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ON DrugDelivery 189

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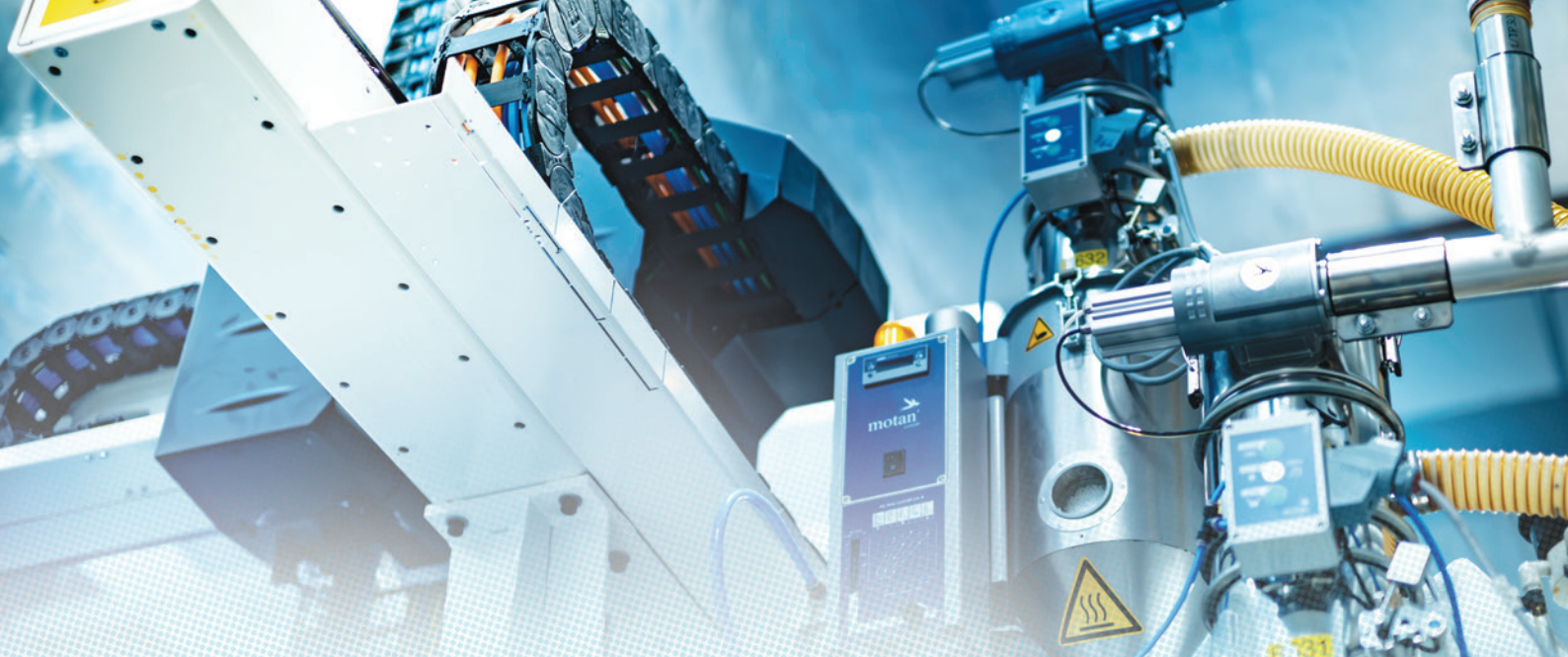

Wearable injectors: The next commercial breakthrough lies beyond device design.

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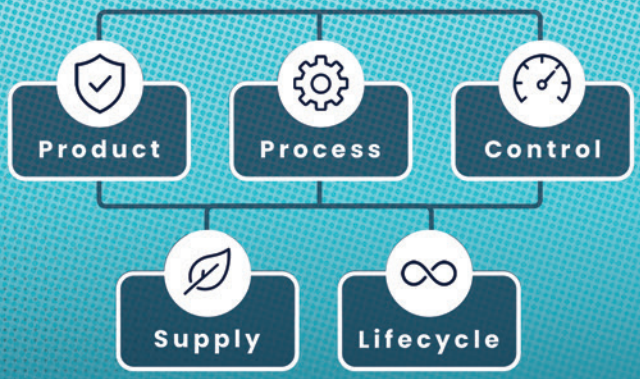

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WEARABLE INJECTORS

ONdrugDelivery Issue N° 189, September 4th, 2026

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, "Sorrel™ On-Body Injector", courtesy of LTS Device Tehcnologies & Ventura Solutions (see this issue, Page 64). Reproduced with kind permission.

