Next, **ZwickRoell** considers the process and requirements for testing these devices (Page 24). Lastly, we hear from **Kymanox** and **Johnson MedTech** on how structuring development using a modular approach, with expert teams given space to focus on their specific part of the design being co-ordinated by a systems integration specialist, can accelerate and de-risk the development process (Page 58).

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2025/26 Editorial Calendar

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

SEP/OCT 2025 **NEW ISSUE TOPIC** Dual Chamber Delivery Systems DEADLINE PASSED	**OCT** Prefilled Syringes & Injection Devices DEADLINE PASSED	**OCT/NOV** Sustainability in Drug Delivery DEADLINE: **Sep 18, 2025**
NOV Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 2, 2025**	**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**

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20 YEARS ON drugDELIVERY

DIVERGENT DESIGN PHILOSOPHIES IN THE WEARABLE INJECTOR SEGMENT

YPSOMED SELFCARE SOLUTIONS

Reto Jost and **Daniel Käser** of **Ypsomed** detail how the company is approaching wearable injector design with YpsoDose and achieving large-volume requirements, consistent dosing and low residual waste, going on to explain how the company's design choices are integrated with patient-centric features to ensure adherence and comfort.

As subcutaneous (SC) biologics increase in volume and complexity, the demand for wearable injectors enabling safe and effective at-home delivery continues to grow. Yet unlike the autoinjector and pen segments, which have largely converged on common standards, wearable injectors remain highly diverse in design. YpsoDose – a prefilled and ready-to-use large-volume wearable injector developed by Ypsomed – reflects a deliberate design philosophy that differentiates it within the fragmented design landscape of wearable injectors. YpsoDose prioritises consistent delivery, low residual volume and ease of use, helping to shape the large-volume wearable category.

IV LEAGUE DROPOUTS

Over the past decade, the biopharmaceutical industry has shifted towards higher-volume SC drug delivery. Driven by the rise of monoclonal antibodies, bispecifics, antibody-drug conjugates and other complex biologics, SC injection is

"COMPARED WITH IV, SC ADMINISTRATION OFFERS FASTER DOSING, GREATER FLEXIBILITY IN TREATMENT LOCATION AND IMPROVED PATIENT EXPERIENCE."

becoming an increasingly preferred alternative to intravenous (IV) infusion for many indications. Compared with IV, SC administration offers faster dosing, greater flexibility in treatment location and improved patient experience. One widely cited example is daratumumab, which transitioned from a 3–7 hour IV infusion to a SC version deliverable in under five minutes, which now accounts for around 93% of usage in the US (Figure 1).

This trend is made possible by advances in drug formulation, permeation enhancers and injection devices. As more therapies move into the home or outpatient setting, there is a growing need for delivery systems capable of handling volumes well beyond the 2 mL traditionally supported by autoinjectors. In a systematic review, Ypsomed found that over 100 large-volume SC candidates aim for doses of 5 mL or above. With more biologics entering the pipeline and patient care moving closer to home, the need for devices that support safe, convenient SC administration continues to grow.

This evolution concerns more than just dosing increase, it is a shift in how and where care happens. For device developers, the challenge is to design large-volume injection systems that not only meet clinical and technical requirements but also fit seamlessly into the realities of self-care, delivering efficiency, reliability and usability.

PATCH WORK: THE FRAGMENTED DESIGN LANDSCAPE OF WEARABLE INJECTORS

Pen injectors and autoinjectors have, over time, coalesced around a set of widely accepted design norms. Since the 1980s, cartridge-based pen injectors have evolved from prefilled reusable to prefilled multidose disposable, geared devices with easy-to-read displays, which are either manually or spring-driven. Single-use autoinjectors were first launched in 2006, and today they are usually based on two-step, push-on-skin mechanisms that are activated once the needle is fully inserted into the skin. The volumes delivered by single-use autoinjectors have increased to cover 1.0, 2.25 and most recently 5.5 mL prefilled syringes.

Figure 1: From IV to SC injection – YpsoDose enables the shift from hospital-based IV therapy to self-administered SC delivery.

"FOR DEVICE DEVELOPERS, THE CHALLENGE IS TO DESIGN LARGE-VOLUME INJECTION SYSTEMS THAT NOT ONLY MEET CLINICAL AND TECHNICAL REQUIREMENTS BUT ALSO FIT SEAMLESSLY INTO THE REALITIES OF SELF-CARE."

Traditionally, larger-volume SC injections have relied on reusable infusion pumps for delivering drugs in niche applications, such as apomorphine for treating Parkinson's disease or gamma-globulins for immunomodulatory therapies. The emergence of new antibody therapies over the past 10–15 years has driven the need for larger-volume SC injections in the 5–20 mL range. In response, wearable injection devices have evolved alongside large-volume handheld autoinjectors to meet the requirements of these new treatment regimens.

It is the wearable nature of these systems, and the relatively recent emergence of the segment in comparison with pens and autoinjectors, that has led to considerable design divergence. While pens and autoinjectors tend to centre on faster injection times, simplified handheld actuation and integrated sterile drug paths (a cartridge with pen needle or a staked needle syringe), wearable injectors show a remarkable diversity in design. Differences span device shape, fluid path, patch technology, drive mechanisms, filling methods, user-assembly requirements and sterilisation strategies.

Against this backdrop, selecting the right design is more critical than ever. With so many design directions being followed in parallel by different design manufacturers, the implications for usability, reliability, cost-effectiveness and scalability are significant, making it even more critical for pharmaceutical companies to carefully consider their options when deciding on potential delivery devices.

Faced with this open design space, Ypsomed pursued a focused, pragmatic approach. Rather than following completely novel but unproven architectures, Ypsomed made foundational decisions that reflect real-world use cases and pharmaceutical constraints. The first such decision was to create a consistent injection experience for every dose.

FORCE MAJEURE: INJECTION CONSISTENCY AND EXTERNAL VARIABLES

While mechanical injection systems may appear simple and cost-efficient, they can introduce inconsistency into the drug delivery process. Spring-driven mechanical devices often exhibit declining force profiles as the spring decompresses, leading to fluctuating flow rates during the injection. In handheld autoinjectors we can already see variance in injection time, though the variance is negligible given the injection event lasts a matter of a few seconds. These limitations naturally become more pronounced with large-volume or high-viscosity formulations, where an injection may last up to 30 minutes.

YpsoDose avoids these pitfalls through its motor-driven push-on-plunger system. Unlike spring-based systems, the motor delivers consistent force throughout the injection event, independent of external conditions. This design enables a steady, controlled flow profile even under assumed worst-case conditions and reliable delivery of 10 mL at viscosities up to 50 cP in 10 minutes (Figure 2). The result is a system that delivers not just the correct volume but a consistent experience.

External factors such as variations in temperature, orientation and injection site can also adversely affect delivery. As YpsoDose is motor-driven and sensor-supported, it performs reliably across a range of environmental and patient-specific variables. Skin-contact sensors verify correct placement before initiating the injection, reducing the risk of user error, and its motor drive allows for delivery across a wider range of temperatures. This stability translates into a smoother experience for patients and more dependable outcomes for healthcare providers. For treatments requiring long-term therapy adherence, this consistency supports trust and ongoing engagement. While this represents real value for patients, there is another key aspect that provides more direct value for pharma customers – minimising residual drug volume.

RESIDUAL VOLUME: THE SILENT DRAIN ON DRUG DELIVERY

Two major factors contribute to drug loss in wearable injectors. Firstly, manual filling or transfer steps may introduce variability and loss; secondly, residual drug left in the device after injection due to fluid path design. These factors can lead to significant cumulative waste, particularly for high-cost biologics.

In contrast to, for example, suction-based delivery, YpsoDose was designed from the outset to minimise residual volume. YpsoDose integrates a prefilled cartridge with a simplified, optimised fluid path consisting of two cannulas and a short connecting tube. The result is a total residual volume for the system of <0.262 mL (<0.015 mL device fluid path, <0.247 mL cartridge) and zero waste from manual patient filling (Figure 3).

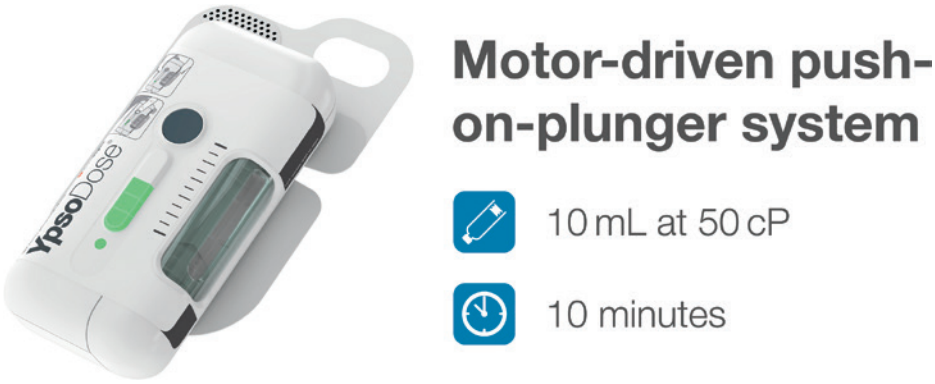

Figure 2: YpsoDose administers 10 mL at 50 cP in 10 minutes using a motor-driven push-on-plunger system – ensuring reproducibility even with challenging formulations.

These numbers matter for pharma and this efficiency is not a secondary feature; it is integral to the device's value. By minimising drug waste, YpsoDose reduces the overfill requirement and helps to preserve valuable APIs. Yet the implications extend beyond pharmacoeconomics. Reduced residual volume contributes to environmental sustainability by minimising chemical waste and reducing the carbon footprint associated with manufacturing and disposal. For pharmaceutical companies facing cost pressures and environmental, social and governance expectations, this design choice makes a compelling case.

MORE THAN JUST VOLUME AND FLOW

While minimal residual volume and consistent injection performance are foundational, they are only part of what makes YpsoDose a complete solution. Usability, safety and reliability are also central to the device's value, each informed by human factors testing and industrial design decisions made to reduce user burden and improve confidence.

YpsoDose incorporates several other features designed to improve usability and confidence for both patients and pharmaceutical partners. An example of core patient centricity is the audio and visual feedback features, providing real-time cues that guide the user through the injection process, making it intuitive and reassuring. Likewise, electronic skin-contact sensors ensure that the injection is only initiated when proper contact with the skin is detected, reducing the risk of improper use and providing peace of mind. Flexibility is also built in, with the device supporting programmable injection speeds of up to 3.0 mL/min, allowing for the accommodation of different formulations and individual patient tolerances. Additionally, built-in sterility enables final assembly outside a cleanroom, reducing manufacturing and integration complexity for pharmaceutical companies.

"BY MINIMISING DRUG WASTE, YPSODOSE REDUCES THE OVERFILL REQUIREMENT AND HELPS TO PRESERVE VALUABLE APIs."

Figure 3: YpsoDose achieves a total residual volume for the system of <0.262 mL, helping to reduce overfill, cut drug waste and protect valuable biologic formulations.

"YPSODOSE OFFERS A SOLUTION THAT BALANCES INNOVATION WITH RELIABILITY, REVOLUTIONISING SELFCARE AND HELPING PARTNERS BRING THERAPIES TO MARKET WITH CONFIDENCE."

Taken together, these design choices deliver not only a technically advanced device but one that is practical, scalable and aligned with the real-world demands of pharmaceutical development and patient use. YpsoDose offers a solution that balances innovation with reliability, revolutionising self care and helping partners to bring therapies to market with confidence.

CONCLUSION

As the number of large-volume SC biologics increases, careful evaluation of device design is critical. YpsoDose addresses primary sources of delivery inefficiency – residual volume and injection inconsistency – with a platform built for reliability. Yet advanced features alone are not enough. YpsoDose is part of a broader solution ecosystem, supported by partnerships across the supply chain, including the primary container (SCHOTT Pharma, Mainz, Germany), fill-finish, and final assembly (ten23 health, Basel, Switzerland), ensuring a smooth, integrated path to clinic and market for customers (Figure 4). Clinically and commercially ready, YpsoDose enables easier adoption and faster market access for pharmaceutical partners.

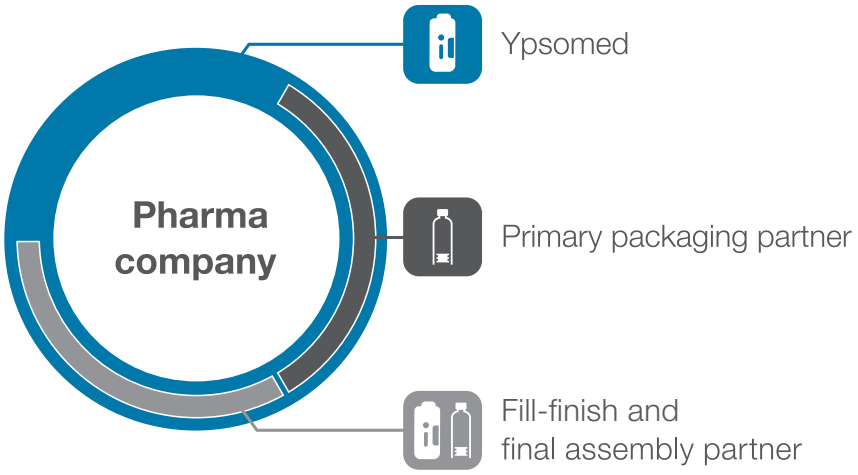

Figure 4: YpsoDose is a complete, clinic- and market-ready solution, supported by expert partners in primary packaging (SCHOTT Pharma) and final assembly (ten23 health), ensuring end-to-end project confidence.

Reto Jost

Reto Jost is Category Lead for Large-Volume Injectors at Ypsomed Delivery Systems. He has been with Ypsomed since 2014 in various roles in product management and business development, working with pharmaceutical companies to develop self-injection systems and bring them to market. Since 2018, his main focus has been on new product innovation, with a particular focus on large-volume injections. Mr Jost holds an MSc in Mechanical Engineering from ETH Zurich (Switzerland) and a CAS in Business Administration from HES-SO (Fribourg, Switzerland). He has broad experience in medical devices, having worked in the industry since 2006.

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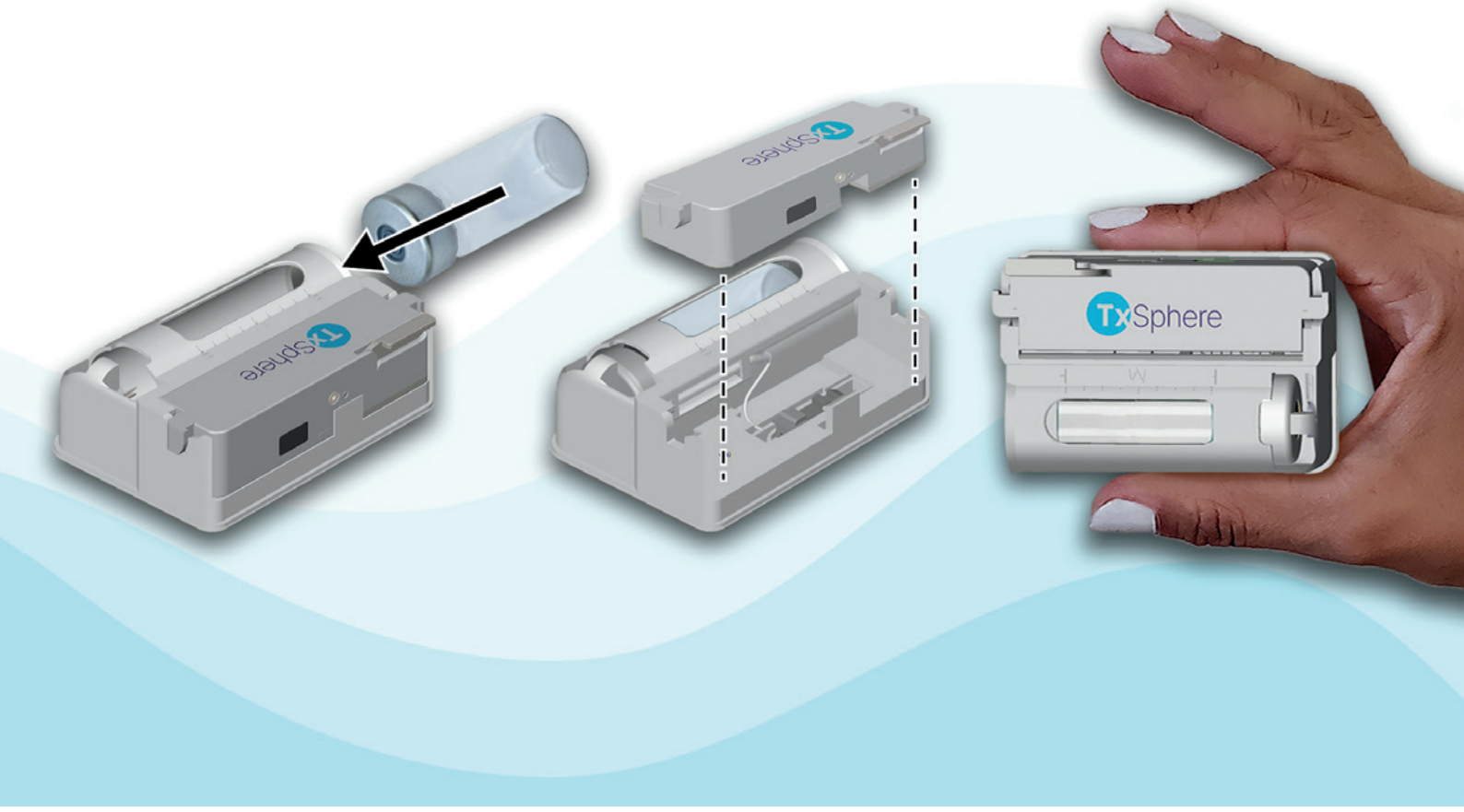

VISTA BY TXSPHERE: TRAVERSING THE LIMITATIONS OF SMALL-VOLUME BIOLOGICS

Dr Chaoyoung Lee and **Mike Stout**, both at **TxSphere**, unveil an innovative addition to their wearable platform, Vista, designed to improve on efficiency goals, adapt to varied drug formulations and advance beyond the requirements of low-volume drug delivery.

INTRODUCTION

Bringing a biopharmaceutical to market represents an enormous undertaking. Furthermore, the choice of how to deliver the preparation is much more complex than most pharmaceutical products. The push to transition from intravenous (IV) to subcutaneous (SC) delivery, especially for self-administration, adds even more considerable challenges. How best to meet these challenges is a strategic decision that impacts the entire lifecycle of a therapeutic product. The resulting development goal is to balance the best patient experience, time to market, dose cost and sustainability.

THE SHIFT FROM IV TO SC ADMINISTRATION

Historically, the high doses required for many biologic therapies have necessitated IV administration in clinical settings – a method that is costly, time-intensive and inconvenient for patients. In response, the pharmaceutical industry is increasingly shifting towards SC delivery. This transition is fuelled by several compelling

"THE RESULTING DEVELOPMENT GOAL IS TO BALANCE THE BEST PATIENT EXPERIENCE, TIME TO MARKET, DOSE COST AND SUSTAINABILITY."

drivers – the convenience of at-home self-administration, improved patient adherence and a substantial reduction in the economic burden associated with infusion-based care.

Transitioning to SC delivery presents significant technical challenges, particularly in formulation and device design. SC injections are constrained by limited volume tolerance, meaning that the high doses required for protein-based biopharmaceuticals introduce additional complexities such as increased viscosity and formulation instability.

Formulation Challenges

SC formulations traditionally involve increasing drug concentration to reduce injection volume, enabling rapid administration via autoinjectors or manual injection. These small-volume, highly concentrated formulations present significant technical hurdles not found in low-concentration preparations.[1] Elevated protein concentrations lead to increased solution viscosity, which can complicate manufacture and hinder injectability. Additionally, high concentrations elevate the risk of protein aggregation, opalescence and physical instability.[2]

Another approach involves the use of permeation enhancers, which can dramatically increase the volume of fluid that can be delivered subcutaneously. However, they also contribute to the overall formulation volume, often exceeding the capacity of conventional delivery devices.

Delivery Device Challenges

The autoinjector is a widely used device for the self-administration of biologic drugs. Its design focuses on facilitating simple and rapid drug delivery for the user, enabling self-administration of a therapeutic dose in a single action. The primary engineering consideration in autoinjector development is to deliver a complete dose of viscous drug formulations within a period generally regarded as suitable for patients (usually 15–20 seconds or less).[3]

This situation creates a complex relationship between device mechanics, formulation properties and clinical pharmacology. To achieve the necessary injection force, manufacturers frequently employ stronger springs, which can place greater stress on the primary container, increase device size and raise the amount of force during injection. This increased stress also necessitates more robust container designs and materials.[4] Autoinjectors are also constrained by volume limitations, with most commercially available devices supporting doses in the 0.3–2.25 mL range, with some emerging devices expanding this up to 5 mL.

While some of these formulation and delivery challenges can be mitigated, further increases in concentration and reductions in dose volume are ultimately constrained by the physical limits of formulation and the capabilities of current delivery technologies. As viscosity, stability and device performance thresholds are approached, trade-offs become increasingly difficult to manage without compromising safety, efficacy or patient usability.

> "AN ALTERNATIVE TO FORMULATING OR DELIVERING BIOLOGICS AT HIGH CONCENTRATIONS IS TO PLACE LESS EMPHASIS ON SMALL VOLUMES AND MORE ON OPTIMAL FORMULATIONS."

THE LARGE-VOLUME ALTERNATIVE

An alternative to formulating or delivering biologics at high concentrations is to place less emphasis on small volumes and more on optimal formulations. This approach offers numerous benefits.

Transitioning to large-volume protein formulations removes the limitations associated with small-volume delivery. This strategy has far-reaching implications for the drug development process, including:

- **Viscosity Reduction Benefits**: This can ease manufacturing processes, enhance formulation stability and reduce the need for high-force delivery mechanisms.
- **Accelerating Development**: Large-volume alternatives help to reduce the necessity to re-formulate, potentially shortening development timelines and lowering associated costs.
- **Enabling High-Dose Biologics**: Certain biologic molecules, particularly at high doses, are difficult, or even impossible, to concentrate at levels compatible with conventional self-administration devices.[5]

Large-Volume Delivery Benefits

Capitalising on the benefits of large-volume formulations will require a different approach to administration. Large-volume on-body delivery systems are expected to be part of the solution.[6] Devices that deliver at slower rates can further expand the utility by mitigating discomfort.[4,7]

Slow infusion allows for gradual absorption and dispersion of fluid through SC tissues and the lymphatic system, minimising discomfort and improving tolerability. When administered at a controlled rate, even relatively large volumes can be delivered comfortably and effectively. A notable example is the transition of immunoglobulin therapies from IV to SC delivery, where volumes of 50–60 mL per injection site are successfully administered over a 60-minute period.

Addressing the challenge of delivering larger volumes via the SC route without compromising patient comfort can be achieved through innovative wearable technologies with adaptable delivery profiles. Large-volume wearable devices embody this shift in philosophy – moving away from the rapid, forceful injections of autoinjectors and prefilled syringes towards a more patient-friendly approach that emphasises comfort, tolerability and extended wear. By prioritising volume capacity over injection speed, these devices unlock new possibilities for SC administration, including the delivery of biologics and other complex therapies.

TXSPHERE'S MODERN APPROACH TO WEARABLE DESIGN

Higher dose volumes pose design challenges for wearable devices as well. Extended wear times require careful consideration of patient acceptance, such as the clarity of its user interface, size and comfort. For the pharmaceutical company, it is also important for delivery devices to be adaptable to various dosing regimens. TxSphere develops wearable devices

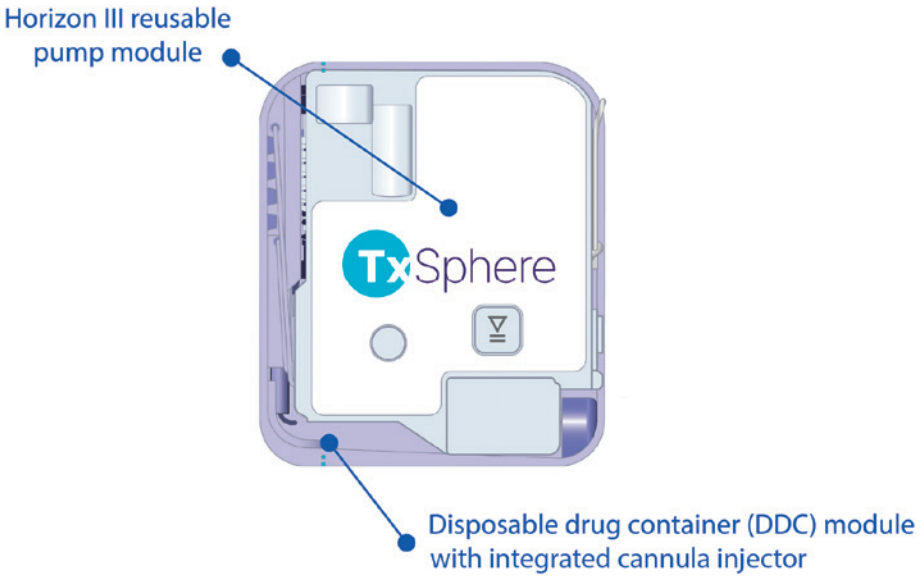

Figure 1: The Horizon III Wearable.

capable of administering biopharmaceuticals across a range of dose volumes and concentrations. This adaptability can enable pharmaceutical manufacturers to reduce the amount of time spent adjusting formulations to suit various delivery devices. In other words, TxSphere's philosophy is that devices should adapt to the drug formulation, not vice versa.

Last year, TxSphere launched Horizon III, a small wearable device capable of delivering at least 10–20 mL of medication while not much larger than an insulin patch pump (Figure 1).

This small size was made possible through miniaturisation of TxSphere's fluid delivery technology and an internal reservoir. The internal reservoir of the Horizon III has the advantage of reducing the overall size of the wearable and does not require stoppers, movable plungers or lubricants.

Nevertheless, this approach involves a trade-off in terms of reduced pre-filling efficiency. Filling at the point of care is another suitable option, however it introduces additional complexity for self-administration.

THE NEW VISTA WEARABLE – STANDARD PRIMARY PACKAGING

Out of its commitment to tailoring our devices to the requirements of the drug product, TxSphere is pleased to announce the addition of Vista to its wearable platform (Figure 2). Vista retains much of the innovations of Horizon III, but instead of an internal reservoir, Vista delivers medication from standard vials or cartridges. The addition of primary packaging for Vista required a moderate increase in size, but it still maintains the compact, patient-friendly form factor and other benefits of Horizon III.

> "TXSPHERE'S PHILOSOPHY IS THAT DEVICES SHOULD ADAPT TO THE DRUG FORMULATION, NOT VICE VERSA."

With the addition of Vista, TxSphere now offers two versatile wearable designs, each providing a discrete combination of benefits:

- **Horizon III** is designed to prioritise the patient experience while offering a less efficient filling process
- **Vista** is primarily focused on greater efficiency in filling, storage and distribution processes.

The TxSphere Wearable Platform

Both the Vista and Horizon III wearables are built on TxSphere's two-piece modular platform, which consists of a reusable pump and a disposable drug container (DDC).

The pump module is based on TxSphere's core technology – a linear volumetric peristaltic pump, which is derived from the company's extensive experience in infusion pump development. The disposable module contains the drug reservoir and an automated soft cannula injector.

The integration of TxSphere's miniature pump module with the DDC works seamlessly across a range of primary packaging systems. This design enhances the patient experience, supports drug-specific dosing needs – including concentration, volume and viscosity – and addresses critical factors in container filling, storage and distribution throughout the product lifecycle.

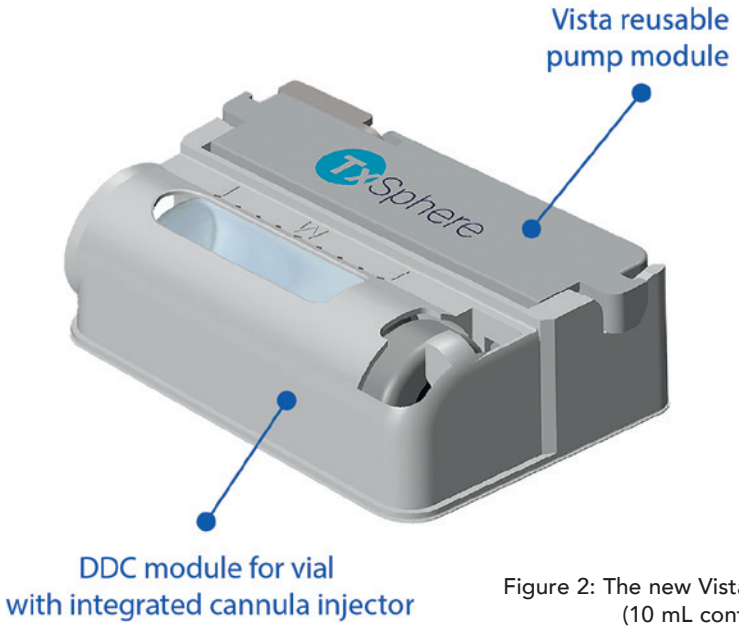

Figure 2: The new Vista wearable (10 mL configuration).

"NEITHER THE MEDICATION NOR CONTAINERS ARE SUBJECT TO HIGH PRESSURES AND THE RELATED VISCOUS FLOW CONCERNS, SUCH AS THE NECESSITY OF SPECIALISED, ROBUST CONTAINER SOLUTIONS."

Improved Patient Experience

If a device is truly "wearable", it must meet the practical expectations of wearability – ensuring comfort, discretion and ease of use for the patient throughout the intended wear period.

- **Comfort:** The compact and lightweight design means it is less noticeable and easier to conceal. The automated cannula injector is hidden from the patient and provides extended wear comfort when compared with a needle. Cannula insertion is quick and much gentler than typical autoinjectors (Figure 3).
- **Simple Operation:** Requires just a few steps – insert the vial into the DDC, connect the pump, adhere it to the skin and press Run. Sensors verify each action before medication delivery, reducing user errors and preventing mistakes that can lead to device incapacitation and wasted doses (Figure 4).
- **Hands Free:** Does not need to be held in place during delivery, which typically takes around 15 seconds with an autoinjector. This hands-free method allows the patient to carry out regular activities during the infusion.

Container Simplicity and Flexibility

Because TxSphere wearables pull medication from the drug reservoir, many container challenges are reduced or eliminated. Neither the medication nor containers are subject to high pressures and the related viscous flow concerns, such as the necessity of specialised, robust container solutions.

The two reservoir configurations offer increased flexibility to meet diverse development and manufacturing needs:

- **Internal Reservoir (Horizon III):** This integrated, prefillable reservoir eliminates the need for stoppers, movable plungers and lubricants – reducing potential sources of variability.
- **Standard Primary Packaging (Vista):** Traditional vial formats offer proven stability, ease of filling and compatibility with existing infrastructure. This approach can accelerate development timelines by minimising the need for new packaging solutions. Cartridges provide another familiar and scalable option.

Figure 3: Vista's compact size.

Formulation and Dosing Flexibility

The versatile design of TxSphere's wearable devices accommodate a wide range of different dose volumes, delivery rates and viscosities, enabling developers to leverage the advantages of lower-concentration formulations, including added permeation enhancers:

- **Reduced Time and Cost:** A more efficient development process can result in substantial cost and time savings.

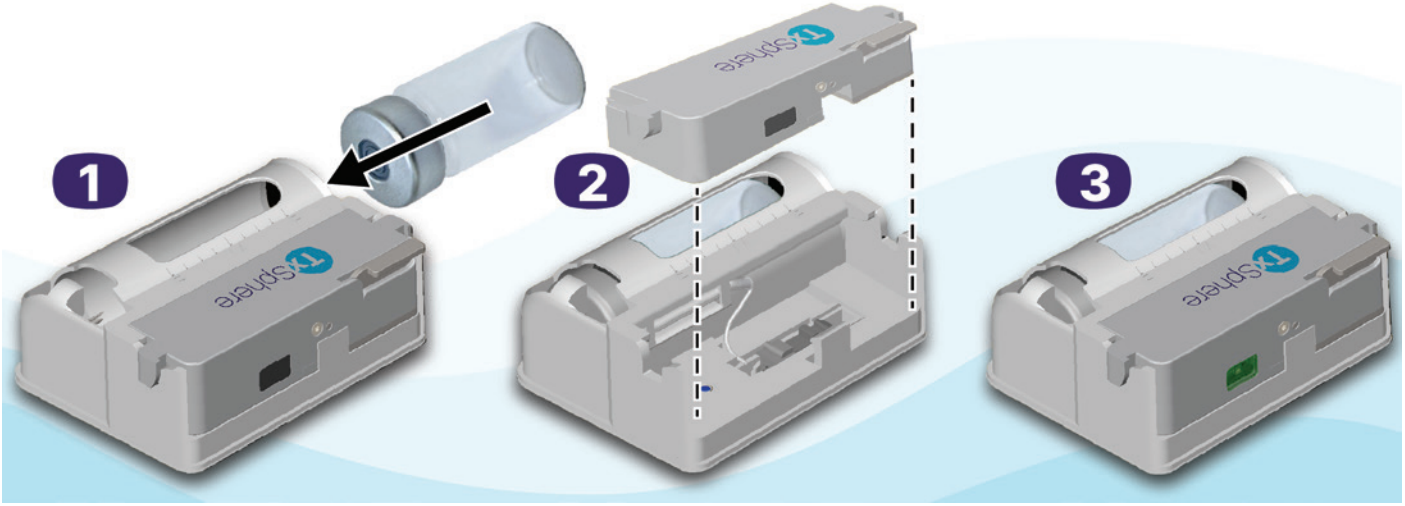

Figure 4: Vista preparation – three steps.

- **Accelerated Time to Market:** Less time spent on costly formulations and container challenges, helps to get products to the market faster.

Sustainability

Sustainability has emerged as an increasingly important consideration in recent years. Nevertheless, many wearables and autoinjector devices in the market require the disposal of the entire unit following each use. Vista's modular design addresses this challenge by enabling the reuse of electromechanical components, with only the sterile fluid path elements being discarded after each dose. This approach also offers the added advantage of reducing the cost per dose.

SUMMARY

The transition from IV to SC delivery for biopharmaceuticals presents new challenges across an already intricate product lifecycle. Navigating these complexities requires strategic decisions that shape every stage of development. Equally important is the selection of a delivery device, which plays a pivotal role in product strategy and should be integrated into lifecycle planning as early as possible.

TxSphere's wearable platform – Horizon III and Vista – offers a modern alternative to meeting many of these challenges. Supporting a broad range of volumes, formulations and packaging formats, these devices align with the evolving needs of today's drug-device combination products.

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"THE VERSATILE DESIGN OF TXSPHERE WEARABLES ACCOMMODATE A WIDE RANGE OF DIFFERENT DOSE VOLUMES, DELIVERY RATES AND VISCOSITIES, ALLOWING DEVELOPERS TO LEVERAGE THE ADVANTAGES OF LOWER-CONCENTRATION FORMULATIONS."

Dr Chaoyoung Lee

Chaoyoung Lee, PhD, is a software engineer by training and an entrepreneur who has founded and grown multiple software and medical device companies. He is the founder and president of TxSphere, with a passion for developing simple and intuitive technologies to improve patient experience in self-administrate medication therapies at home to manage disease states.

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Mike Stout

Mike Stout, RPh, Head of Strategic Partnerships and Clinical Applications at TxSphere, began his career in home infusion pharmacy, including roles as Director of Pharmacy for a major health system and branch manager for a national organisation. His interest in infusion devices eventually led him to the ambulatory infusion device industry. His contributions have primarily involved sales, marketing and product development. In June 2005, Mr Stout received the Outstanding Design Team award from MDDI Magazine for his role in developing the AmBit® ambulatory infusion pump. He has also shared his knowledge as a lecturer on infusion therapy, pain management and human factors design, presenting both domestically and internationally.

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FLEXIBLE

- Robust Linear Peristaltic Drive
- Variable Delivery Rates
- Large Volume Capacity

PATIENT FRIENDLY

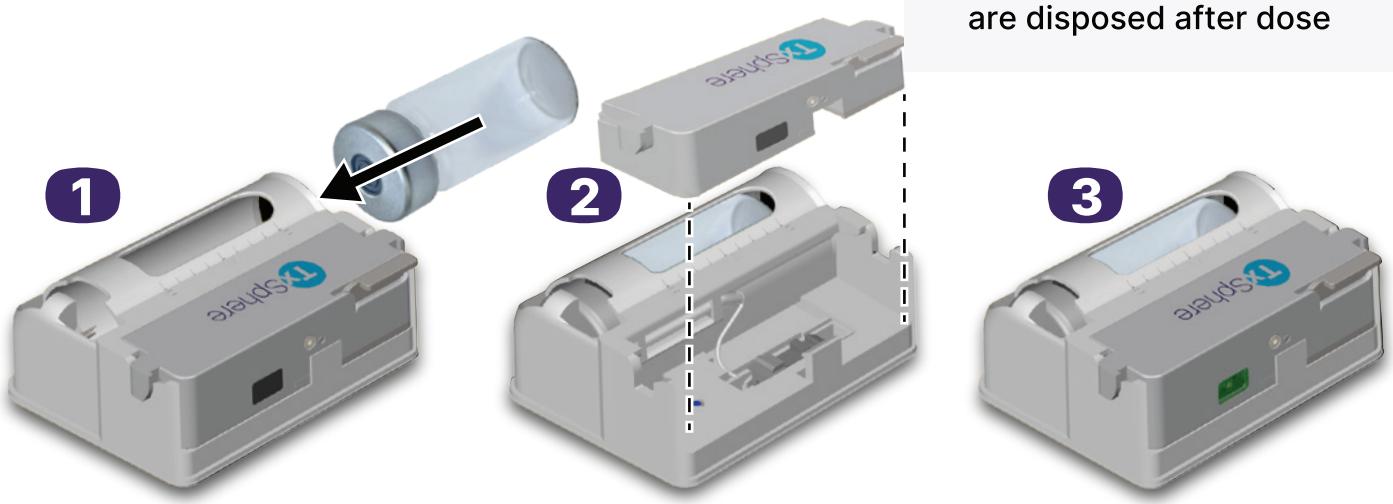
- Simple Operation
- Compact, Lightweight
- Soft Cannula
- Hands Free Delivery

STANDARD PRIMARY CONTAINERS

- Vials
- Cartridges

SUSTAINABLE

- Reusable Pump Module
- Only Reservoir & Cannula are disposed after dose



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SAFE AND SKIN-FRIENDLY MANUFACTURING OF MEDICAL WEARABLES WITH ULTRASONIC WELDING

Michael Boerner of Herrmann Ultraschall looks at the key factors for designing skin-friendly medical wearables and how to manufacture them safely, automatically and sustainably.

Figure 1: The appropriate joining technology is crucial for optimal wearing comfort and reliable functionality of medical wearable devices, such as CGMs and patch pumps.

The rising global prevalence of diabetes is driving a rapidly increasing demand for medical wearable devices, such as continuous glucose monitors (CGMs) and patch pumps (Figure 1). These devices offer patients enhanced freedom, safety and, ultimately, an improved quality of life.

However, studies indicate that up to 81% of users experience skin irritation from these wearables.[1] This is often caused by allergens such as isobornyl acrylate (IBOA), commonly found in the chemical adhesives used in medical devices.[2] Additionally, other factors can also compromise the comfort and functionality of medical wearables, such as the use of unsuitable materials or joining processes for plastic components.

SKIN-FRIENDLY WEARABLES START WITH THE DESIGN

To prevent skin irritation, product designers must consider the moisture vapour transmission rate (MVTR) during development. This factor significantly impacts both skin compatibility and comfort during wear; however, it can be effectively managed through the use of appropriate joining technology.

The MVTR measures the amount of moisture vapour that passes through a material within a day. A high MVTR value allows the skin to breathe more easily, reducing the risk of irritation. However, medical wearables, such as CGMs, which are worn directly on the skin, can limit breathability. This issue becomes particularly critical when stronger adhesive formulations or higher adhesive coating weights are used. These factors hinder moisture escape, increasing the likelihood of skin irritation.

To minimise irritation caused by prolonged use of medical wearables, it is crucial to consider MVTR early in the product development process.

CRITICAL FACTORS FOR THE MVTR

Medical wearables are typically attached to the skin using a skin adhesive with

"TO MINIMISE IRRITATION CAUSED BY PROLONGED USE OF MEDICAL WEARABLES, IT IS CRUCIAL TO CONSIDER MVTR EARLY IN THE PRODUCT DEVELOPMENT PROCESS."

a nonwoven backing, forming a skin-adhesive patch. The sensor or device is then affixed directly to this patch. Even when the adhesive plaster has a high MVTR, the device itself can still restrict or completely block the skin's breathability.

Additional barriers may arise if unsuitable joining technologies are used to attach the sensor or device to the nonwoven material on the back of the skin patch. Traditionally, this has been achieved through heat sealing or adhesive bonding.

However, conventional adhesives and heat-based bonding methods often have limitations. The chemicals in adhesives can trigger allergic reactions and further restrict skin breathability. While additional sensor mounting tape or reactive adhesives can provide a secure hold, they also introduce another barrier, increasing the risk of skin irritation.

Thermal joining processes, on the other hand, can negatively impact the soft material properties of nonwoven patches, reducing their flexibility and comfort. Moreover, excessive thermal loads during joining can create microchannels that weaken the bond, compromising the device's secure attachment to the wearer's skin.

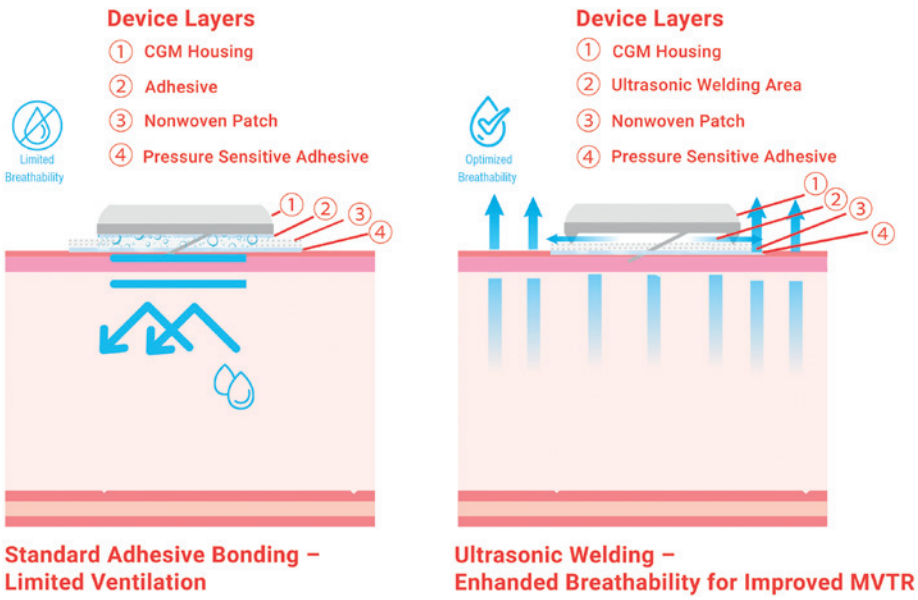

Figure 2: While using adhesives as a joining technology can restrict the skin's breathability, ultrasonic welding makes it possible to include microchannels to ensure optimum MVTR.