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Autumn of Injection Part I:
Wearables & On-Body Devices

As summer comes to a close and the autumn conference season approaches, ONdrugDelivery returns to the injectables space with a series of three issues focusing on this key sector within drug delivery. This first entry into our parenteral trilogy focuses on wearable devices and on-body injectors. ONdrugDelivery's first issue focusing exclusively on this topic was published back in 2014 and, while the sector has come a long way since then, this issue features long-standing veterans present in that first Wearables issue alongside new entrants into the space.

The issue begins with **LTS Device Technologies**, our Outstanding Sponsor, and its Sorrel™ platform, making the case that the additional complexity of electro-mechanical wearable devices is not, in fact, a drawback of the device category, but an opportunity to achieve enhanced reliability over purely mechanical systems by taking advantage of on-board software (Page 8). Alongside that, Key Sponsors **Jabil** and **TxSphere** discuss the necessity of pairing advanced device design with proven manufacturing, and how the companies' partnership achieves this for the TxSphere wearable devices (Page 14). Our final Key Sponsor, **Synolus Medical**, introduces its MiniGo device and puts forward a challenge to the traditional division of autoinjectors and wearables (Page 20).

Further contributions come from the other major players in the wearable injection device space. **Enable Injections**' article zeros in on the root cause of misconceptions about the 3 mL limit for subcutaneous injection and how its enFuse® system counters them (Page 35); **Gerresheimer** discusses the role of backpressure and how it is handled by the Gx InPuls™ and Gx InPuls Flex platforms (Page 42); **West Pharmaceutical Services** comments on how its SmartDose® platform has been enhanced by continuous development (Page 52); **Ypsomed** covers the broader strategy of selecting an on-body system and how this has shaped the design of YpsoDose (Page 58); and **Torramics** introduces its novel, miniaturised NanoFlow platform based on semiconductor architecture rather than a traditional mechanical pump system (Page 78).

But, of course, there is more to the wearables sector than device design alone. Also featured in this issue is a Company Showcase from **Grand River Aseptic Manufacturing** (Page 28), an in-depth look at design verification practices for infusion systems from **Cambridge Design Partnership** (Page 30) and a discussion on ensuring the safety of wearable devices from **Sanner** (Page 48). Alongside them, **Ventura Solutions** and **LTS** consider the role and value of partnerships in combination product development, and how the timing of bringing partners in can be a critical factor in development timelines (Page 64); and **Quvara Medical** puts forward the importance of considering the industrial architecture of a wearable device as a key competitive advantage (Page 70). Finally, rounding out the issue, **Herrmann Ultraschall** examines the value of ultrasonic welding in wearable applications, using a novel, non-invasive continuous glucose monitor as a case study (Page 74).

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

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WHY SMARTER WEARABLES ARE THE SIMPLE ANSWER TO INTELLIGENT DRUG DELIVERY

Dr Greg Moakes of **LTS Device Technologies** considers how complex devices, such as the company's Sorrel™ on-body delivery system, can facilitate the self-administration of injectable therapies while continuously monitoring and verifying the device's critical delivery functions.

Jeopardy is unwelcome in the world of drug delivery. For healthcare professionals (HCPs) and their patients, the proven model of "the right dose, in the right way, at the right time" is fundamental to the aim of securing positive treatment outcomes.

Failure in any of these three aspects is likely to have consequences. This could be as serious as failing to safely and accurately deliver life-saving medication or, in less grave circumstances, it could result in financial loss from wasted doses of complex, high-value biologics.

Often, of course, it is patients themselves who can be the root cause of these problems. From those with needle phobias to those who struggle to adhere to the structure of a treatment regimen, there are a myriad of personal reasons why individuals fail to engage with their therapy correctly. Subsequently, these points of friction all have the potential to hinder compliance and hamper the chances of a prescribed drug having the desired pharmacological effect.

In parallel with this ongoing issue of patient compliance is the growth of at-home self-administration. By removing the need to attend a medical facility and directly involve HCPs, devices that enable self-administration answer the ever-increasing demand for greater patient convenience, which, in turn, contributes to an enhanced experience, improved compliance and preferential outcomes.[1] It is for these reasons that combination devices in their various forms continue to be a primary focus for innovation in drug delivery.

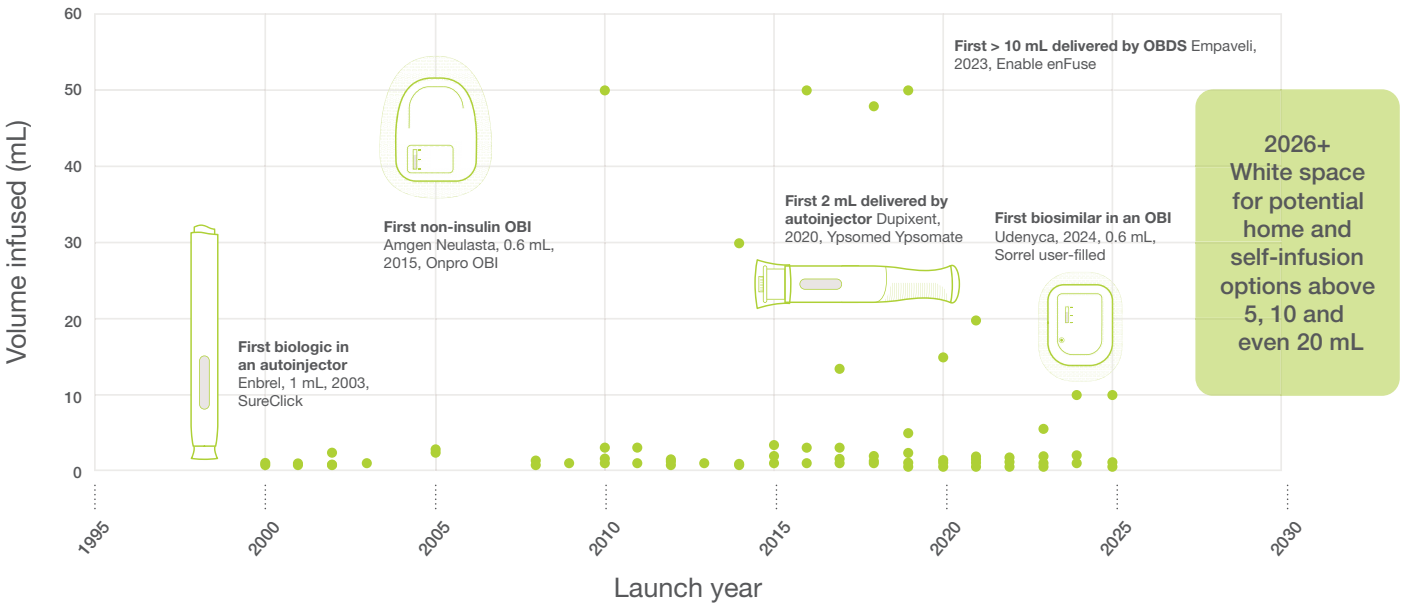

Figure 1: Increasing volumes of subcutaneous FDA-approved drug products, 2000–2025.

"BY REMOVING THE NEED TO ATTEND A MEDICAL FACILITY AND DIRECTLY INVOLVE HCPs, DEVICES THAT ENABLE SELF-ADMINISTRATION ANSWER THE EVER-INCREASING DEMAND FOR GREATER PATIENT CONVENIENCE."

COMPLEX DEVICES DESIGNED TO SIMPLIFY PATIENTS' LIVES

A broad spectrum of devices have emerged into the combination device space, all providing the means for patients to self-inject, but with varying levels of convenience, functionality and capability built in. Building on the foundations of the pen injector, autoinjectors further reduce the level of manual manipulation required. On-body delivery systems (OBDSs) represent yet another step forward, providing a platform for discreet automated dosing, while also supporting higher drug volumes and extended injection times to overlap into territory previously only occupied by infusions.

These OBDSs, with their advanced "hands-free" functionality, provide particular benefits for those affected by chronic conditions, where treatment is required on a sustained, long-term basis. The potential for slower delivery via finer gauge needles can help to reduce injection pain. Moreover, they have the potential to be configured to great effect. As well as accommodating formulations with a wide range of viscosities and volumes, OBDSs can integrate sensors and connectivity functions to support activity logging and data transfer, and they can also be programmed to deliver formulations at specific rates and to specific absorption profiles (Figure 1).[2]

For patients, caregivers and payers, the potential for an OBDS to facilitate subcutaneous injections of drugs in higher volumes, even viscous biologics, has only increased the momentum behind the shift to treat chronic illnesses at home. Key questions then surround how far wearable devices can reasonably push beyond autoinjectors and into infusion territory, and whether they can provide a truly patient-centric platform for the safe, reliable delivery of valuable drugs in higher volumes.

In recent decades, milestones in this area have continually been targeted and exceeded. Currently, the clinical "pinch point" is around 15 mL therapies, where patients still largely rely on HCP-led administration via a manual syringe infusion system involving multiple preparatory steps. With OBDS platforms, however, the gap between higher-volume therapies and patient autonomy is closing fast. Already, devices with volumes 15 mL are on the market, pointing to acceptance and tolerance of these devices for infusion-type applications (Figure 2).

"FOR PATIENTS, CAREGIVERS AND PAYERS, THE POTENTIAL FOR AN OBDS TO FACILITATE SUBCUTANEOUS INJECTIONS OF DRUGS IN HIGHER VOLUMES, EVEN VISCOUS BIOLOGICS, HAS ONLY INCREASED MOMENTUM BEHIND THE SHIFT TO TREAT CHRONIC ILLNESSES AT HOME."