USING ULTRASONIC WELDING TO IMPROVE BREATHABILITY

Ultrasonic welding presents an innovative alternative to conventional bonding methods. This technology uses high-frequency mechanical vibrations to weld materials together at precise points. The heat generated is confined to these predefined joining zones, protecting the surrounding areas of the application.

This process offers several key advantages. As no chemical adhesives are required, the risk of allergic reactions caused by IBOA is eliminated. Additionally, the soft material structure remains intact, as thermal exposure is minimal and occurs only in the designated weld zone. The resulting bond is highly durable, ensuring a long shelf life.

Furthermore, ultrasonic welding enables the integration of ventilation gaps and drainage channels, enhancing airflow and reducing the likelihood of moisture buildup (Figure 2).

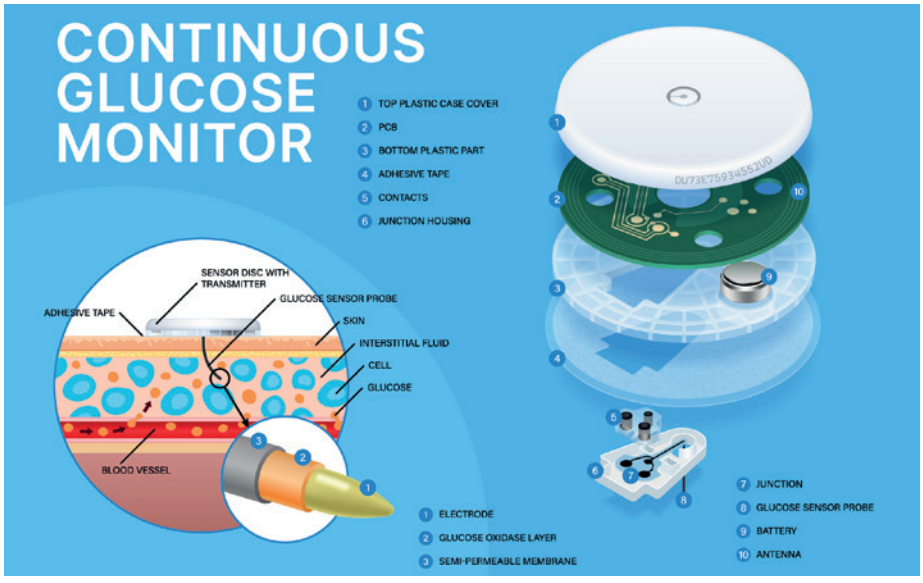

Figure 3: Precise control of process parameters enables ultrasonic technology to join even sensitive components and parts hermetically and securely.

CHOOSING THE RIGHT MATERIAL FOR MEDICAL WEARABLES

To date, medical wearables have been made primarily of polyvinyl chloride (PVC). PVC is robust, chemically resistant and inexpensive, but is made flexible by the addition of plasticisers, which poses risks for both the environment and the health of the patient.

As such, manufacturers are increasingly switching from PVC to thermoplastic elastomers (TPEs). Even if PVC and TPEs differ fundamentally in their chemical composition, they have similar physical properties, which simplifies the switch. The benefits of TPEs are that they are naturally flexible, require no plasticisers and are more biocompatible (Figure 3).

DIFFERENT JOINING PROCESSES FOR TPE

When joining TPE components, the material's smooth surface structure presents a key challenge. Bonding TPEs requires

"ULTRASONIC WELDING IS PARTICULARLY WELL-SUITED FOR JOINING PLASTICS SUCH AS TPEs."

specialised adhesives that are chemically compatible and provide sufficient elasticity. However, these adhesives tend to be more expensive and complex to handle compared with conventional ones. Additionally, TPE surfaces often require chemical pre-treatment to ensure proper adhesion, adding extra production steps and costs.

Hot welding of TPEs also demands precise temperature control and specialised equipment, as excessive heat can damage the material. Furthermore, the smooth surface makes it difficult to achieve stable joints, as the melting properties of TPEs are less predictable than those of PVC.

Ultrasonic welding is particularly well-suited for joining plastics such as TPEs. The precise application of energy enables a controlled and uniform fusion of the TPE components. In addition, this technology minimises material changes and ensures consistent quality of the products.

CHALLENGES WITH MATERIAL SELECTION

However, due to the unique properties of each material, not all plastics can be welded together with the same efficiency. When designing a component intended for ultrasonic welding, selecting the right material is the crucial first step towards a successful welding process.

All thermoplastic materials can be joined using ultrasonic technology. However, homogeneous (uniform) welding is only possible with identical thermoplastics.

The most commonly processed thermoplastics in ultrasonic welding include:

- Acrylonitrile butadiene styrene (ABS)
- Polystyrene (PS)
- Polypropylene (PP)
- Polyethylene (PE)
- Polyvinyl chloride (PVC)
- Polymethyl methacrylate (PMMA)
- Polycarbonate (PC).

Additives can also affect the weldability of thermoplastics – both positively and negatively. Additionally, various external factors influence how well plastics can be welded (Table 1).

IMPROVED SAFETY IN MANUFACTURING THANKS TO REAL-TIME QUALITY CONTROL

A major advantage of ultrasonic welding is the precise control it offers throughout the entire joining process. Intelligent software within the generator regulates the operation, storing optimised welding parameters that have been determined through extensive laboratory testing.

Once the welding modules are integrated into the production system, these predefined parameters can be consistently and reliably replicated in every individual weld. This ensures a stable process, delivering high-quality connections with every cycle.

The intelligent software controlling the welding process not only ensures hermetic seals but also enables manufacturers to implement digital quality control in their production. Because the component is in direct contact with the welding tool during the joining process, real-time data collection is possible. Up to 150 data points per weld are transmitted to the generator and stored, which can then be accessed from anywhere in the world. Analysing data from thousands of welds can help to identify valuable opportunities for further process optimisation, making production even more efficient.

Seamless process monitoring also enhances traceability. In the event of a product recall by the US FDA or similar regulatory body, defective products can be quickly and accurately identified (Figure 4).

GREAT POTENTIAL FOR AUTOMATED MANUFACTURING

Ultrasonic welding offers an ideal solution for high-volume manufacturing, thanks to its precise and automated process control. Unlike adhesive or heat-based welding systems, ultrasonic welding is ready for use immediately – without the need for tool heating or curing agents. This ensures consistent results from the very first weld.

Negative Influences	Positive Influences
Additives (such as fire protection): Additives protect plastics from degradation caused by external influences. However, this also means that additives make it harder to process the plastic using ultrasonics.	**Glass fibres**: Increase the stiffness, toughness and strength of the plastic, thus improving sound conductively, especially in semi-crystalline plastics.
Moisture (especially in polyamides): If the plastic has a high moisture level, it can evaporate during welding. This leads to gas bubbles in the joining area, resulting in porous weld joints.	**Glass beads**: Increase the pressure resistance of the plastic, thus improving sound conductivity, especially in semi-crystalline plastics.

Table 1: Positive and negative influences on plastic welding.

Figure 4: Seamless process monitoring makes the manufacture of medical wearables using ultrasonic technology process-safe and traceable.

A key advantage of this technology is its efficiency. Since no additional joining agents are required, time-consuming cleaning and regular maintenance are eliminated. This minimises system downtimes and maximises production output. Moreover, ultrasonic welding operates at extremely high speeds, creating strong connections in as little as 80–500 milliseconds, depending on the application.

Another significant benefit is its resilience to environmental influences. Adhesives, for example, often require recalibration when moved to a new production site, as temperature fluctuations during transport can alter their properties – sometimes leading to weeks of downtime.

Ultrasonic components, however, function reliably regardless of temperature changes or material batch variations. This eliminates the need for adjustments when relocating modules to different climates, allowing for seamless production transitions and immediate operational readiness.

SUPPORTING SUSTAINABLE PRODUCTION AND PRODUCTS

By switching to ultrasonic joining technology, manufacturers can enhance the sustainability of both their products and production processes. This is primarily possible because additional joining agents, such as adhesives, are no longer required. These chemical agents must first be produced, transported and heated – steps that consume large amounts of CO_2, particularly if they need to be distributed globally.

The use of adhesives also means that medical devices are no longer made from a single material, preventing them from being integrated into the circular economy.

These negative environmental impacts do not apply to ultrasonic welding. The technology only requires energy for joining plastics, which can be sourced locally from renewable sources.

Furthermore, the energy usage can be precisely controlled, enabling a reduction of about 60% in energy consumption compared with alternative joining processes. This significantly improves the carbon footprint of manufacturing.

CONCLUSION

Ultrasonic welding offers a promising solution to address the challenges faced in the production of medical wearable devices. By eliminating the need for chemical adhesives, which are often responsible for skin irritation, and by providing precise control over the joining process, this technology can ensure both skin compatibility and product reliability.

Additionally, the energy-efficient and sustainable nature of ultrasonic welding makes it an ideal choice for manufacturers aiming to meet the growing demand for medical wearables while enhancing patient comfort, safety and quality of life. With its ability to reduce the environmental impact and improve the overall functionality of wearables, ultrasonic welding paves the way for a more sustainable and user-friendly future in medical device manufacturing.

ABOUT THE COMPANY

As a specialist in ultrasonic welding of plastic components, Herrmann has been developing safe and efficient welding systems for over 60 years. With the services of Herrmann Engineering, more than 600 employees assist customers all over the world. Herrmann ensures a sustainable and economical welding process in the long term as a trusted adviser.

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INJECTING DRUGS DIRECTLY INTO THE BODY: HOW ON-BODY DELIVERY SYSTEMS ARE REVOLUTIONISING THERAPY

Zwick / Roell

Peter Schmidt of **ZwickRoell** discusses the advantages of on-body delivery systems and what makes them special, going on to consider the significant role that they are expected to play in the future of injection technology for the pharmaceutical and medical fields, as well as the role that comprehensive testing plays in bringing this technology to patients.

Medicine is becoming portable – while going to the clinic used to be routine for many patients with chronic illnesses, modern on-body delivery systems (OBDSs) can now enable painless and discreet self-administration of medications via a device worn directly on the body, in the patient's own home. This has long been a reality and has not only changed the quality of life of those affected, but also the processes in the healthcare system.

WHAT MAKES OBDS SO SPECIAL

OBDSs are portable injection systems that are attached to the skin and administer medication over a longer period of time in a controlled, precise and virtually unnoticed manner. These devices offer a real alternative to traditional administration methods, particularly for highly viscous biologics, which are difficult to administer using conventional autoinjectors.

Biologics – usually proteins – often must be delivered via an injection, as they would be broken down in the gastrointestinal (GI) tract. Biologically active molecules often have a large, complex and fragile structure, which makes them susceptible to degradation in the body. Their low permeability through biological barriers and complicated transport to the intracellular target make it difficult for them to maintain efficacy. However, an injection can significantly increase the bioavailability of these molecules, as it allows direct access to the bloodstream, bypassing degradation in the GI tract.

Treatment with OBDSs can be administered alone at home – without the need for a healthcare professional. This means that patients have to go to hospital less often, which places less of a burden on healthcare systems. OBDSs are easy to use, meaning that more people adhere to their treatment and digital aids, such as apps, make it easy to monitor treatment. Delivery via an OBDS can also save money because it reduces the necessary number of clinical appointments for infusion. As such, OBDSs enable a new form of patient autonomy, giving people back their time and freedom, while maintaining a consistently high level of therapeutic safety.

A GROWING MARKET WITH COMPLEX REQUIREMENTS

The market for OBDSs is growing rapidly. More and more companies are investing in the development of new generations of devices that are not only functional but also user-friendly and aesthetically pleasing. The variety of models – ranging from disposable to reusable devices, as well as offering different drug reservoirs and drive technologies – presents developers and test engineers with new challenges. A key issue is the reliability of drug delivery; with highly viscous substances in particular, it is crucial that the entire volume is injected correctly – right to the last drop. Simultaneously, these devices must be tested under realistic conditions, such as at body temperature. As a specific example, cytostatic drugs are used in cancer therapies, but they are hazardous to health if inhaled, therefore, to counteract this hazard, ZwickRoell has already installed devices for air extraction as part of its testing technology.

TESTING EXPERTISE FOR THE NEXT GENERATION OF INJECTION TECHNOLOGY

As one of the leading suppliers in the field of testing technology, ZwickRoell, together with a well-known manufacturer of injection systems, has developed an innovative testing system for OBDSs. This system now makes it possible to perform all relevant tests in a single pass – efficiently, modularly and adaptably to different injector types (Figure 1). A particular highlight is the option to combine several testing tasks, such as peeling off the adhesive film and injection testing (Figure 2), in one machine. This saves time and resources and increases the validity of the tests. ZwickRoell's testing systems are designed so that they can be flexibly adapted to new requirements, which is crucial, since the variety of OBDS models is constantly growing.

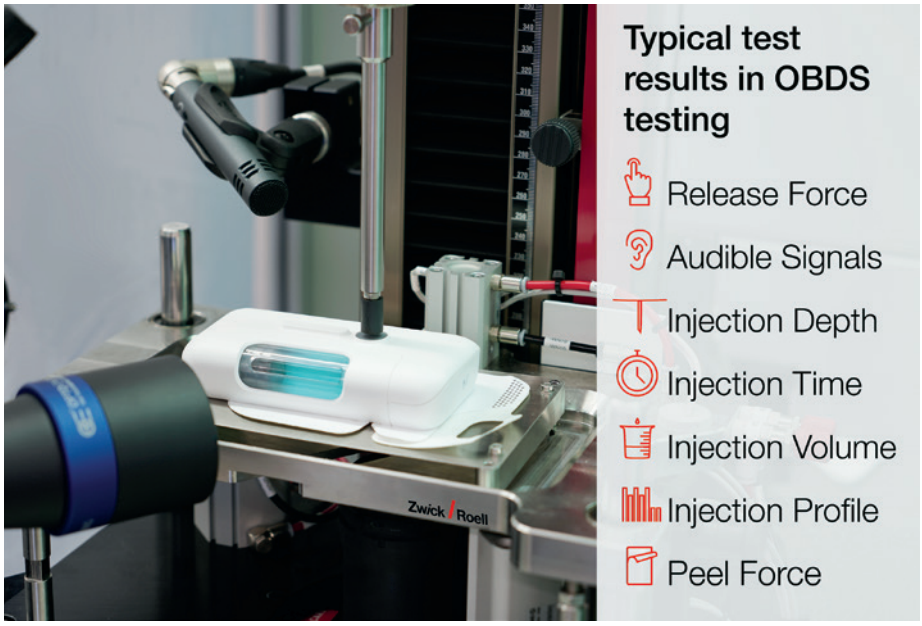

Figure 1: Typical test values that are preferably determined in a single test run.

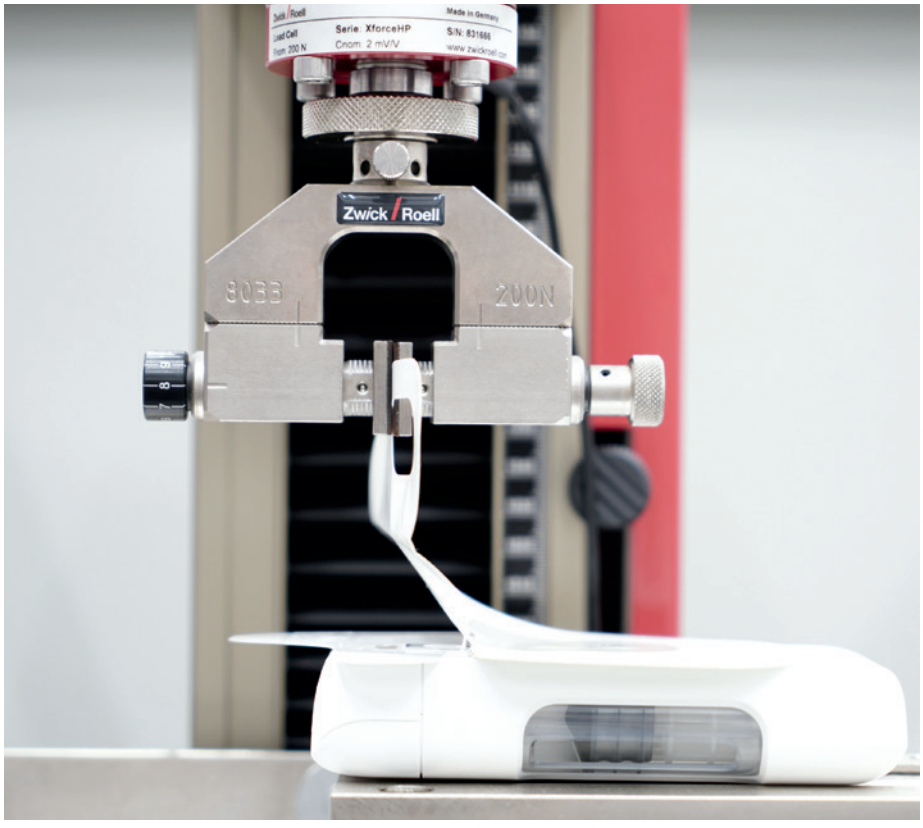

Figure 2: Peel forces for the film are determined in the peel test.

FROM THE INITIAL IDEA TO QUALIFICATION – EVERYTHING FROM A SINGLE SOURCE

ZwickRoell supports its customers throughout the entire project, from the initial user requirement specification (URS) to the final qualification. Standardised checklists, URS templates for all common injection systems, a standardised process and an experienced project team ensure that no detail is overlooked. The company's own qualification department offers both standardised and customer-specific solutions, including on-site measurement system analyses.

ZwickRoell's range of testing machines is supplemented by testXpert III testing software with integrated user administration. Complete traceability and tamper-proofing in accordance with US FDA 21 CFR Part 11 is made possible by an optional integrated software module. The integrity of data cannot be negotiable, as it is the only way to guarantee the security of results and their traceability, as well as provide protection against manipulation.

DIGITAL NETWORKING IS THE FUTURE

The future of OBDSs lies not only in the mechanics of the devices, but also in digital networking, versatility and patient comfort. The results of injections and raw data can be precisely documented using connectivity – more and more systems are equipped with sensors that document the injection process, communicate with apps or even transmit real-time data to medical professionals. This development opens up new possibilities for personalised therapies and close monitoring, especially for cancer and chronic diseases. ZwickRoell takes this development into account by also providing connectivity and data management solutions. This means that not only mechanical but also functional and software-based aspects of OBDS can be reliably tested.

REGULATORY REQUIREMENTS AND FUTURE PROSPECTS

As technology advances, so do the regulatory requirements for OBDSs. Authorities such as the FDA and EMA not only require proof of mechanical safety but also functional reliability and data integrity. Compliance with standards such as ISO 11608-5 and ISO 11608-6 is an essential part of this, especially when digital components are integrated. ZwickRoell supports manufacturers in implementing these requirements with validated test processes, documented testing software and comprehensive qualification services.

"THE FUTURE OF OBDSs LIES NOT ONLY IN THE MECHANICS OF THE DEVICES, BUT ALSO IN DIGITAL NETWORKING, VERSATILITY AND PATIENT COMFORT."

"NEW MATERIALS, MINIATURISED ELECTRONICS AND AI-SUPPORTED EVALUATION SYSTEMS ARE SET TO OPEN UP COMPLETELY NEW POSSIBILITIES."

Looking into the future, it seems inevitable that OBDSs will continue to gain in importance. New materials, miniaturised electronics and artificial intelligence (AI)-supported evaluation systems are set to open up completely new possibilities. For example, systems that automatically recognise the optimal injection time or adapt the administration of medication to individual vital parameters are conceivable.

The industry is only at the beginning of a development that will permanently change the healthcare sector. The combination of medical technology, digitalisation and patient focus will produce many new solutions in the coming years – and ZwickRoell is ready to help shape them.

OBDSs ARE MORE THAN JUST A TREND

OBDSs are exemplary for the change in medical technology away from centralised, clinic-based therapies towards patient-centric, digital and flexible solutions. They not only improve quality of life for patients but also the efficiency of healthcare systems. The integration of smart wearables into medication administration opens up new avenues for patient-centric care. The combination of digital monitoring, automated dosing and AI-supported analysis promises not only greater adherence to treatment but also more efficient use of medical resources. With innovative testing systems, standard-compliant implementation and comprehensive project support, ZwickRoell is making an important and decisive contribution to improving the quality and safety of this new technology – and thus to the future of drug delivery.

Peter Schmidt

Peter Schmidt, Product Manager Medical/Pharma at ZwickRoell, has several decades of experience in the pharmaceutical and medical technology industry. Mr Schmidt is a product specialist for testing solutions for injection devices and primary packing.