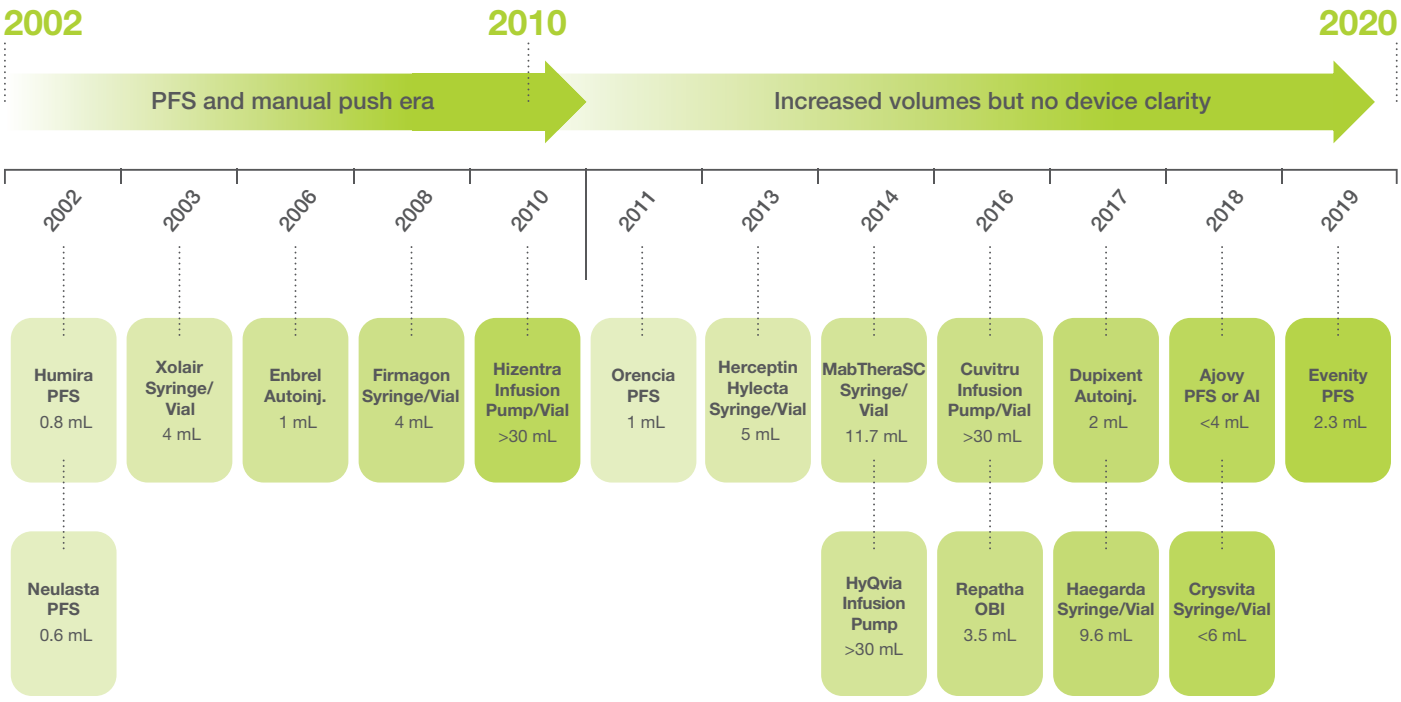

Figure 2: Subcutaneous delivery – a volume journey over 25 years.

UNCOVERING EVIDENCE OF OBDS TOLERABILITY

LTS conducted a study to assess patient tolerability of OBDS-based drug delivery for a dose volume typically delivered either by HCPs via multiple syringes or by infusion via a durable pump.

In a clinical trial, 22 healthy subjects were subject to two high-volume injections of ~15 mL using LTS's Sorrel™ electro-mechanical OBDS. The injections were delivered into the lower abdomen and thigh of subjects, with each lasting around 15 minutes (Figure 3). Patients self-reported pain scores at various times after device placement and during delivery, while also completing post-treatment questionnaires to provide an evaluation of their overall experience. Injection sites were visually assessed to check for bleeding, bruising, irritation, rash, bleb formation or leakage. Dosing accuracy was measured by weighing the device pre- and post-injection to verify the on-board device readings.