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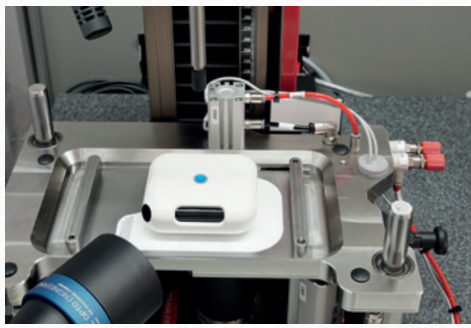
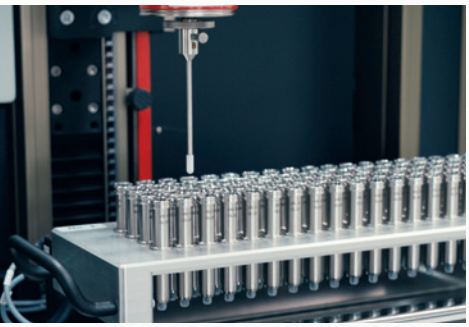
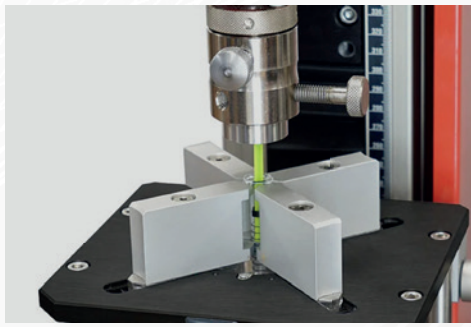

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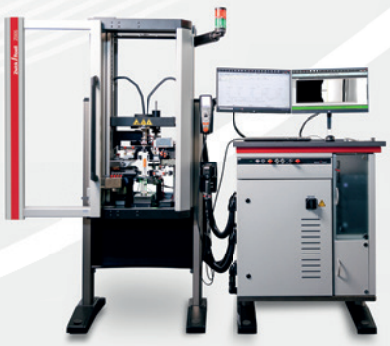

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DEVICE DESIGN TO ADDRESS USABILITY AND MITIGATE USE-RELATED RISKS – A MEDICAL AFFAIRS AND HUMAN FACTORS PERSPECTIVE

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Dr Sylvine Raverdy-Wilson at **BD Medical – Pharmaceutical Systems Medical Affairs**, deep dives into the device constituent of drug-device combination product design and shares perspectives through the Use-Related Risk Analysis methodology with a focus on the BD Libertas™ Wearable Injector.

As the global population ages and chronic diseases become more prevalent, healthcare systems are facing mounting pressure to reduce the burden of care delivery. The demand for patient-centric care models that extend beyond traditional clinical settings is also accelerating. To meet these shifting needs, medical device and pharmaceutical companies are developing drug delivery solutions and drug-device combination products designed for the safe and effective delivery of biologics to enable a transition from intravenous (IV) infusion to subcutaneous (SC) injection or direct development of SC solutions. For the patient, these products may be designed for treatment flexibility and accessibility, potentially enabling care in both clinical and alternative care settings. In all cases, the drug and its delivery system are required to meet stringent safety and efficacy standards, supporting effective outcomes for patients and providers alike.

Meeting these evolving needs requires pharmaceutical companies and their partners to explore new approaches on how therapies are administered (including the possibility of self-administration) while carefully considering the key factors that influence effective delivery of the drug, such as concentration, viscosity and dose volume. While self-administration of dose volumes up to 2.25 mL is commonly facilitated by prefilled, handheld autoinjectors, these injectors may be suboptimal for the SC delivery of larger-volume biologics with longer injection durations, especially in non-traditional care settings.[1] In such cases,

larger-volume wearable injectors are an opportunity for administration of single bolus doses greater than 2 mL.

Wearable injectors are medical devices or device constituents designed to administer large-volume SC drug formulations over durations ranging from minutes to hours. These device constituents, combined with drug formulation, enable the transition from IV to SC delivery. The diversity of device designs available or in development[2] is extensive and provides both healthcare providers and patients with a choice that can meet their individual needs.

The development of a drug-device combination product, including its formulation, is a complex, lengthy and costly process. Initially, the drug molecule undergoes rigorous laboratory testing as part of its preclinical drug discovery and development process. This is followed by multiple clinical studies to demonstrate safety and efficacy and to determine the appropriate dosing regimen, volume and frequency required to achieve therapeutic benefit.[3] Throughout this process, it is important to anticipate the possibility of using a delivery device and then ensure a seamless integration within a drug-device combination product. It is good practice to select a device constituent whose potential impact on patient safety has been minimised to the greatest extent possible. This approach aligns with regulatory expectations and the risk management standards applicable to combination products.

"WEARABLE INJECTORS ARE MEDICAL DEVICES OR DEVICE CONSTITUENTS DESIGNED TO ADMINISTER LARGE-VOLUME SC DRUG FORMULATIONS OVER DURATIONS RANGING FROM MINUTES TO HOURS."

RISK MANAGEMENT FOR DRUG AND DEVICE CONSTITUENTS

Ensuring the safe and effective use of device constituents within the drug-device combination product requires comprehensive risk management strategies throughout the combination product's life cycle. Figure 1 is a graphical representation of the risk management cycle for the device constituent (per ISO 14971:2019) and how it integrates with the drug risk management cycle (following ICH Q9 (R1)) to result in the overall drug-device combination product risk evaluation. As such, it is important to proactively control and mitigate risks prior to integration of the device constituent to avoid a negative impact on the overall drug-device combination production risk evaluation.

ISO 14971:2019 lists the three risk-control mechanisms available to manufacturers to reduce identified risks, with the following priority order:

1. Inherently by design
2. Through the medical device itself or its manufacturing (barrier or alarm) and, finally
3. Through important safety information provided to the patient in the Instructions For Use (IFU).

According to the ISO 14971:2019 standard for medical device risk management, high-level residual risks must be mitigated *"as far as possible without adversely affecting the benefit-risk ratio"* of the medical device. As a best practice, manufacturers of device constituents should evaluate how their devices will be used across the intended patient populations and indications to ensure seamless integration into the final combination product. Throughout the injector's use by the patient, caregiver or healthcare provider, there are multiple opportunities for hazardous situations to occur, impacting both the patient and the drug they receive. Evaluating the occurrence of these hazardous situations and the severity of the harm allows for the assessment of residual risk.

While user compliance with instructions and proper technique is essential across all injector designs for combination products, some technologies rely more heavily on these "user-directed controls". Manual steps – for example, drug transfer using a separate syringe, surface disinfection with antiseptic wipes or other manual assembly steps such as drug cartridge insertion – introduce opportunities for use error. The effectiveness of "user-directed risk

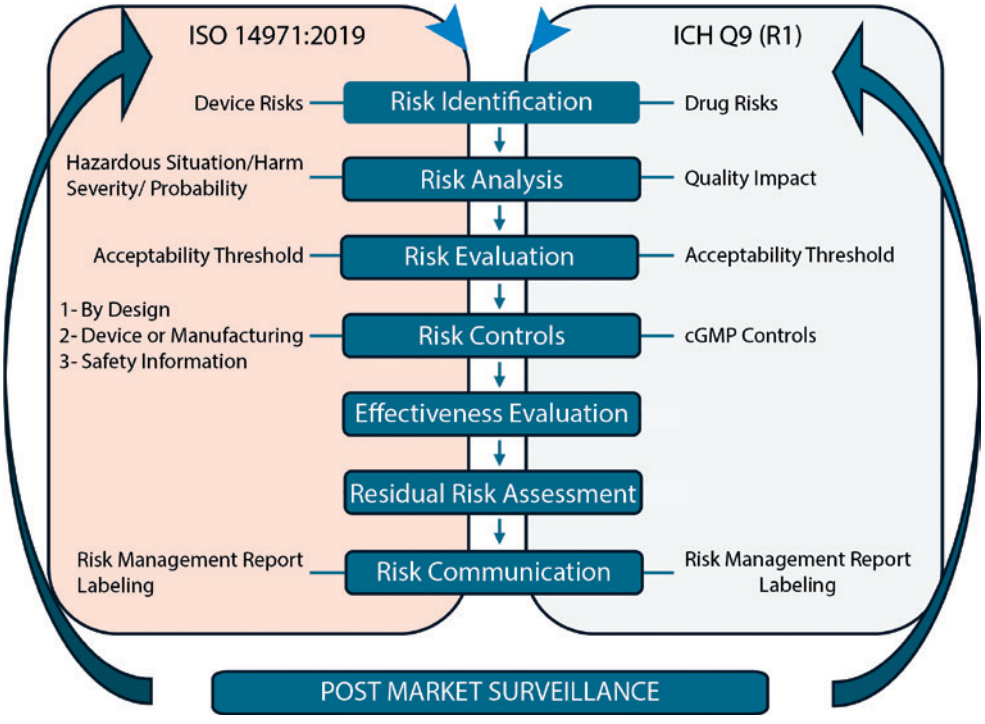

Figure 1: Risk management cycle for medical devices and drugs based on ISO 14971:2019 and ICH Q9 (R1).

controls" depends on multiple factors, including user compliance with labelling, clarity of the IFU, and consistency of technique at first treatment and subsequent treatments when treating chronic diseases. These challenges are further compounded in real-world settings, where distractions and interruptions may compromise user performance, particularly in chronic treatment scenarios.

USE-RELATED RISK ANALYSIS

The Use-Related Risk Analysis (URRA) draft guidance was formally issued by the US FDA in 2024,[4] but the tool was previously described in the 2016 FDA draft guidance "Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development".[5] It has also been mentioned in several guidances issued by the Center for Devices and Radiological Health, the Center for Drug Evaluation Research and the Center for Biologics Evaluation and Research.[6,7]

The URRA is a document that systematically analyses each use step of a medical device or drug-device combination product, along with the associated clinical risks. It is a suggested and recommended component of FDA submission packages, including INDs, NDAs and BLAs. It links potential use errors at each step to their clinical risk. Conducting this analysis early in development supports informed decisions on risk-mitigation strategies. The FDA recommends that the URRA includes detailed evaluation methods of the effectiveness of the risk controls during human factors validation testing. Figure 2 summarises the steps of a complete URRA.

APPLICATION OF URRA METHODOLOGY TO WEARABLE INJECTOR USE

There are generally three technology options (commercially available with drug or in development) for administering drug with a wearable injector device constituent. These technology options, represented in Prašnikar *et al*,[2] involve varying preparation steps for patients or caregivers immediately prior to treatment, depending on the technology. The technology options are:

- **Transfer Drug from Vial or Syringe to Wearable Injector:** Requires patient or caregiver to fill a syringe with drug from a vial and transfer the drug to the wearable injector prior to treatment.
- **Loading Drug-filled Container into Wearable Injector:** Requires patient or caregiver to clean and load a prefilled drug cartridge into the wearable injector prior to treatment.
- **Prefilled, Pre-assembled Wearable Injector:** Wearable injector does not require filling or assembly by patient or caregiver prior to treatment.

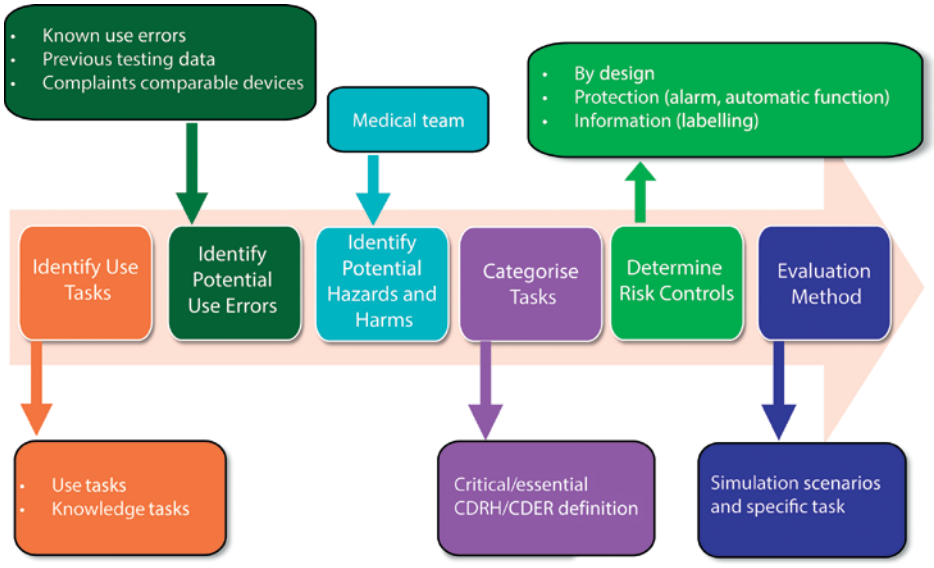

Figure 2: Graphical representation of a URRA per FDA guidance (draft, 2024)[4].

A simplified analysis was conducted by the author, based on the FDA URRA draft guidance (2024). This analysis focused on the applicability of the steps for use of the third technology. The analysis evaluated the potential effect of mitigating use-related risks through design based upon the range of potential usage steps required when using a wearable injector technology. The BD Libertas™ Wearable Injector is a prefilled, pre-assembled device component designed to deliver single-dose SC injections of large-volume (2–5 or 5–10 mL) and high-viscosity (up to 50 cP) fixed-dose biologics, and it is representative of the third technology.

This paper evaluated user interaction, handling complexity and potential clinical risks associated with wearable injector technologies, with a focus on the BD Libertas™ Wearable Injector. The steps followed in this illustrative analysis were:

- **Use Step Identification:** IFUs from three wearable injector technologies were reviewed to inform the range of potential usage steps required when using a wearable injector technology. Use steps were grouped by functional category (e.g. warming the package, preparing the injection site). While the order of steps may vary, the core actions are consistent across devices.
- **Use Error Identification:** One representative potential use error was selected per use step to simplify the comparison.
- **Clinical Risk Assessment:** Each potential use error was linked to the most direct and plausible clinical harm that could affect both general and immuno-compromised patient populations.

Severity ratings, criticality assessments and evaluation of risk control effectiveness were excluded from the analysis. Design and manufacturing-related risks were also excluded.

The analysis was not exhaustive in nature, but it was intended to represent the URRA principles and the value of URRA in the development of a drug-device combination product. The analysis only covered the use-related risk. Results of the analysis are not indicative of clinical performance or outcomes.

"THE BD LIBERTAS™ WEARABLE INJECTOR FEATURES A PREFILLED AND PRE-ASSEMBLED DESIGN THAT HELPS TO REDUCE HANDLING STEPS, THEREBY SIMPLIFYING THE PROCESS AND LOWERING THE POTENTIAL FOR USER ERROR, CONTAMINATION AND DOSAGE INACCURACIES."

Table 1 summarises the information and key findings related to user handling, preparation complexity and potential risk associated with a delivery system.

RESULTS FOR GENERAL PATIENT POPULATION

The analysis for applicability of the use-related risks associated with combination product use steps for general patient population highlights the varying levels of complexity, contamination risk and dosage accuracy depending on the technology used. This complexity may increase the likelihood of contamination and discrepancies in dosing. The BD Libertas™ Wearable Injector features a prefilled and pre-assembled design that helps to reduce handling steps, thereby simplifying the process and lowering the potential for user error, contamination and dosage inaccuracies.

Overall, by reducing the number of use steps and mitigating by design the potential risks of contamination and dosage issues, the BD Libertas™ Wearable Injector aims to offer a user-friendly design, providing a safe and consistent experience for general patient population.

Use Steps[8,9]		Potential Use Error	Clinical Risk
Warm the injector package		User does not wait the appropriate time	Painful injection
Gather all supplies and wash hands		User fails to wash hands properly	Contamination leading to infection
Inspect the drug/device		User does not detect degraded drugs	Compromised treatment
Injector preparation	Clean drug container (vial or cartridge)	Inadequate cleaning of stopper	Use-related contamination leading to infection **Not applicable to pre-assembled injector**
	Transfer drug into intermediate container (drug in vial)	Incorrect filling technique, air bubbles	Incorrect dosage, potential overdose or underdose **Not applicable to prefilled injector**
	Assemble cartridge and injector/Fill injector with drug	Spillage/breakage or contamination during transfer	Use-related contamination leading to infection **Not applicable to prefilled injector**
	Unlock the device	User does not know how to unlock the device	Delay in therapy
Select the injection area		Incorrect site selection	Ineffective delivery
Clean the injection area		Inadequate cleaning of injection area	Infection at injection site
Apply injector		User error in application	Pain, improper delivery, delay in treatment
Injection	Activate the injector	User does not understand how to start the injection	Delay in therapy
	Monitor injection progress	User does not understand how to track progress	Confusion or annoyance
	Confirm end of injection	User removed the injector too early	Lower dosage
Remove the injector from the skin		User pulls injector too hard from skin	Pain, annoyance
Dispose of the injector		User throws away the injector in regular trash	Third party exposure to used injector

Table 1: Potential use error and clinical harm associated with combination product steps and how they apply for the BD Libertas™ Wearable Injector.

RESULTS FOR IMMUNOCOMPROMISED PATIENT POPULATION

The immune system has two functions – to recognise foreign elements and to defend the body against infection. Several causes can lead to a compromised immune system, such as genetic mutation or a disease, resulting in a higher risk of infection for immunocompromised patients. When comparing the summary of risks for immunocompromised patients with that for general patients, it becomes evident that the heightened vulnerability of immunocompromised patients amplifies the potential consequences of user errors and contamination. The BD Libertas™ Wearable Injector, by mitigating the risk by design, seems to be a suitable drug-device combination product from the use-related risk standpoint for both patient populations.

CONCLUSION

Risk management standards, such as ISO 14971:2019, clearly state that mitigation of risk through design is the highest priority of the three available options (1 – design, 2 – alarm, 3 – IFU). The URRA required by the FDA for medical device and drug-device combination products is a tool that can be used during design development of a medical device or device constituent to identify risk-control measures that will have the most impact on the use-related risks identified.

This paper exercise highlights that reducing the number of use steps can lead to an overall reduction in use-related risks. This aligns with FDA's 2016 guidance on Applying Human Factors and Usability Engineering to Medical Devices,[10] which states: "*Design modifications to the device and its user interface are generally the most effective means for eliminating or reducing use-related hazards. If design modifications are not possible or practical, it might be possible to implement protective measures through labeling. These strategies are not the most preferred, though, because they rely on the user to remember or refer back to the information, labeling might be unavailable during use, and knowledge gained through training can decay over time.*"

The analysis highlights the importance of drug delivery systems that prioritise ease of use and risk reduction, especially for vulnerable populations, such as immunocompromised patients. One of the inherent benefits of the BD Libertas™ Wearable Injector is its prefilled and pre-assembled design, which simplifies dose preparation and eliminates the potential for breakage, use-led contamination, and dosing errors associated with end-user filling and/or assembly of the drug delivery system at the time of use.

The BD Libertas™ Wearable Injector is designed in accordance with fundamental principles of risk management outlined in ISO 14971:2019 by featuring a prefilled,

pre-assembled format. Its *Peel, Stick & Click*™ mechanism simplifies the injection process, minimising user error and infection risk by shifting preparation responsibilities to the pharmaceutical manufacturer. This not only enhances consistency and reliability in treatment but also reduces the burden on patients. By focusing on user-centric innovation, BD continues to advance drug delivery solutions that support both patient safety and pharmaceutical success.

BD Libertas™ Wearable Injector is a product in development; some statements are forward looking and are subject to a variety of risks and uncertainties. BD Libertas™ Wearable Injector is a device component intended for drug-device combination products and not subject to FDA 510(k) clearance or separate EU CE mark certification.

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REDEFINING PATIENT-CENTRIC DRUG DELIVERY: A CLOSER LOOK AT VERTIVA® ON-BODY DELIVERY SYSTEM

Anna Allegro of **Stevanato Group** explores current challenges in wearable injectors and how the next generation of on-body delivery systems, such as the company's Vertiva® platform, aims to close the gap between technical performance and true patient centricity.

Over the past decade, the drug delivery landscape has evolved rapidly to accommodate growing patient needs and therapeutic complexities. One significant advancement has been the emergence of on-body delivery systems (OBDSs), which have introduced greater flexibility and autonomy in managing chronic conditions outside clinical settings. These devices are gaining traction for their ability to simplify the administration of subcutaneous therapies, especially high-volume or high-viscosity drugs that would otherwise require frequent hospital visits or complex at-home procedures.

However, the promise of wearable injectors has been accompanied by equally important questions surrounding usability, safety and patient adherence. As more therapies transition towards the home environment, patients are increasingly expected to take on responsibilities

"AS MORE THERAPIES TRANSITION TOWARDS THE HOME ENVIRONMENT, PATIENTS ARE INCREASINGLY EXPECTED TO TAKE ON RESPONSIBILITIES TRADITIONALLY MANAGED BY HEALTHCARE PROFESSIONALS."

traditionally managed by healthcare professionals. This shift underscores the importance of intuitive, streamlined drug delivery solutions that minimise cognitive and physical burden. In this context, the user experience becomes not only a matter of comfort but a crucial factor in treatment adherence and overall outcomes.

MARKET LANDSCAPE: EVOLUTION OF OBDS DEVICES

Since 2016, six OBDSs have been introduced to the market:

- **Repatha® Pushtronex® System** (Amgen, CA, US, 2016): A 3.5 mL device delivering evolocumab for lowering LDL cholesterol.[1]
- **Ultomiris® OBDS** (Alexion Pharmaceuticals, MA, US, 2022): A 3.5 mL device for ravulizumab, used to treat paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome.[2]
- **Skyrizi® On-Body Injector** (AbbVie, IL, US, 2022): A 3.5 mL device delivering 2.4 mL of risankizumab for plaque psoriasis, psoriatic arthritis and Crohn's disease.[3]
- **Furoscix® On-Body Infusor** (scPharmaceuticals, MA, US, 2022): A 10 mL device administering furosemide for heart failure.[4]
- **Empaveli® On-Body Injector** (Apellis Pharmaceuticals, MA, US, 2023): A 20 mL device delivering pegcetacoplan for PNH.[5]
- **Lasix® ONYU Infusor** (SQ Innovation, MA, US, 2024): A 3 mL device that received the US FDA's Tentative Approval for home treatment of fluid overload in congestive heart failure with 2.67 mL of furosemide. Final approval is still pending and market exclusivity for a competing product expires in October 2025.[6]

All these marketed OBDSs require either manual filling or loading of a drug-filled cartridge – a feature that increases complexity and introduces potential use errors during the critical moment of injection preparation. In fact, it is reasonable to expect that patients may feel the most stressed or nervous before treatment, which can make even simple steps difficult to perform accurately, thereby increasing the likelihood of errors. These challenges may

Figure 2: A patient completing the attribute assignation task during Stevanato Group's patient preference study.

Figure 1: - Stevanato Group's Vertiva 10 mL OBDS, featuring reusable electronics.

have contributed to the discontinuation of some of these marketed user-loaded devices, with pharmaceutical providers acknowledging the importance of prioritising optimal patient experience.[7,8] This calls for more patient-centric solutions that streamline the treatment process, minimise use steps, and enhance both safety and usability. Technologies such as Stevanato Group's Vertiva® OBDS can play a role in addressing these gaps.

STEVANATO GROUP'S READY-TO-USE OBDS: VERTIVA®

Stevanato Group's Vertiva® OBDS is a versatile device supporting programmable flow rates and injection times, making it suitable for basal infusions and bolus injections across diverse therapies, up to 10 mL in volume. Vertiva® features a single-use injection unit with a prefilled, preloaded drug cartridge and a reusable, multi-use smart controller connected via a proprietary magnetically-coupled drive mechanism (Figure 1). Its ready-to-use design significantly reduces complexity for users, allowing patients to begin treatment with greater ease and confidence while minimising potential use errors.

This advantage of Vertiva® has been observed in a patient preference study conducted by Stevanato Group in the UK in July 2024 (Figure 2). The study compared Vertiva® with a user-loaded OBDS available on the market, highlighting critical attributes that influence patient preferences for comparable delivery devices. Twelve participants, representing diverse demographics, medical conditions and varying levels of familiarity with injection devices, were involved. The study began with patients exploring the design and functionalities of the two OBDSs, watching an instructional video and reading summarised instructions for use. Patients were then asked to rank a list of pre-determined product attributes by importance, followed by assigning each attribute to the device they believed best fulfilled the criterion.

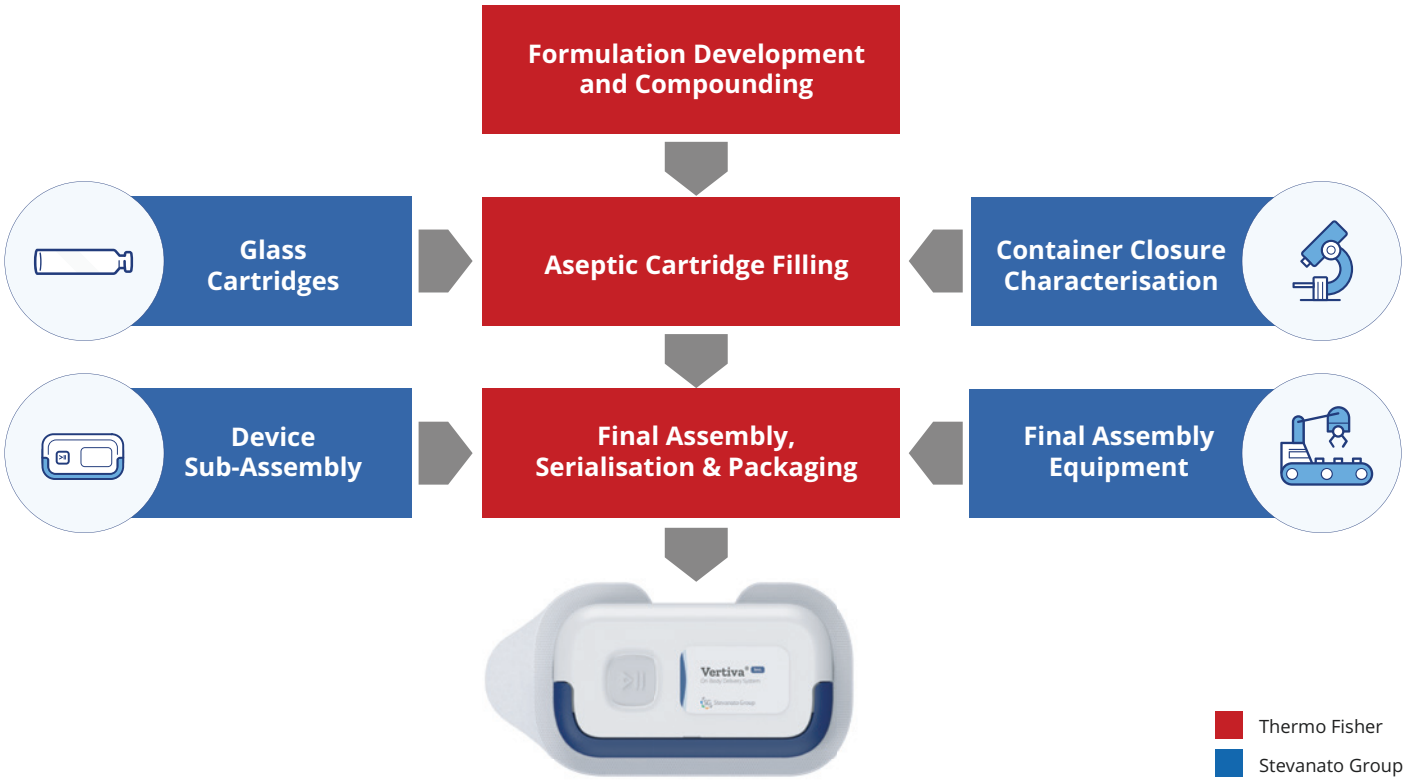

Figure 3: Stevanato Group and Thermo Fisher's integrated Vertiva® offering.

The study results highlighted that ease of administering treatment and the total number of use steps were the most critical attributes for patients. Notably, 10 out of the 12 patients considered it easier to administer treatment with Vertiva®, citing its preloaded and prefilled design, which reduces complexity and eliminates risks associated with manual cartridge loading, particularly during moments when patient stress and nervousness are at their peak.

Sustainability is another key focus of the Vertiva® system. By incorporating reusable electronics, it minimises environmental impact and offers cost-effective solutions for long-term treatments. This approach addresses growing environmental concerns while aligning with healthcare providers' goals to adopt eco-friendly practices without compromising usability. In fact, while reusability adds some extra steps, such as the need for patients to store and possibly recharge the electronic unit, these occur after the injection, when patients are more at ease with their treatment.

Another advantage for pharmaceutical manufacturers stems from Stevanato Group's comprehensive end-to-end offering, which provides a variety of optional products and services to optimise Vertiva®'s supply chain. In addition to device development and manufacturing, Stevanato Group can provide proprietary primary packaging solutions, including ready-to-use EZ-fill® cartridges optimised for integration with Vertiva®. Additionally, Stevanato Group's Technology Excellence Centers offer a suite of testing services, including drug-container-device interaction assessments. To further streamline operations, Stevanato Group also provides automated final assembly and packaging equipment. These capabilities are complemented by a strategic collaboration with a leading contract manufacturing organisation, Thermo Fisher Scientific (Waltham, MA, US).

"STEVANATO GROUP CAN PROVIDE PROPRIETARY PRIMARY PACKAGING SOLUTIONS, INCLUDING BULK AND READY-TO-USE EZ-FILL® CARTRIDGES OPTIMISED FOR INTEGRATION WITH VERTIVA®."

THERMO FISHER AND STEVANATO GROUP PARTNERSHIP

In March 2023, Stevanato Group and Thermo Fisher announced a collaboration to offer an integrated, end-to-end solution to help streamline the supply chain management of the Vertiva® OBDS. Along with the proprietary device platform and the integrated services provided by Stevanato Group, Thermo Fisher will provide fill-finish and final assembly services (Figure 3). This has been supported with investment in a low-volume final assembly line at Thermo Fisher's site in Ferentino (Italy) for final assembly of Vertiva® devices, with minimal changes required to the manufacturing equipment components when switching between the different device configurations.

The collaboration between Thermo Fisher and Stevanato Group is designed to address critical challenges in drug delivery system supply. By focusing on mitigating risks related to drug container compatibility and fill-finish techniques, the partnership ensures seamless integration with existing pharmaceutical workflows.

"THE COLLABORATION BETWEEN THERMO FISHER AND STEVANATO GROUP IS DESIGNED TO ADDRESS CRITICAL CHALLENGES IN DRUG DELIVERY SYSTEM SUPPLY."

Additionally, the partnership will simplify supply chain management, reduce operational complexity and allow pharmaceutical manufacturers to focus on innovation. Upfront preparation, work capabilities and scalable production solutions minimise customer investment, making the process more accessible and efficient. Ultimately, these advantages accelerate time-to-market, enabling companies to deliver therapies to patients more quickly, meeting urgent healthcare needs.

CONCLUSION

The future of drug delivery lies in advancing patient-centric, technology-driven solutions that align with modern therapeutic demands. OBDS platforms such as Vertiva® exemplify this progress, addressing critical challenges, such as larger-volume, high-viscosity and complex drug delivery while ensuring patient convenience and adherence. In this context, collaborative efforts between industry leaders, such as Stevanato Group and Thermo Fisher, will be vital in fostering innovation, optimising manufacturing processes and ensuring efficient supply chains for these transformative technologies.

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ON-BODY INJECTORS: A PROMISING SOLUTION TO THE UK'S SYSTEMIC ANTI-CANCER THERAPY CRISIS

Omar Rahman, PharmD, of **Enable Injections**, **Catherine Loughran** of **University Hospitals of Leicester NHS Trust** and **Rachel Senior** of **Leeds Teaching Hospitals NHS Trust**, consider how on-body injectors, such as Enable's enFuse, can help to reduce the administrative burden on the healthcare system as well as giving patients more autonomy and dignity in managing their disease.

The UK's systemic anti-cancer therapy (SACT) infrastructure is under immense pressure. This crisis, well documented in national press and peer-reviewed literature, centres on a collision of increasing patient volume, complexity of treatments and use of maintenance therapies over fixed-duration regimens, resulting in demand exceeding capacity. Despite ongoing innovations in oncology drug development, the ability of the health system to deliver these therapies safely and efficiently is under significant strain. Patients are experiencing increasing delays, and these interruptions are not merely operational hurdles, they represent missed therapeutic windows, deteriorating prognosis and rising patient anxiety.[1]

Historically, drug preparation for monoclonal antibodies resided within the aseptic environments of pharmacies. However, many UK NHS cancer centres have shifted this responsibility onto nursing staff to increase preparation capacity for cytotoxic treatments in pharmacies. Nurses now find themselves responsible for preparing and administering complex large-volume subcutaneous (LVSC) therapies – often in suboptimal conditions. The result is a rise in occupational hazards.

"NURSES NOW FIND THEMSELVES RESPONSIBLE FOR PREPARING AND ADMINISTERING COMPLEX LVSC THERAPIES – OFTEN IN SUBOPTIMAL CONDITIONS."

Data from the British Journal of Nursing show that transitioning drug handling tasks to the ward increases risks such as accidental exposure to hazardous medications and needlestick injuries.[2] While well-intentioned as a solution to capacity challenges, this approach has added pressure to an already overburdened workforce. Home administration of SACT is increasingly available in the UK, both within the NHS and via private providers. Initially expanded in response to the covid-19 pandemic, it has since become a standard strategy to ease pressure on hospital services, enhance the patient experience and reduce unnecessary hospital visits.

Nurses face physical strain from manual administration of viscous, large-volume therapies via traditional syringes. Delivering LVSC injections often involves prolonged application of force while maintaining awkward postures – factors closely associated with repetitive strain injuries. These injuries, while sometimes dismissed as minor, are among the leading causes of absenteeism and attrition in the nursing profession. In busy oncology units, even minor delays in care caused by injury-related absences can ripple through patient scheduling, creating further backlogs. The prevalence of injection-related musculoskeletal disorders underscores a pressing need for ergonomic innovation in drug delivery workflows.[3]

Healthcare professionals (HCP) face other difficult trade-offs, too. Traditionally, many biologic therapies are warmed to near-ambient temperatures before administration, which helps to reduce injection pain, improve flow characteristics and enhance patient tolerability. However, mounting workloads and the pressure to maintain high throughput have led some HCPs to bypass warming procedures altogether on occasions. While this speeds up patient throughput, it compromises both comfort and compliance, increasing the risk of negative patient experiences and potentially undermining adherence.

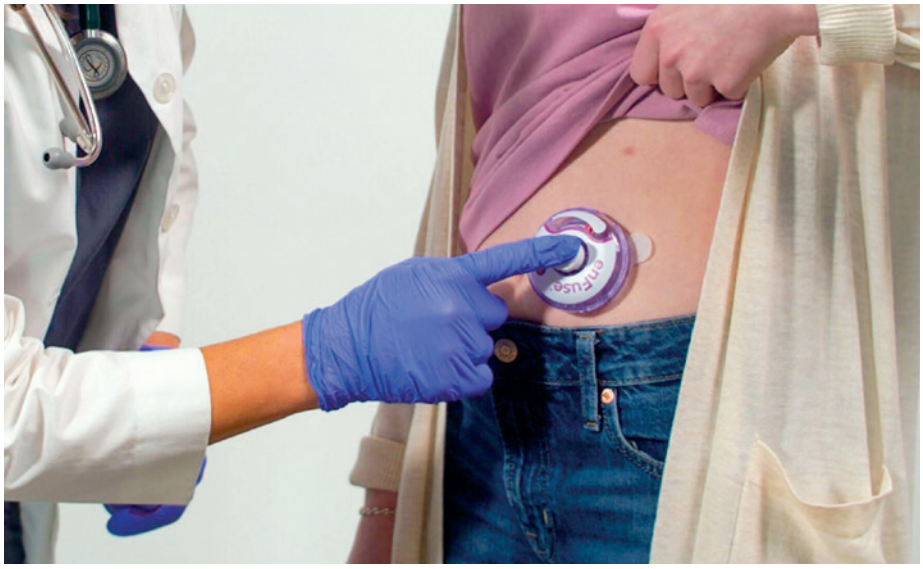

Figure 1: Starting administration with the push of a button, the enFuse OBI is designed to minimise complexity, reduce discomfort and decentralise care, addressing key barriers across patients, nurses and pharmacists.

Meanwhile, patients face persistent challenges in their experiences of treatment. Among the most underappreciated yet influential of these is needle anxiety. The visibility, size and invasiveness of standard syringe-needle technology contribute to pain, fear and psychological discomfort, especially in oncology, where long-term treatment regimens can involve dozens of injections. According to Alsbrooks *et al*, visible needles are a key driver of treatment-related anxiety, with needle phobia cited as a leading barrier to adherence in patients receiving injectable biologics. This challenge goes beyond psychological discomfort, however. Studies have shown that anxiety related to injections is associated with increased pain perception and lower patient satisfaction, even when the effectiveness of the treatment is unchanged.[4]

In this environment, Enable Injections' enFuse® on-body injector (OBI) offers a unique opportunity to alleviate pressure across the oncology care continuum. The enFuse device is a wearable, hands-free OBI that delivers large drug volumes subcutaneously at a controlled, patient-responsive rate. It is designed to minimise complexity, reduce discomfort and decentralise care, addressing key barriers across patients, nurses and pharmacists amid the ongoing SACT crisis (Figure 1).

For nurses, the enFuse OBI meaningfully reduces the procedural burden of administration. Unlike traditional manual injection methods (e.g. syringe and needle), enFuse does not require consistent manual effort or force to deliver the drug and

"FOR NURSES, THE ENFUSE OBI MEANINGFULLY REDUCES THE PROCEDURAL BURDEN OF ADMINISTRATION. UNLIKE TRADITIONAL MANUAL INJECTION METHODS (E.G. SYRINGE AND NEEDLE), ENFUSE DOES NOT REQUIRE CONSISTENT MANUAL EFFORT OR FORCE TO DELIVER THE DRUG AND INVOLVES SIGNIFICANTLY FEWER STEPS."

involves significantly fewer steps. This ergonomic simplicity limits the strain associated with repeated administration of viscous drugs and may help to reduce the incidence of injection-related repetitive strain injuries. Importantly, clinical data support this. In the IZALCO crossover study, the majority (78.9%) of HCPs preferred using the OBI for subcutaneous (SC) delivery of isatuximab. Notably, none preferred manual injection and 21.1% had no preference for either modality (OBI or manual syringe). All respondents agreed that the device was easy to use and reliable – important aspects in environments where clinical efficiency and safety are paramount.[5] In addition to clinical data, two separate surveys showed a strong nurse preference for the enFuse OBI over traditional syringe and needle methods for LVSC administration, with preference rates of 97.8% and 90%.[6,7]

While the enFuse system is not labelled for reducing drug warming time, its integrated design offers meaningful risk mitigation in scenarios where warming is not being performed out of necessity due to ongoing systemic pressures. The system's automatic filling and inherent ability to warm fluid during preparation and administration supports efficient workflows without compromising protocol adherence. A recent study of the enFuse system's rapid warming capabilities highlighted that near-ambient temperature delivery can reduce patient discomfort, improve flow rates and shorten injection times. In practice, the enFuse system offers a pragmatic balance of efficiency, patient experience and regulatory alignment in high-pressure care environments.[8]

For patients, the benefits are particularly noteworthy. The enFuse injector uses a small, 30-gauge needle, significantly thinner than the 23- to 25-gauge needles typically used for other LVSC drugs, and it remains out of sight throughout the injection process, helping to reduce anxiety and discomfort. The device automatically adjusts delivery speed based on tissue backpressure, promoting a smoother and more comfortable injection experience. These features are not merely cosmetic, as they translate to measurable improvements in tolerability and satisfaction.

In the IZALCO trial patients received both manual and OBI delivery of isatuximab subcutaneously and were asked to express a preference after cycle six. A remarkable 74.5% of patients preferred the OBI over manual injection, while 17% preferred manual injection and 8.5% had no preference.[5] These findings resonate beyond oncology. In the Wasserman *et al*, randomised crossover study in patients with primary immunodeficiency, all surveyed participants preferred a wearable OBI over an SC pump for immunoglobulin therapy, citing ease of use, greater mobility during infusion, less time for device set-up and less pain at the injection site.[9] These results highlight the universal appeal of patient-centric delivery technologies such as enFuse.

The enFuse OBI also exhibits a strong safety performance. In the IRAKLIA study, the incidence of injection site reactions

(ISRs) was significantly lower – nearly 17-fold – compared with intravenous (IV) administration.[5] This has been attributed to both the smaller gauge of the needle and the adaptive pressure-based delivery system. As an example, the incidence of infusion-related reactions with daratumumab delivered subcutaneously or intravenously was 13% and 35% respectively, representing a threefold difference between the two routes of administration.[10] This striking contrast suggests that the mode of delivery, given the similar mechanism of action, may meaningfully contribute to the improved tolerability profile observed with enFuse.

In the IZALCO trial, ISR rates were similarly low between manual injection and enFuse – under 1% in both groups – and all reactions were mild and self-limiting.[5] These outcomes suggest that wearable OBI technology offers safety benefits without compromising reliability or dosing fidelity.

Another compelling advantage of the enFuse OBI is its potential to support treatment outside traditional hospital settings. The device is fully wearable and intuitive, allowing patients to receive treatment in or out of hospital treatment locations with minimal supervision. This decentralisation of care holds significant promise for relieving bottlenecks in infusion clinics and SACT centres. By transitioning appropriate patients to at-home treatment supported by remote monitoring, healthcare systems can free up in-clinic resources while maintaining therapeutic standards. This strategy aligns with broader NHS initiatives to decentralise chronic care management and represents a scalable solution to SACT congestion.

Importantly, this shift does not just help hospitals, it also empowers patients. For many, treatment is not only physically taxing but logistically disruptive, involving travel, time off work or dependence on caregivers. OBI technology such as enFuse gives patients more autonomy and dignity in how they manage their disease. In diseases where long-term treatment is required, such as haematological malignancies or autoimmune disorders, the value of home administration cannot be overstated (Figure 2).

Figure 2: The enFuse OBI allows patients to receive treatment in or out of a hospital setting, using a small 30-gauge needle that remains out of sight throughout the injection process.

The enFuse OBI, therefore, addresses pain points across the entire delivery chain. It improves patient experience, reduces physical strain on nurses and supports pharmacists in maintaining best practices without sacrificing workflow. It also enables flexible site-of-care options, helping the system adapt to changing patient volumes and evolving expectations.

The SACT crisis in the UK has made clear that current infrastructure alone cannot scale fast enough to meet rising demand. What is needed is innovation, particularly innovation that supports the workforce, protects quality and empowers patients. Enable Injections' enFuse OBI offers a compelling example of how targeted drug delivery technology can serve not just as a convenience, but as a systemic remedy. Its ability to integrate into clinical workflows, improve tolerability and shift care outside the hospital makes it more than a novel device – it becomes a practical component of care transformation.

While no single technology can resolve the entire SACT crisis, OBI systems such as enFuse are poised to play an essential role in building a more resilient, patient-centred model of oncology care. The future of SACT lies not only in the drugs we discover but in how we deliver them.

The enFuse on-body injector (OBI) and syringe transfer (ST) system were recently registered in the UK with the United Kingdom's Medicines and Healthcare products Regulatory Agency (UK MHRA) and received European Union Medical Device Regulation (EU MDR) CE Mark approval for in-clinic use earlier this year. The enFuse OBI and ST have also received combination product US FDA approval with a specific drug for at-home self-administration, as well as approval for the enFuse System (syringe and vial transfer) from the Brazilian Health Regulatory Agency (Agencia Nacional de Vigilancia Sanitaria or ANVISA) for a range of drug viscosities and in-clinic or at-home use.

"BY TRANSITIONING APPROPRIATE PATIENTS TO AT-HOME TREATMENT SUPPORTED BY REMOTE MONITORING, HEALTHCARE SYSTEMS CAN FREE UP IN-CLINIC RESOURCES WHILE MAINTAINING THERAPEUTIC STANDARDS."

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SYMBIOZE® – THE ELECTROMECHANICAL ON-BODY DRUG DELIVERY SYSTEM FOR LARGE-VOLUME IMMUNOTHERAPIES

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we put patients first

Corinne Malica and **Cécile Gross** of **Nemera** discuss the challenges involved in developing a wearable device for on-body drug delivery of advanced biologics, with a focus on the immunotherapy sector, and the technical solutions that can overcome them, using Nemera's Symbioze® as an example.