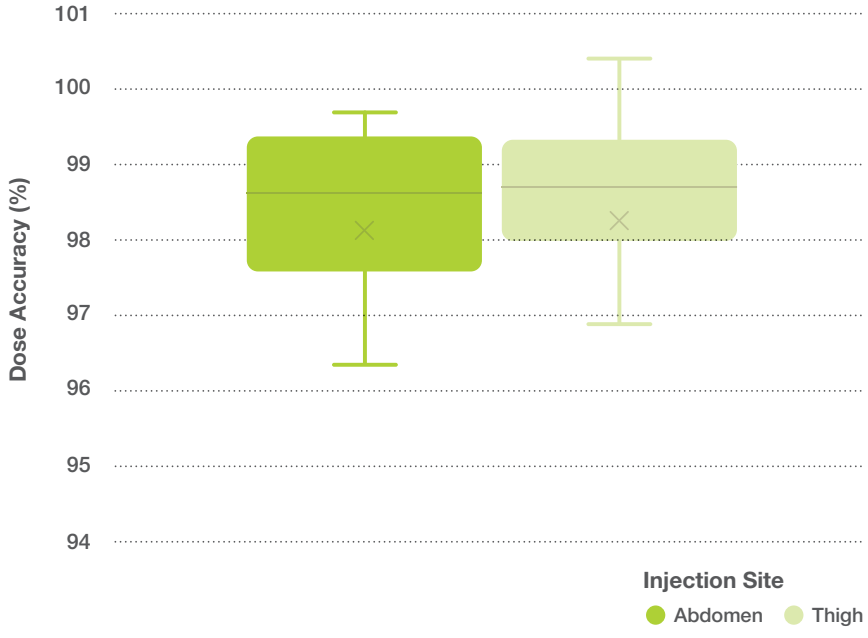

Figure 3: Dose accuracy of delivery by Sorrel into the thigh and abdomen during a clinical trial.

From a device perspective, the results showed that doses were delivered in full, with no errors or inconsistencies, and there was no evidence of fluid reflux onto the skin following removal. Skin reactions were limited and in line with predictions. Out of 19 reports of redness, the majority cleared within 60 minutes of device removal, and the remainder cleared within 24 hours. Mild skin warmth was reported in two cases, but this dissipated within 15 minutes.

In terms of tolerability, peak levels of patient-reported pain occurred five minutes into the injection, but the level was low for most subjects, indeed, some described the experience as an unfamiliar sensation rather than pain. There were no requests to abort treatment, and for all subjects, pain was fully resolved 15 minutes after treatment, underlining the speed of recovery.

Overall, the vast majority of participants (91%) agreed that the device was comfortable to use, with the same proportion saying they felt confident in handling it independently at home without medical supervision.

A COMPELLING CASE FOR DEVICE COMPLEXITY

These study results send an unequivocal message regarding the significant untapped potential of OBDSs. They can enable patients with chronic conditions to benefit from convenient home-based treatment rather than relying on subcutaneous infusion in a medical facility. With LTS's Sorrel™ OBDS, the entire process is supported by data that confirm when an infusion occurred, if it was successful, how long it took, the precise volume of drug delivered and any potential user- or device-related errors.

Admittedly, however, this extensive technical capability comes with compromise: compared with other subcutaneous self-administration modalities, and indeed other OBDS platforms, Sorrel™ is inherently more complex from a design and engineering perspective.

As such, for applications where drug volumes are pushing the 2.25 mL threshold for autoinjector delivery, pharmaceutical and biotech organisations must consider which delivery route is more reliable for their injectable formulation, with the simpler option of a handheld, patient-controlled autoinjector pitted against the more sophisticated, software-controlled OBDS.

In this scenario, many factors will filter into the final calculation, from compliance and clinical outcomes to the cost of development and manufacture. Faced with such a complex decision-making process, there is a risk that judgement may be clouded by an inherent human bias towards simplicity, resulting in a tendency, in the pursuit of cognitive efficiency, to favour options that do not require more intense reasoning or analysis.[3] In this example, fewer device components and simpler functionality appear to signal fewer points of risk (and vice versa), leading to a flawed conclusion that autoinjectors are the preferable route.

"THIS EXTENSIVE TECHNICAL CAPABILITY COMES WITH COMPROMISE: COMPARED WITH OTHER SUBCUTANEOUS SELF-ADMINISTRATION MODALITIES, AND INDEED OTHER OBDS PLATFORMS, SORREL™ IS INHERENTLY MORE COMPLEX FROM A DESIGN AND ENGINEERING PERSPECTIVE."

SOFTWARE: ADDING A LAYER OF INVISIBLE DEVICE INTELLIGENCE

Upon closer inspection, the relationship between device complexity, functionality and reliability is not as simple as it seems. Perhaps counterintuitively, there is a strong argument that an OBDS, despite being a more technically advanced platform, represents a more reliable and predictable delivery option. This logic is explained by one of the core features that differentiate an electro-mechanical device from a purely mechanical one: software.

The control software within an OBDS is akin to the device's "brain", with responsibility for orchestrating operations and elevating the hardware into an "intelligent" system. One key aspect of this intelligence is the ability to capture the exact time, duration and successful completion of an infusion. Such data have the potential, permissions allowing, to be integrated into companion apps or healthcare provider networks.

Another key aspect is the ability of an OBDS to continually perform self-checks and encode this activity into memory, meaning that every device contains a fully traceable status history that can bring critical insights into product integrity. This provides valuable support for dosing reliability, as data on compromised integrity and the potential for a failed injection can be relayed from the device in the field, triggering its removal from circulation.