The increasing use of biologic therapies such as large-molecule drugs, especially monoclonal antibodies and other immunotherapies for cancer and autoimmune diseases, has led to new advanced drug delivery systems entering development. Historically, many of these biologics require intravenous (IV) infusions in clinics due to their high doses and volume requirements, placing a significant burden on patients and healthcare systems. Subcutaneous (SC) administration offers a patient-friendly alternative – reducing infusion times from hours to minutes and enabling treatment outside of hospitals. However, delivering the large volumes (>2 mL) and high viscosities necessary via the SC route has proven challenging with conventional drug delivery systems.

In response, on-body delivery systems (OBDSs) have emerged as a promising solution to enable the safe SC delivery of high-dose or higher-concentration biologics. These motorised wearable drug delivery systems are attached to the patient's body and autonomously administer the medication at a controlled rate over an extended period, thereby facilitating at-home administration of complex cancer immunotherapies and other biologics that would otherwise require clinic-based infusions.

ENABLING SC DELIVERY OF LARGE-VOLUME BIOLOGICS

Conventional autoinjectors administer up to 2 mL of drug substance and rely on spring forces to deliver the drug in a rapid

timeframe (10–15 seconds) – a method that can become impractical and painful for patients as volume or viscosity increases. OBDSs address these challenges by enabling the delivery of volumes of 20–30 mL over extended periods (from several minutes up to an hour) at controlled flow rates that can potentially mitigate pain and tissue stress. In the future, the industry may see more IV oncology drugs reformulated for SC delivery – using OBDSs if the required volumes are very large – to offer patients the flexibility of receiving treatment in the comfort of their home or local clinic.

SYMBIOZE® – THE STATE-OF-THE-ART ON-BODY DELIVERY SYSTEM PLATFORM

Nemera's Symbioze® is an OBDS platform designed to accommodate the demanding requirements of biologic drug delivery. It incorporates several key trends in its design – a reusable/disposable hybrid architecture for sustainability, large-volume capacity and connectivity. The reusable subassembly contains the motor, battery and electronics, and can be recharged and used across multiple injections, with the user inserting a new disposable module each time. This design prioritises sustainability, reducing the electronic waste generated per dose by having a lifelong core module with a two-year shelf life. The disposable unit includes a preloaded standard glass pharmaceutical cartridge, meaning that the patient does not manually handle the cartridge.

During injection, Symbioze® features a soft cannula, which is automatically inserted using a hidden needle, and is supplemented by connectivity via Bluetooth and near-field communication (NFC), enabling injection tracking and even drug identification by verifying the correct drug cartridge via an NFC tag. The user interface features a simple one-button activation approach and offers audio-visual feedback, along with an optional smartphone app for guidance. The combination of a modular reusable design with high-volume capability, typically from 20 to 30 mL, and digital integration positions Symbioze® as a flexible platform for a range of biologics and chronic conditions.

> "IN THE FUTURE, THE INDUSTRY MAY SEE MORE IV ONCOLOGY DRUGS REFORMULATED FOR SC DELIVERY – USING OBDSs IF THE REQUIRED VOLUMES ARE VERY LARGE – TO OFFER PATIENTS THE FLEXIBILITY OF RECEIVING TREATMENT IN THE COMFORT OF THEIR HOME OR LOCAL CLINIC."

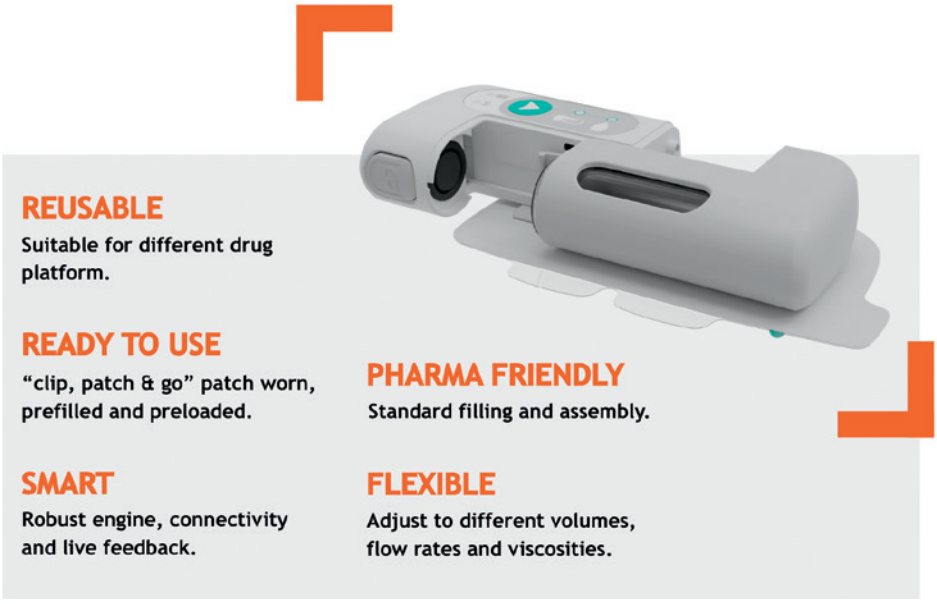

Figure 1: Symbioze® OBDS platform key features and benefits.

DESIGN CHALLENGES AND TECHNICAL SOLUTIONS

Injectability of High-Viscosity Drugs

Large biologic formulations often have high viscosities, making them difficult to push through a conventional thin needle. The Symbioze® OBDS tackles this with a powerful miniaturised motor that can sustain controlled flow rates for highly viscous solutions (50 cP or above). It also facilitates programmable delivery profiles to accommodate drug characteristics and minimise injection force (Figure 1).

Patient Comfort and Tolerability

Drug delivery devices must be designed to avoid pain and fear as much as possible. OBDSs address this through slower flow rates, thereby reducing the acute tissue distension that causes pain, and ergonomic cannula designs. To this end, Symbioze® was designed with the following features:

- Injection via a soft cannula to improve comfort during long injections
- The rigid needle for inserting the cannula is retracted at the start of injection, meaning that the patient never sees the needle and any risk of needlestick injury is avoided
- An adhesive patch that secures the device to the skin without any side effects
- Audible and visual feedback to reassure the user that the dose is being delivered correctly
- Large, tactile button and intuitive indicators that make the injection experience as seamless as possible for patients of all ages, including those with limited dexterity
- A combination of controlled flow, user-friendly and intuitive interface that maximises comfort and confidence during long SC injections.

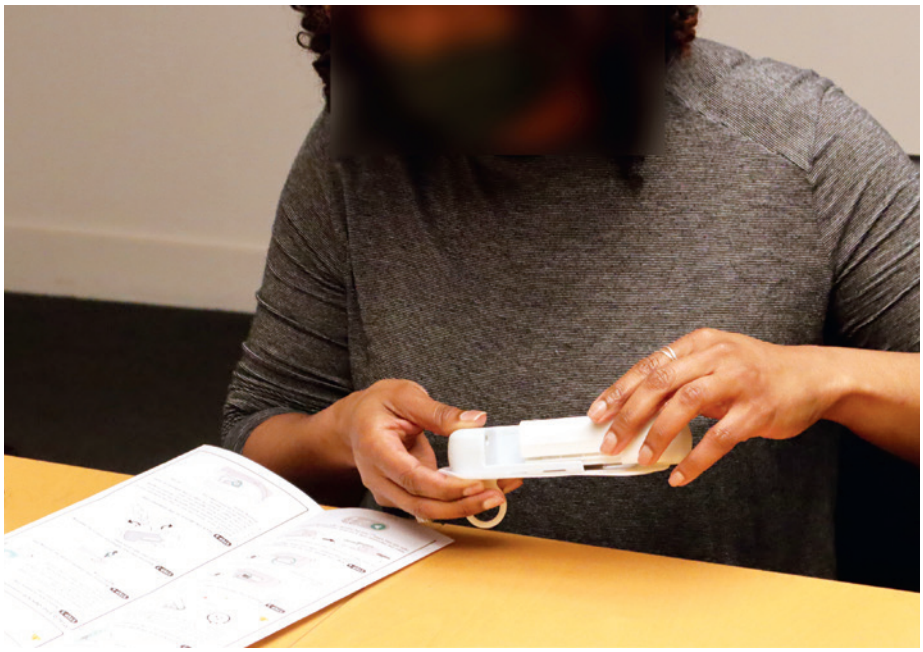

Figure 2: Clear instructions for use are crucial for therapy success.

Figure 3: Human factors studies by Insight by Nemera.

"THE DEVICE IS ACTIVATED BY ONE BUTTON AND IS READY TO USE AS SOON AS THE DISPOSABLE UNIT IS ASSEMBLED, PREVENTING USER ASSEMBLY ERRORS AND MAKING TRAINING EASIER."

Usability and Human Factors

Effective solutions include minimising user steps and providing clear instructions (Figure 2). For Symbioze®, extensive human factors studies were conducted to streamline the injection steps and optimise its intuitiveness (Figure 3). The device is activated by one button and is ready to use as soon as the disposable unit is assembled, preventing user assembly errors and making training easier. Furthermore, the Symbioze® platform incorporates multiple feedback mechanisms, including lights, an injection progress meter and audio cues at the start and completion of the injection.

Symbioze® is designed to ensure a safe connection between its disposable and reusable parts, guaranteeing that sterility is maintained throughout the injection (Figure 4). In addition, the device will not inject drug unless it is well positioned on the body, as well as assembled with the expected drug. These features guide users through the process and significantly lower the risk of misuse, which is crucial given that patients may be self-administering. Robust risk mitigation, including an automatic signal if an error is detected, is built-in to avoid any device malfunctions.

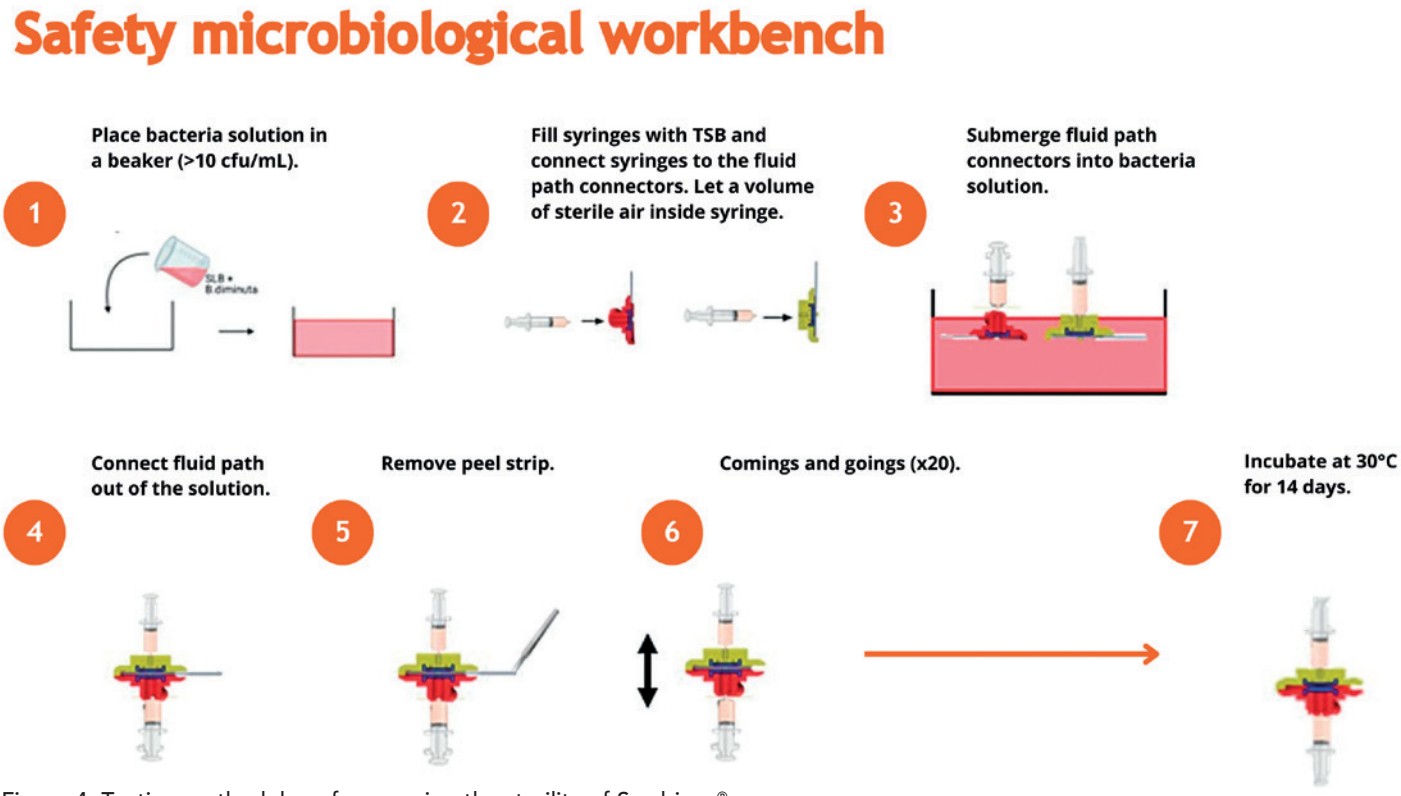

Figure 4: Testing methodology for ensuring the sterility of Symbioze®.

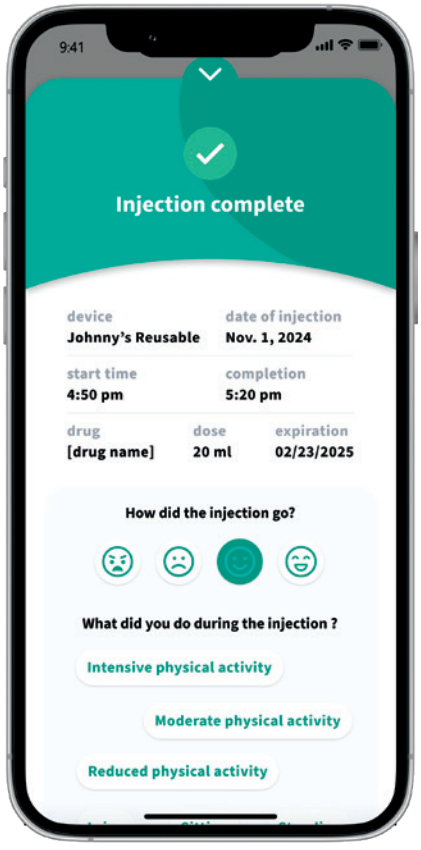

Figure 5: Symbioze® offers the possibility for connected accessory support.

Connectivity and Digital Health Integration

The Symbioze® platform increasingly offers connectivity features to support adherence and integrate with digital health ecosystems (Figure 5). This platform was conceived with connectivity in mind – it has built-in Bluetooth and can pair with a dedicated app or cloud system to manage injection schedules and monitor the device. The benefits of connectivity include reminders, training prompts and real-time feedback for patients, as well as enabling clinicians to remotely monitor dosing compliance.

OVERCOMING THE CHALLENGES

Taken together, the technical solutions discussed here enable Symbioze® to overcome the major hurdles of large-volume SC delivery. Through careful engineering, this OBDS ensures that even high-dose immunotherapies can be administered safely, comfortably and conveniently – meeting both the pharmaceutical requirements of biologic drugs and the practical needs of patients in the real-world use.

"SYMBIOZE® INTEGRATES SEVERAL CUTTING-EDGE FEATURES INTO ONE PLATFORM – LARGE-VOLUME CAPACITY, REUSABLE CORE FOR SUSTAINABILITY, SOFT CANNULA FOR COMFORT, PREFILLED DISPOSABLE UNIT FOR EASE OF USE AND FULL CONNECTIVITY FOR SMART THERAPY MANAGEMENT."

In summary, Symbioze® integrates several cutting-edge features into one platform – large-volume capacity, reusable core for sustainability, soft cannula for

comfort, prefilled disposable unit for ease of use and full connectivity for smart therapy management. Additionally, the modular, reusable design of Symbioze® reduces waste and enables the platform to be adapted across therapies. For pharmaceutical companies, Nemera's Symbioze® platform can be customised according to the needs of a given drug's profile (volume, viscosity, injection time) and market needs (target patient population and lifecycle management), and maximises sustainability with a reusable model.

CONCLUSION

Motorised OBDSs represent an innovative approach for administering large-volume biologics, bridging the gap between potent new therapies and patient-centric care. By learning from past devices and addressing challenges in injectability, comfort, sterility and connectivity, Symbioze® has demonstrated how to offer a more flexible solution for home-based immunotherapy that could enhance quality of life for patients. This potential could enable the pharma industry to unlock new opportunities and improve patient outcomes in cancer care through the power of innovative drug delivery.

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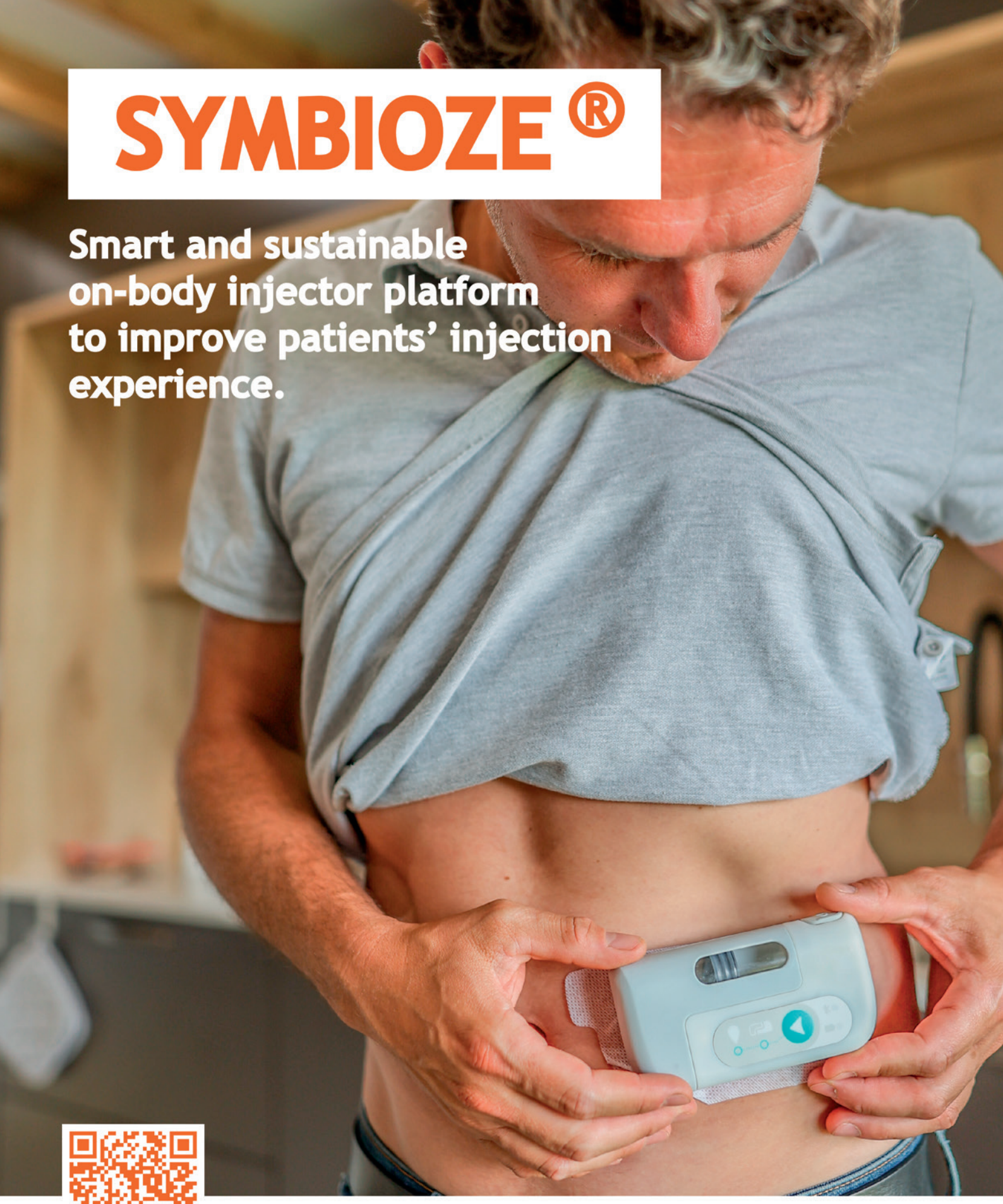

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Smart and sustainable on-body injector platform to improve patients' injection experience.

Nemera
we put patients first

Expert View

ADVANCING CANCER CARE THROUGH ON-BODY SUBCUTANEOUS INJECTIONS: THE ONCOLOGY COMMUNITY'S PERSPECTIVE

Dr Greg Moakes of LTS Device Technologies discusses the role that on-body delivery systems have to play in modernising the delivery of oncology drugs, digging into the survey results of over 200 attendees of the American Society of Clinical Oncology 2025 Global Meeting as to their opinions on the place of this pivotal technology in oncological practice.

"TOO MANY CANCER PATIENTS CHOOSE TO DISCONTINUE THEIR TREATMENT REGIMENS, STATING A MYRIAD OF REASONS INCLUDING FEELING RESISTANT TO TREATMENT, THE SEVERITY OF THE SIDE EFFECTS OUTWEIGHING THE BENEFITS AND THE SHEER FINANCIAL BURDEN OF TREATMENT."

The drug delivery industry is currently seeing a continued rise in the popularity of on-body delivery systems (OBDSs). As many industry experts recognise, this growth is driven by the increasing prevalence of chronic diseases, continued innovation in injectable drug delivery, a continued focus on at-home healthcare and the growing range of therapy areas that OBDSs can be configured to treat, including diabetes, Parkinson's disease, pain management, autoimmune diseases and many types of cancer.

In the case of oncology care specifically, new therapies are being discovered and existing therapies continue to evolve rapidly, driven by advances in biologics and immunotherapies. However, the method of drug administration has, until recently, remained a persistent barrier to delivering what should be regarded as better patient-centric outcomes. This is because traditional intravenous (IV) infusions, although often effective, place huge demands on both clinicians and patients, involving emotionally demanding and lengthy visits to healthcare facilitates by patients and the provision of dedicated, specialist and expensive healthcare professionals (HCPs) by hospitals and clinics.

In response to this, the industry is witnessing a growth in pharmaceutical R&D projects either innovating in or repurposing for subcutaneous (SC) delivery methods, particularly large-volume SC injections, and the development of OBDSs that can deliver high-volume, high-viscosity therapies. This article explores the real-world insights from a survey conducted during the American Society of Clinical Oncology (ASCO) 2025 Global Meeting, highlighting both the promise and practical limitations of shifting towards SC delivery.

THE CHALLENGES WITH THE STATUS QUO

Oncology patients undergoing hospital-based treatments face significant challenges, including frequent unplanned hospitalisations, emotional distress, significant variations in access to care and an overall reduction in quality of life. As a result, too many cancer patients choose to discontinue their treatment regimens, stating a myriad of reasons including feeling resistant to treatment, the severity of the side effects outweighing the benefits and the sheer financial burden of treatment.

There are other reasons too, ones that an effective, patient-centric solution could mitigate. Hospitalisation is taxing both physically and psychologically, with patients often reporting deterioration in wellbeing, constant fatigue and an overall sense of a lessening quality of life, particularly at a time when patients and their families are confronted with the reality of a shortened life expectancy. Even the burden of travel is often cited as a tangible reason for discontinuation.

Unacceptable delays in treatment and navigating the complexity of a disjointed, multi-stakeholder healthcare system, including problems accessing daycare support and pain management, further add to challenges that patients face, leaving them feeling isolated and giving them the sense that they have to manage their care on their own. And, of course, there is the economic burden of oncology care,

"TO BETTER UNDERSTAND HOW THE ONCOLOGY COMMUNITY REGARDS THE POTENTIAL OF OBDSs AS AN EFFECTIVE DELIVERY MECHANISM, 200 ONCOLOGISTS ATTENDING THE ASCO 2025 MEETING WERE SURVEYED TO ASCERTAIN THEIR OPINIONS."

which can be considerable to say the least, placing even greater levels of anxiety on the patient or the payer.

SC DELIVERY VIA AN OBDS IS EMERGING AS A VIABLE ALTERNATIVE

SC delivery therefore presents an appealing alternative to the status quo. It offers faster administration and improved patient comfort. However, up until recently, transitioning complex oncology drugs to highly viscous SC formulations has presented unique challenges in terms of patient tolerance and administration feasibility. Some therapies also require follow-up visits with the physician.

One demonstrable example of how these challenges have been overcome is the recent market commercialisation of UDENYCA ONBODY™ (Coherus, CA, US), a state-of-the-art on-body injector system designed to deliver the biosimilar pegfilgrastim-cbqv for cancer patients undergoing chemotherapy or radiation therapy. Based on the approved dosing regimen, pegfilgrastim is to be administered 27 hours after oncology treatment to reduce the risk of infection.

Conveniently, this device can be securely applied directly to the skin at the end of a chemotherapy session. The retractable needle mechanism will then automatically deploy at the predetermined delivery time, with an indicator, status light and audible signal to provide patients with reassurance that the dose has been correctly administered. Furthermore, the injection time is around five minutes, which ensures that the disruption to patients' daily lives is kept to an absolute minimum. This is, of course, on top of the invaluable benefit of not having to visit an HCP for treatment, with all the time, disruption and anxiety that brings.

A LANDMARK STUDY INTO THE ATTITUDES WITHIN THE ONCOLOGY COMMUNITY

To better understand how the oncology community regards the potential of OBDSs as an effective delivery mechanism, 200 oncologists attending the ASCO 2025 meeting were surveyed to ascertain their opinions. The ASCO has a stated aim of "Conquering cancer through research, education and promotion of the highest quality patient care" and attracts a range of highly experienced and diverse oncology expertise, making it an ideal environment for such a study.

Survey Demographics

The study targeted a broad spectrum of oncology specialists, including haematologist, medical, surgical and radiation oncologists, as well as nurse practitioners and physician assistants working across academic centres, community hospitals and private practices. Ranging from recent graduates to seasoned experts, over 88% of respondents had more than six years in practice, with 31% practicing for over 16 years. The majority of those surveyed (45%) were haematologist oncologists who frequently administer SC therapies, while another 38% were medical oncologists.

Current Use and Perceived Barriers of SC Therapies

While SC therapies are gaining traction, they still remain underused in many practices, with just 5% of oncologists reporting that more than 50% of their patients receive SC therapy (excluding supportive care). A significant proportion of respondents (48%) administer SC drugs to just 11–25% of patients. That said, usage is growing where clinicians are looking to reduce the number of frequent IV infusions for chronic therapy or to better manage limited resources.

As shown in Table 1, the greatest barrier to widespread adoption appears to be patient-reported pain or discomfort (44%), followed by administration complexity and staff burden (26%). These concerns underscore the need for better drug delivery systems, particularly for volumes exceeding 2.25 mL.

Tolerability Thresholds

Tolerability thresholds are critical to patient adherence and comfort. In this section, the survey explored the respondents' perceptions of volume tolerance for SC injections via handheld syringes – 46% of oncologists identified 3.5 mL as the upper limit, another 33% considered up to 5 mL as tolerable and only 5% believed that up to 10 mL was acceptable. On this basis, the upper limit for standard SC injections lies between 3.5 and 5 mL, which is clearly a considerable constraint, as many biologics require much higher doses than that.

Paradoxically, the overall tolerability rating of large-volume SC injections (>2.25 mL) was favourable, with 55% rating them as "well tolerated" and only

Percentage of Patients Receiving SC Therapy (non-supportive care)	Most Significant Challenge With SC Injections as Identified by Clinicians >2.25 mL
26–50%: 29%	Patient-reported pain or discomfort: 44%
11–25%: 48%	Administration time and complexity for staff: 26%
0–10%: 18%	Injection site reactions: 15%
More than 50%: 5%	Patient anxiety or apprehension: 10%
	Reimbursement or billing issues: 5%

Table 1: Barriers to large-volume SC use.

5% indicating that they were "poorly tolerated". No respondents rated them as "very poorly tolerated"; the remaining 40% reported them as "moderately tolerated". So, while clinicians believe there is a volume threshold, many acknowledge real-world tolerability is better than expected, opening the door to alternative methods for larger-volume delivery.

Response Option	Percentage
Enabling at-home administration	62%
Freeing up staff time in the clinic	18%
Reducing patient-reported pain	11%
Improving patient adherence	7%
Allowing for administration of viscous drugs	2%

Table 2: Primary potential benefit of an OBDS.

OBDSs: The Promise and the Unease

The emergence of OBDSs is generating cautious optimism among clinicians. A total of 76% of the respondents rated the potential of OBDSs to improve the patient experience as "substantial" or "significant". The primary benefit identified by the respondents was their potential to enable at-home administration (62%), followed by freeing up staff time (18%) and reducing pain via slower, controlled injection (11%), as shown in Table 2.

However, the optimism is tempered by practical concerns such as device failure (43%) and the ability of patients to manage the device at home (35%). Other concerns cited included reimbursement (14%) and potential side effects (6%), although these were seen as somewhat lesser barriers to adoption.

Notably, 73% of respondents saw the greatest potential for OBDSs as enabling technology platforms in at-home settings, reflecting the strong appetite for decentralising treatment while maintaining therapeutic efficacy and safety. The respondents thoughts on the potential of OBDSs to improve quality of life for patients are shown in Table 3.

Response Option	Percentage
5 – Significant Improvement	25%
4 – Substantial Improvement	51%
3 – Moderate Improvement	20%
2 – Minor Improvement	4%
1 – No Improvement	0%

Table 3: Belief that an OBDS could improve patient experience (Scale 1–5).

The Future Outlook Suggests a Shift From IV to SC is Imminent

Finally, the survey turned to the respondents' outlook on the future, which provided some telling statistics. Notably, 48% of oncologists expect 26–50% of their patients to shift from IV to SC biologics within the next five years, with another 40% predicting that between 10% and 25% will make the switch. Only 3% expect the transition to affect fewer than 10% of their patient population. This projection aligns with the conversations drug delivery device developers are having with pharma partners and the broader industry, with all stakeholders making concerted efforts to make cancer therapies more convenient and patient centric to enhance patient quality of life.

"THIS PROJECTION ALIGNS WITH THE CONVERSATIONS DRUG DELIVERY DEVICE DEVELOPERS ARE HAVING WITH PHARMA PARTNERS AND THE BROADER INDUSTRY, WITH ALL STAKEHOLDERS MAKING CONCERTED EFFORTS TO MAKE CANCER THERAPIES MORE CONVENIENT AND PATIENT CENTRIC TO ENHANCE PATIENT QUALITY OF LIFE."

CONCLUSION

Oncology treatment stands at a pivotal crossroads. Scientific advances, together with novel delivery platforms, are creating unprecedented potential for improved

patient outcomes. The landmark survey of oncology professionals discussed here reinforces an increasingly popular view that SC drug delivery, particularly through OBDSs, is both feasible today and inevitable in the future of modern oncology, supporting the clinical motivation to improve patient experience, reduce strain on resources and modernise delivery methods for increasingly complex therapies.

In many ways, OBDSs can be seen as the absolute manifestation of a patient-centric healthcare approach. By integrating drug product, injection hardware and software-controlled activation mechanism into a single automated device, these devices offer significantly greater levels of convenience when compared with the need to regularly self-inject or the requirement to attend a clinic for medicine to be administered by an HCP. This not only removes a burden from patients but can also support improved compliance with sometimes complex therapy regimens, as well as removing a proportion of the costs where travel to care would otherwise be required.

Greg Moakes

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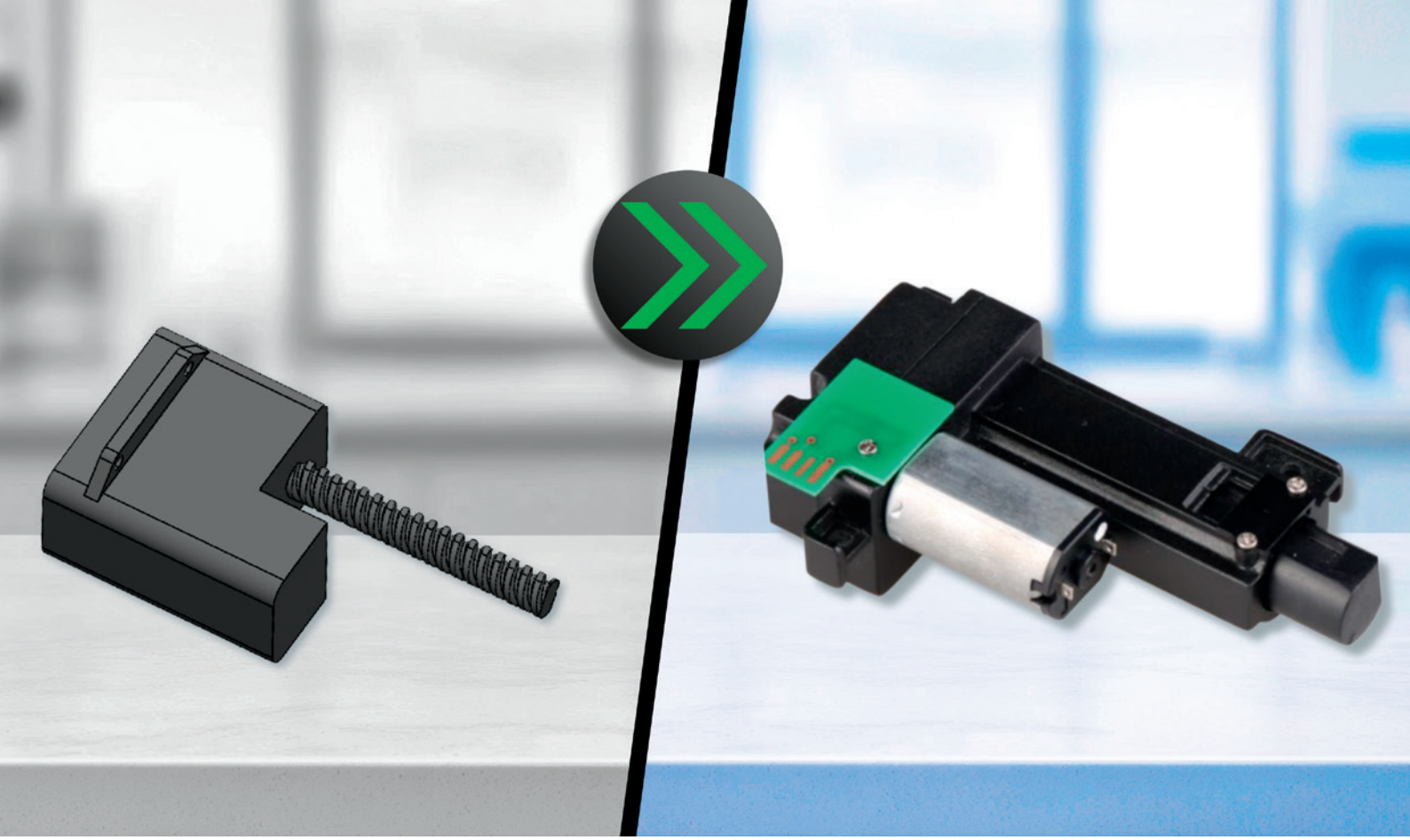
ABOUT THE COMPANY

LTS is a pharmaceutical technology company that develops and manufactures drug delivery systems for pharma partners, with a focus on transdermal therapeutic systems, oral thin films on-body delivery devices and microneedle-array patches. Its systems are applied in more than 20 marketed products.



ACCELERATING DEVELOPMENT OF ELECTROMECHANICAL DELIVERY SYSTEMS VIA MODULAR INTEGRATION

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Nicholas Ciccarelli and **Andrew King** of **Kymanox**, along with **Dr Marcus Herrmann** and **Dr Thomas Roschke** of **Johnson MedTech**, discuss the insights gained in the product development process from the recent collaboration between the two companies, with Kymanox managing the overall system integration and Johnson MedTech tackling the specific design of the drive system within the designated product specification.

Reusable, electromechanical drug delivery systems are becoming increasingly sought after for their superiority over their disposable counterparts, specifically for their increased sustainability and precision dosing. At the heart of many advanced drug delivery systems lies a precision motion subsystem – a custom motor and gearbox designed to deliver exacting performance in a compact, long-lasting package.

This article explores the system integration of highly customised subsystems through a collaborative partnership between Kymanox, an expert in drug delivery device design and development, and Johnson MedTech (JMT), a specialist in miniaturised dosing and needle insertion systems. Both companies embraced a collaborative development approach, wherein Kymanox defined clear interfaces and performance criteria and JMT was free to engineer the internal workings. With that, both companies were able to accelerate development and deliver innovative solutions.

The clarity of the proper technical interfaces was the result of this joint co-operation, leading to a mutual understanding of the drug delivery and motion system needs. One of the most impactful

outcomes of this approach was the ability to test and verify the subsystem independently from the final product, significantly reducing risk and increasing efficiency.

INTERFACE DEFINITION: FOUNDATION FOR MODULAR DEVELOPMENT

The cornerstone of this collaboration was the thoughtful definition of the interface between the drug delivery device (Kymanox module) and the motor-gearbox subsystem (JMT module). Kymanox's goal was to precisely define what the subsystem needed to achieve – without dictating how it was achieved. This interface definition typically includes:

- **Mechanical Parameters:** Mounting geometry, shaft alignment, space envelope and tolerance allowances.
- **Electrical Requirements:** Supply voltage range, current limits and connector standards.
- **Performance Expectations:** Speed and torque profiles, positional accuracy, response times and lifecycles, as well as environmental conditions.

> "RATHER THAN OVER-PRESCRIBING SUBSYSTEM REQUIREMENTS TO AN INDUSTRY EXPERT, KYMANOX FOCUSED ON DESIGNING THE OVERARCHING SYSTEM ARCHITECTURE, ORCHESTRATING MULTIPLE SPECIALISED PARTNERS, BRINGING IN USER AND PATIENT EXPERIENCE AND INTEGRATING ALL COMPONENTS AND SUB-SYSTEMS."

This modular approach enabled JMT to treat the subsystem as an independent, clearly bounded unit. JMT had full control over the internal design, while ensuring compatibility with the broader device. Simultaneously, JMT provided feedback to Kymanox on how those expectations could be achieved in the most efficient way. Within a few paper-based iterations, the proper system boundaries were able to be clarified and refined. To get the most out of both engineering teams, those boundaries were elaborated on during each system iteration, based on the specific application conditions and requirements.

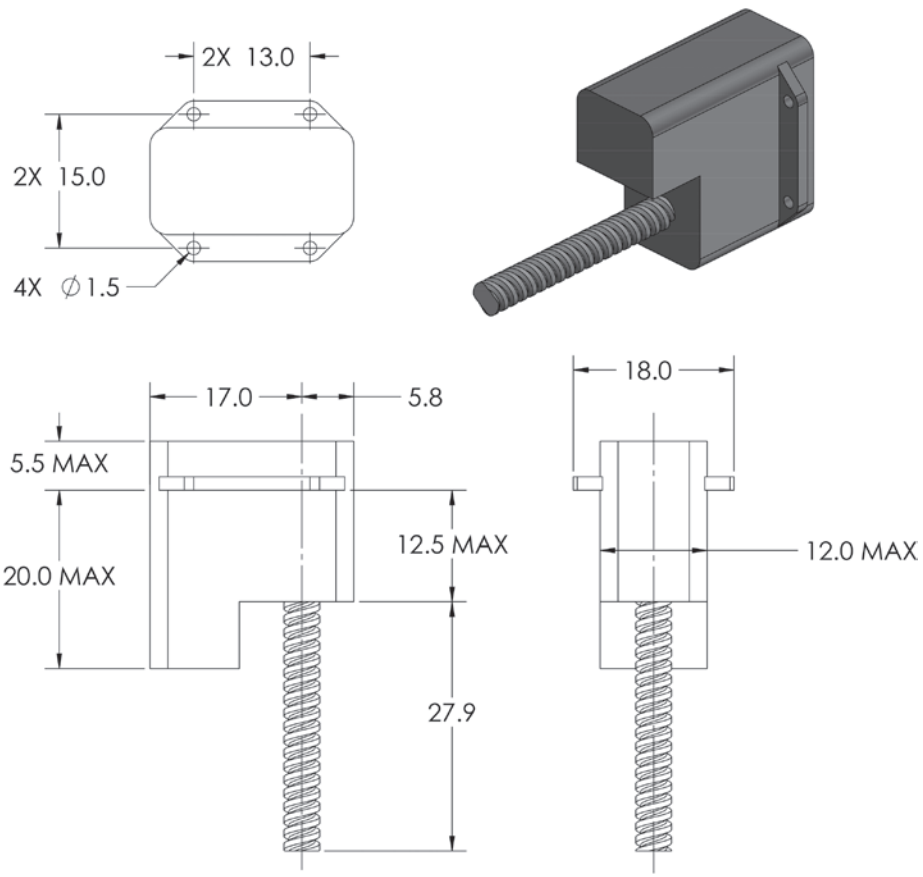


Figure 1: Example of a design envelope from Kymanox for an actuator module showing dimensional maxima, mounting locations and interface points.

KYMANOX'S ROLE: SYSTEM INTEGRATION EXPERTISE IN ACTION

Kymanox brought deep experience in system integration to the table – a strength that proved essential in defining subsystem boundaries and ensuring seamless incorporation into the complete device. Rather than over-prescribing subsystem requirements to an industry expert, Kymanox focused on designing the overarching system architecture, orchestrating multiple specialised partners, bringing in user and patient experience and integrating all components and sub-systems. This effort included:

- **Identifying Critical Parameters:** Knowing which aspects of the motion system truly matter for overall device performance and reliability.
- **Clarifying Functional Interfaces:** Defining the mechanical and electrical connections in ways that are robust yet flexible.
- **Orchestrating Parallel Development:** Co-ordinating efforts across vendors, ensuring that the timeline moves forward without bottlenecks.

By clearly articulating requirements and constraints while trusting experts such as JMT to solve within them (Figure 1), Kymanox ensured that the system-level goals were met without micromanaging the implementation.

JMT'S ROLE: ENGINEER THE "HOW"

Within the agreed boundaries, JMT had full freedom to develop the optimal motor-gearbox-sensor solution. Rather than being constrained by prescribed components or legacy configurations, JMT was able to explore and simulate various design pathways to meet the performance requirements.

Simulation-Driven Design Process

JMT used a suite of advanced tools to optimise the subsystem virtually before committing to physical prototypes:

- **Mathematical Modelling:** Simulating how the motor would perform under load and adjusting parameters such as winding configuration and magnetic characteristics.
- **System Simulation:** Evaluating the overall efficiency, response time and duty cycle compliance to ensure good battery life and dosing precision during the different delivery profiles.
- **Selection of the Best Fitting Motor Principle:** Determining if brushed motors, stepper motors or electronically commuted motors are the best fit for the required drive train (Table 1).
- **Finite Element Analysis (FEA):** Studying gear stress, deformation and long-term durability under cyclic loading.