By way of contrast, it is helpful to highlight the inherent limitations of traditional mechanical delivery systems. Here, there is no ongoing monitoring or feedback on device status, meaning that there is no way to gain insights into the device's functionality or performance. During manufacturing, verification processes provide a layer of quality assurance, but once released into the supply chain, the absence of control software means these "dumb" units are not equipped to assess their own condition, detect degradation from environmental factors or respond to unexpected conditions during patient use. Factors such as temperature exposure, mechanical creep, ageing or transportation stress may significantly impact performance, but in the absence of a software-controlled "flagging" mechanism, such issues can remain undetected, only manifesting themselves through a fault at the moment of injection, resulting in wastage of a potentially high-value dose.

This can be thought of as an "open loop": without control software, there is no monitoring of delivery, detection of mechanical failures or intervention if something goes wrong. If, for example, there is increased tissue resistance, misalignment or incomplete actuation, the suboptimal mechanical device continues its process "blind", potentially resulting in a wet injection, incomplete dosing or patient injury.

"AN OBDS PLATFORM, SUCH AS LTS'S SORREL™, USES SOFTWARE TO CREATE A CLOSED LOOP, WHERE CORRECT PERFORMANCE OF CRITICAL DELIVERY FUNCTIONS CAN BE CONTINUOUSLY VERIFIED THROUGHOUT THE DEVICE'S LIFE AT FOUR KEY STAGES."

Conversely, an OBDS platform, such as LTS's Sorrel™, uses software to create a "closed loop", where correct performance of critical delivery functions can be continuously verified throughout the device's life at four key stages. If post-manufacturing checks highlight deviations, such as loss of intended positioning, the system can immediately detect, respond to and safely interrupt the injection process in real time – a fundamental reliability advantage that mechanical systems simply cannot provide.

- **Production Stage Verification:** During manufacturing, the OBDS software executes a comprehensive suite of automated tests performed on every single device to ensure repeatable and objective quality verification. These checks include position and alignment verification using indexed multisampling measurements, electrical validation and controlled actuation tests that validate movement consistency. All test results, including raw measurements and error events, are automatically recorded in a production database, providing full traceability and facilitating continuous improvement.

- **Pre-Treatment Validation (Pre-Client Test):** Before a patient begins treatment, the OBDS performs an automated, software-controlled self-test to ensure that it remains fully functional after shipping and storage. This sequence includes a built-in test of internal systems, battery validation and position verification to ensure correct alignment prior to delivery initiation. If any deviation is detected, a software-driven gating mechanism prevents treatment initiation and transitions the device to a safe fault state.

- **Real-Time Treatment Monitoring:** During drug delivery, embedded software algorithms continuously monitor device performance. Key functions include tracking delivery progress, verifying positioning and detecting flow-related anomalies inferred from actuation patterns. If any abnormality is detected, the device stops, retracts the on-body needle and registers the error.

- **Post-Treatment Data Traceability:** At the end of the treatment cycle, the device records a complete execution history stored in non-volatile memory, including treatment completion status, the full sequence of operational states and the cause of any fault conditions.

While autoinjectors might log and relay information on activation events, the OBDS lifecycle data log delivers a full, traceable audit of real-world events. It represents a rich seam of insight, even incorporating possible field failure modes that would otherwise remain hidden, thus allowing pharma companies to establish a feedback loop for continuous improvement of manufacturing and device performance.

DETAILING PERFORMANCE, EVIDENCING TOLERANCE

On reflection, it is no surprise that the technology for facilitating self-administration of injectable therapies continues to become increasingly complex. To provide an enhanced experience for patients, a device must have the in-built intelligence to monitor and manage each injection event, controlling the conditions for the safe and complete delivery of a dose, while also fuelling a data feedback loop to optimise manufacturing and treatment efforts. Such a multiplicity of objectives is only possible to achieve with more advanced layers of functionality. Add into this picture the industry's movement towards connected health and personalised medicine, and it is easy to see that complexity, far from being a multiplier of risk, is in fact the intelligent answer to delivering improved outcomes in the face of ever more complicated healthcare challenges.

With a combination of robust data on device performance and higher-volume dose tolerance, software-controlled wearable technologies root patient-centric injectable delivery in evidence and insight. In doing so, stakeholders can be assured that jeopardy is removed at the very moment it matters most, maximising the potential for the right dose to be delivered in the right way at the right time.