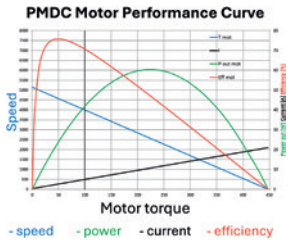
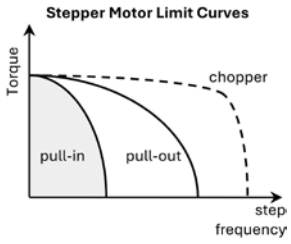
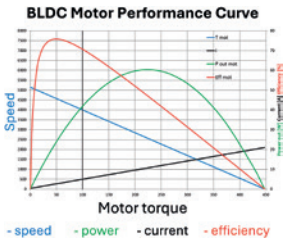
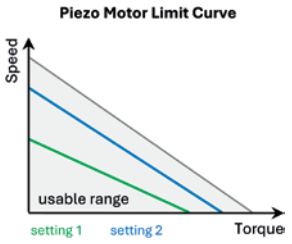
Characteristic	Brushed PMDC Motor	Stepper Motor	Electronically Commutated Motor (BLDC / EC Motor)	Piezo Motor
Reference view				
Size	Ø 4–80 mm	Ø 6–42 mm	Ø 4–60 mm	Ø 8–15 mm
DC Supply	1–240 V	3–48 V	3–240 V	5–120 V
Performance characteristics (example)				
Operational life	300–8,000 hrs	10,000–25,000 hrs	10,000–40,000 hrs	20,000–50,000 hrs
Resolution	Depending on sensor and control	Tin can 7.5°–18° Hybrid 0.36°–3.6°	Depending on sensor and control	Depending on sensor and control (e.g. 4096 CPR)
Reliability	Mainly limited by electrical commutator	Mainly limited by electronic control circuit and bearing	Mainly limited by electronic control circuit and bearing	Mainly limited by tip contact and electronic control
Sensors	Can be added	Can be added	Built-in hall sensors or similar	Built-in hall sensors or similar
Cost	Lowest	Low to medium	Medium	High
Operation temperature	-20°C – +60°C	-40°C – +80°C	-40°C – +80°C	-40°C – +70°C
Notes		Rotary and linear versions available		Rotary and linear versions available

Table 1: Comparison of the common features of miniature brushed PMDC-motors, steppers, electronically commutated motors and piezo motors.

To identify the optimal solution within the given design envelope, JMT investigated a variety of alternative motor technologies and geartrain options. The selected motor principle is one of the base decisions in drive-train design and must be based on the requirements of the application. Common motor technologies are shown in Table 1, together with their key parameters.

As an example, for low speed, high torque applications, a stepper motor is often preferable, featuring open loop control possibilities and precise dosing accuracy. With that selection, the need for additional sensors might be avoided, reducing cost and complexity. On the other hand, it may be preferable to use a direct current (DC) motor for continuous dosing, having the benefit of low power consumption and high efficiency. Both motor principles require a custom geartrain design according to their characteristics. Reliability, operational life or related costs are also often driving factors in the selection of the actuation solution.

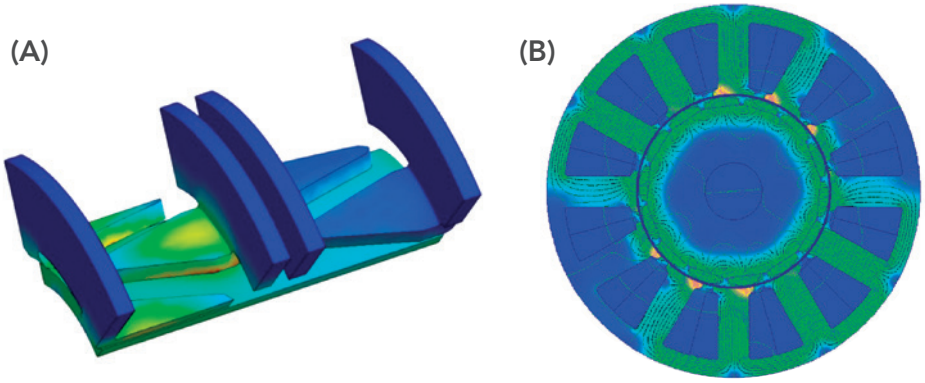


Figure 2: (A) Magnetostatic field analysis of a small stepper motor (ANSYS); (B) Magnetostatic field analysis of a high pole BLDC motor (MotorCAD).

To clearly determine the best technology choice and get Kymanox's buy-in on the proposed solution, JMT used mathematical simulation tools to predetermine performance and life, thereby demonstrating feasibility. FEA and simulations were used for motor performance (Figure 2), as well as dynamic system simulations using either Matlab, Simulink, SimScape or SimulationX (Figure 3). For example, simulated data of motor currents (Figure 3, Right) was typically shared with Kymanox to support their early controller design for drug delivery devices.

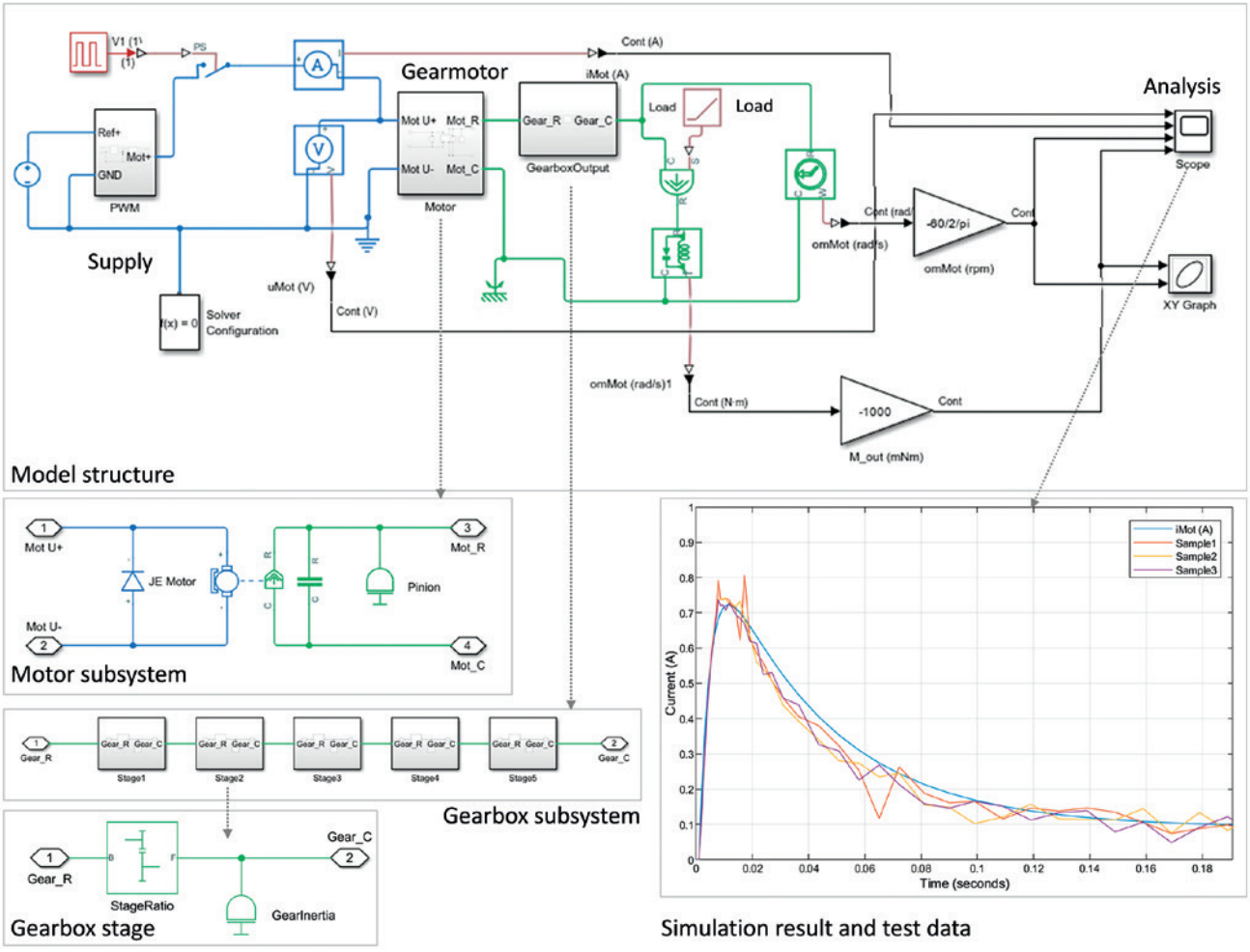


Figure 3: Dynamic simulation model for a PMDC Motor with a multi-stage gearbox (Matlab/Simulink/SimScape) and its simulation result for the motor current during start of operation in comparison to prototype test data.

"THE INHERENT DESIGN TRADE-OFF IN DOSING SYSTEMS IS BETWEEN SIZE AND PERFORMANCE – A SMALLER SIZE IS A KEY CONTRIBUTOR TO PATIENT CONVENIENCE, YET SMALLER COMPONENTS ARE NATURALLY MORE FRAGILE."

The inherent design trade-off in dosing systems is between size and performance – a smaller size is a key contributor to patient convenience, yet smaller components are naturally more fragile. Furthermore, an increasing number of pharmaceutical companies are commercialising higher viscosity drugs that, when coupled with fast injection times, create higher forces inside the geartrain. JMT used advanced analysis software, such as KissSoft and ANSYS, to predict the robustness and endurance of geartrains with respect to the expected device lifespan (Figure 4).

The robustness of the system is determined not only by mechanical loads due to external forces but also by the influence of tolerances – manufacturing tolerances play a major role in the final product performance, especially for small components. To evaluate the assembly interface variations, JMT performed statistical tolerance analyses, also by means of computer-aided engineering software. Eventually, this early-stage analysis on the boundary features gave Kymanox important input for the overall system design.

In summary, these tools allowed JMT to rapidly iterate and test ideas in order to hone the design before any parts were manufactured. The benchmark for all these activities was the actuator module boundary requirements, which were incorporated into a comprehensive verification plan, the results of which were exchanged with Kymanox.

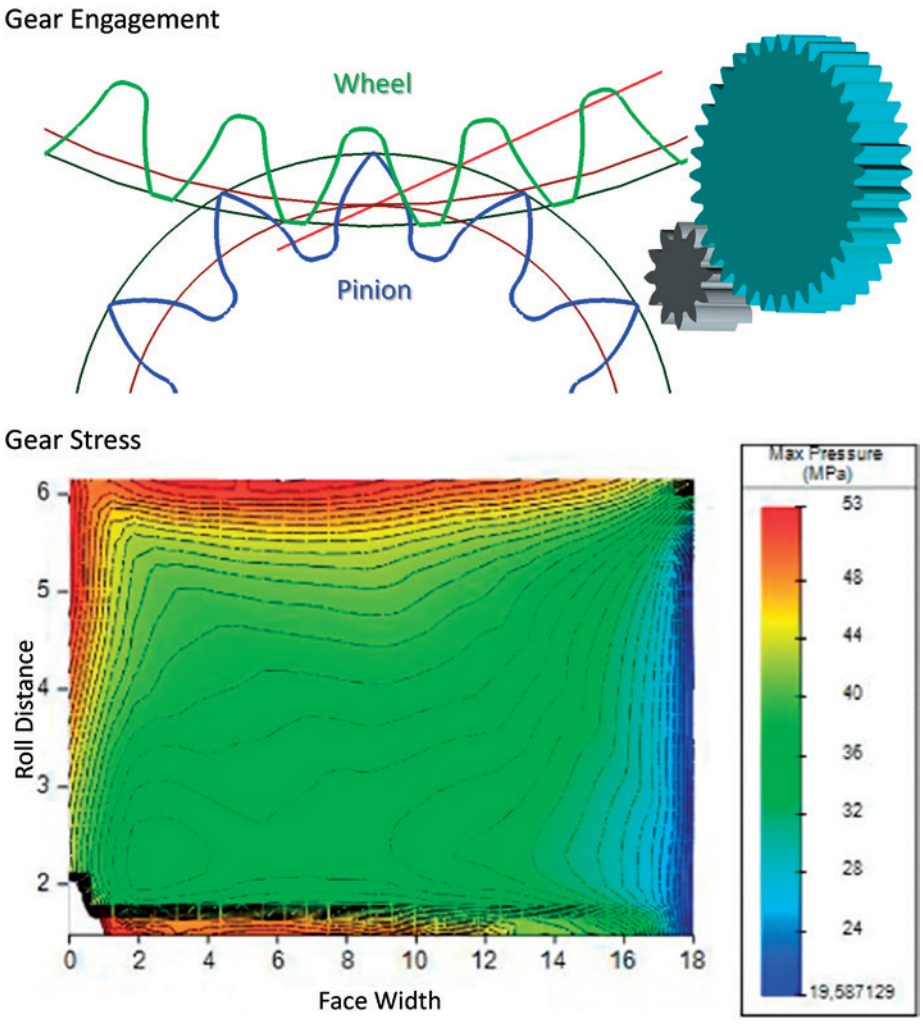


Figure 4: Gear profile optimisation and gear stress simulation (KissSoft).

Independent Subsystem Testing: A Major Advantage

One of the most significant benefits of this modular approach is the ability to test and verify the motor-gearbox subassembly completely independently from the final device.

- **Early Verification**: JMT built test rigs tailored specifically to the subsystem, allowing them to assess critical performance characteristics – such as torque, speed performance and thermal behaviour – well before device-level integration.
- **Parallel Development**: While JMT refined the motion subsystem, Kymanox was able to continue development on other parts of the device. This independent yet collaborative process significantly shortened the development timeline.
- **Reduced Risk**: By confirming standalone subsystem performance upfront, integration challenges were minimised and system-level testing became more of a confirmation step than a debugging phase.

This subsystem testing approach not only improves development speed but also contributes to increased reliability and confidence in the final product. A major benefit of the independent testing scheme is the possibility to test for failure by exaggerating load profiles or cycles. Additionally, various application conditions can be recreated much faster and more easily, gleaning deeper insights than would be achieved with complete device tests. Figure 5 shows a representative motor-gearbox actuator test bench that enables a variety of tests while collecting precise

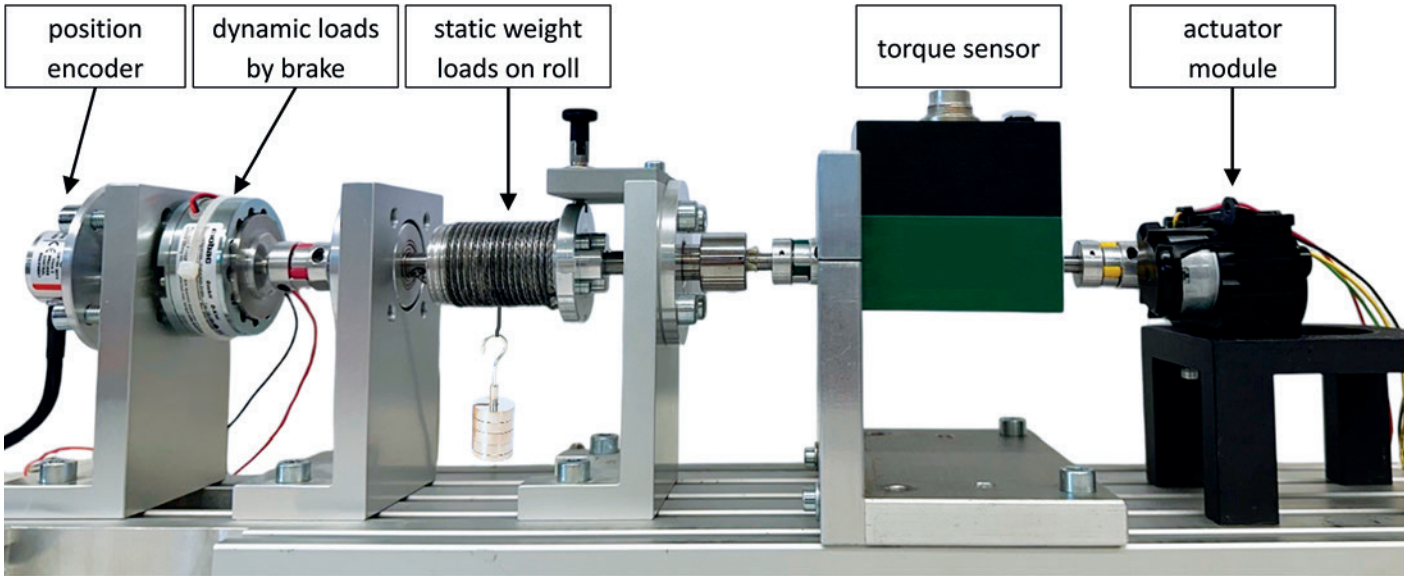


Figure 5: Test bench for a motor-gearbox system used in the modular testing scheme (controller part not shown).

data. The testing is not done in isolation, but results are compared with the upfront simulations to improve the models and gain more knowledge (Figure 3). By sharing the subsystem results early on, JMT provided reliable data to Kymanox that helped its engineers to refine the delivery device design and to advance system development.

RESULTS: HIGH PERFORMANCE WITHIN A CLEAR BOUNDARY

With a collaborative approach, the resulting motor-gearbox-sensor subsystem delivered on all fronts:

- Required specifications were met, with speed and torque profiles optimised to the use case
- The components fit seamlessly within the device envelope without compromising other design goals
- The drive system was verified as a standalone unit, ensuring readiness for integration with minimal reworks.

The disciplined separation of responsibilities and the precise definition of interfaces made this possible, allowing each party to contribute with its core strengths and expertise. In the long term, this definition also allowed for a clear monitoring and revalidation of the motion subsystem's performance during the device's production life.

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Nicholas Ciccarelli, PE, is the Chief Technology Officer at Kymanox, focusing on combination product and medical device development. He brings cutting-edge medical technologies to patients and providers, leading cross functional engineering teams across the US, Europe and China. His expertise spans component design, system integration, design verification, *in vivo* studies and regulatory submissions. Mr Ciccarelli holds a Bachelor of Science in Bioengineering from the University of Maryland, College Park (MD, US) and is a licensed Professional Engineer in Pennsylvania.

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CONCLUSION: CLEAR BOUNDARIES, BETTER OUTCOMES

The collaboration between Kymanox and JMT highlights a powerful model for medical device development using integrated drive systems – define what is needed, then let subsystem domain experts decide how to deliver it. By focusing on the interface and giving the subsystem supplier design freedom, the design teams were able to unlock higher-quality solutions, faster development and lower integration risk.

Above all, however, a shared technical understanding of the dosing systems' function remains essential. The complexity of wearable drug delivery devices requires clear technical specification boundaries and frequent communication. By doing so, independent subsystem testing becomes feasible and effective, enabling early issue detection and smoother final assembly.

As drug delivery devices and medical devices continue to increase in complexity and sophistication, such modular, interface-driven collaboration models are not just beneficial – they are essential. With Kymanox's strength in system integration and JMT's technical depth in electromechanical subsystems, this partnership shows how modern engineering is as much about collaboration as it is about innovation.

Dr Marcus Herrmann

Marcus Herrmann, PhD, is Managing Director of Johnson MedTech Germany, part of the global Johnson MedTech (JMT) organisation. Since 2024, he has worked as Director Engineering Service, focusing on drug delivery systems, medical-grade pumps and valves and diagnostics. He studied Electrical and Precision Engineering in Dresden (Germany) and London (UK), earning his PhD in 2008 on electromagnetic actuators at Munich University (Germany). In 2008, he joined Johnson Electric (JE) as Manager R&D for stepper motors and mechatronic subsystems. Before Johnson MedTech, he was Director Global Engineering at JE's Metering and Circuit Breaker segment, overseeing actuation systems and high-power relays with close ties to high-volume production.

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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.

See **Page 03**

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Johnson MedTech (JMT) is a global CDMO for critical medical device subsystems and vital signs monitoring (VSM) sensors and wearables, established in 2007 with a global revenue of $74M. JMT provides services for surgical tools, medication delivery, medical grade pumps, valves and fans, as well as VSM Sensors and point-of-care diagnostics. Engineering services were recently added to its offering.

To learn more, see **Page 58**

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Kymanox is a life sciences professional services organisation that offers engineering, scientific and compliance support to companies exclusively in the biotechnology, pharmaceutical, medical device and combination product industries throughout the product lifecycle from early development to post-market.

To learn more, see **Page 58**

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Nemera is a drug delivery device solutions and combination product services provider that puts patients first to enable the design and manufacture of devices that maximise treatment efficacy. Nemera is committed to the highest quality standards, from early device strategy to state-of-the-art manufacturing. Nemera works closely with customers to ensure the success of their combination products.

To learn more, see **Page 48**

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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.

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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.

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

To learn more, see **Page 36**

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TxSphere was founded as a spin-off of Intuvie LLC and specialises in drug delivery devices for combination products. With deep expertise in infusion technologies, the knowledge of their multidisciplinary team spans engineering, software, pharmacy and infusion therapy. Manufacturing and related services are supported by a CDMO partner, ensuring scalability, quality and regulatory alignment across development stages.

To learn more, see **Page 14**

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ZwickRoell is a materials testing system developer and manufacturer. The company develops and manufactures both the load frames and all main components itself. With 15 product groups and testing solutions for more than 20 industries, as well as support from the company's approximately 1,900 employees representing over 50 countries, ZwickRoell is an expert partner in the field of materials testing.

To learn more, see **Page 24**

High-volume wearable auto-injector

Shaily Mira is an On-Body Delivery System (OBDS) that allows product customization for the delivered dose volume and injection time.

It can be customized to deliver high-volume drugs from a pre-filled cartridge of 3mL up to 15+ mL. The injection time, regardless of injected volume, can be customized from 1 minute up to 2 hours.

- Shaily Mira is a user friendly auto-injector for high-volume injections.
- Patch and start the injection, sit and relax until the Shaily Mira device tells you that the injection is completed.
- The feedback contains both sound and light signals.

Creating innovative designs for cost-effective drug delivery systems resulting in a better patient experience and supporting sustainable global health.

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