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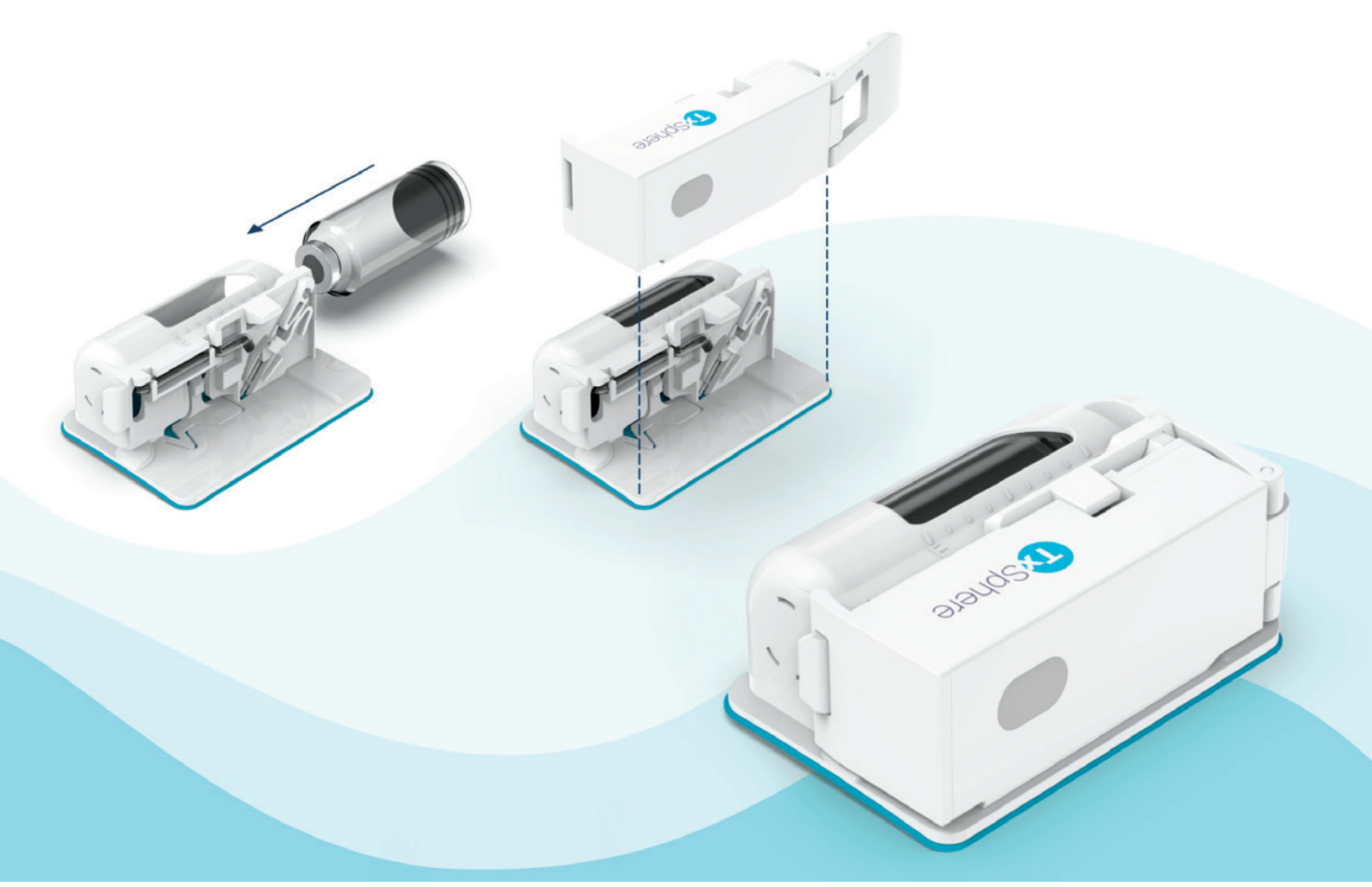

SCALING ON-BODY DELIVERY FOR LARGE-VOLUME THERAPIES

Dr Oliver Eden of **Jabil** and **Mike Stout** of **TxSphere** examine the shift towards large-volume subcutaneous administration, what on-body delivery systems make possible and why bringing them to market at scale depends as much on manufacturing as on design, going on to explore how the two companies' collaboration combines device innovation with engineering-led manufacturing to help bring these technologies to market.

Pharmaceutical development is undergoing one of its most significant transitions in decades. Advances in biologics and other complex injectable medicines are expanding therapeutic possibilities across oncology, immunology and many chronic diseases while simultaneously reshaping how those therapies are delivered to patients.

Unlike traditional small-molecule medicines, many of these therapies cannot be delivered orally and depend on parenteral administration throughout their commercial life. As pharmaceutical pipelines evolve, formulation scientists are increasingly working with larger dose volumes and more viscous drug products, creating engineering requirements that extend beyond the practical design envelope of conventional handheld injection devices.

The result is a broad transition from intravenous (IV) infusion towards subcutaneous (SC) administration wherever clinically appropriate. Patients increasingly expect treatment that fits more naturally around their everyday lives, healthcare systems continue to seek opportunities to reduce reliance on resource-intensive infusion services, and pharmaceutical companies are investing in drug-device combination products that

"AS THE TRANSITION FROM IV TO SC DELIVERY ACCELERATES, WEARABLE ON-BODY DELIVERY SYSTEMS ARE BECOMING AN INCREASINGLY IMPORTANT ENABLING TECHNOLOGY – CHANGING BOTH WHERE AND HOW PATIENTS RECEIVE INJECTABLE THERAPIES."

support self-administration and simplify lifecycle management across growing therapeutic portfolios.

Traditional autoinjectors remain the preferred solution for many injectable medicines. However, their practical operating range typically accommodates doses between approximately 0.3 and 2.25 mL, whereas many emerging biologics require substantially larger SC delivery volumes. Those evolving therapeutic requirements are accelerating innovation in wearable on-body injectors engineered specifically for larger-volume therapies.

In 2024, roughly 15% of all approved or clinical-stage IV and SC biopharmaceuticals were large-volume SC therapies – predominantly monoclonal and bispecific antibodies for cancer (41%) and autoimmune conditions (27%),[1] with most falling within the 2–20 mL range. Non-cancer therapies tend to sit in the lower 2–5 mL tier, within reach of handheld autoinjectors, while most cancer therapies fall within the 5–20 mL range and are still administered in hospitals or clinics – the part of the market where the demand for capable home-delivery systems is now concentrating. And the category is broadening beyond biologics; the US FDA's October 2025 approval of Lasix ONYU (SQ Innovation, Burlington, MA, US), an at-home SC furosemide combination for heart-failure oedema, extends on-body delivery to small-molecule therapies and everyday chronic-care management.

As the transition from IV to SC delivery accelerates, wearable on-body delivery systems are becoming an increasingly important enabling technology – changing both where and how patients receive injectable therapies. Responding to that opportunity increasingly requires collaboration between device innovators and manufacturing partners capable of supporting combination products from development through commercial scale.

ENGINEERING ON-BODY INJECTORS FOR LARGE-VOLUME SELF-ADMINISTRATION

Designing an effective on-body delivery system requires balancing two equally important objectives. It must accommodate the larger volumes, higher viscosities and broader range of formulations emerging from today's pharmaceutical pipelines while also remaining compact, intuitive and comfortable enough for patients to use with confidence. TxSphere has developed its platforms to be mindful of both.

An on-body injector changes the relationship between device and patient. Because it is adhered to the body rather than held in the hand, it is no longer constrained by the delivery window expected of a conventional autoinjector; delivery profiles can instead be optimised around patient comfort and tolerability rather than injection speed.

The slower infusion enabled by on-body delivery allows fluid to disperse gradually through the SC tissue and lymphatic system, reducing patient discomfort while improving tolerability. At a controlled rate, even relatively large volumes can be administered comfortably. For example, the transition of immunoglobulin therapies from IV to SC, where 50–60 mL per injection site is administered over roughly an hour, illustrates what becomes possible at the upper end of the dosing spectrum.[2]

Larger dose volumes also reduce the pressure to reformulate. Compressing larger therapeutic doses into smaller injection volumes requires increasing drug concentration and, as concentration rises, viscosity rises with it, introducing additional formulation and stability challenges for delivery devices designed around conventional handheld injection.[3] Considerations such as this are why the delivery device can no longer be considered a late step in drug product development. Designing and validating the drug and device together in the early phases of development is more crucial than ever for patient success.

By accommodating larger dose volumes, on-body injectors give formulation scientists greater flexibility to optimise the therapy rather than the delivery constraint. Lower viscosities can improve formulation stability while reducing the need for high-force delivery mechanisms that complicate both device design and manufacturing. Together, these advantages simplify development, shorten timelines and expand opportunities for SC self-administration across a broader range of therapies. The device should adapt to the drug formulation, not the other way around.

DESIGNING A WEARABLE THAT PATIENTS WILL ACCEPT

Engineering performance alone does not determine the success of a delivery platform – patient acceptance is equally important. A wearable device intended for long-term therapy must be compact, intuitive and comfortable enough that patients are willing to incorporate it into their everyday lives. Many existing wearables are simply

"THE SLOWER INFUSION ENABLED BY ON-BODY DELIVERY ALLOWS FLUID TO DISPERSE GRADUALLY THROUGH THE SC TISSUE AND LYMPHATIC SYSTEM, REDUCING PATIENT DISCOMFORT WHILE IMPROVING TOLERABILITY. AT A CONTROLLED RATE, EVEN RELATIVELY LARGE VOLUMES CAN BE ADMINISTERED COMFORTABLY."

just too large and cumbersome to be acceptable for consistent use. Ultimately, the success of any wearable platform depends in part on a simple question – will patients actually use it?

Despite exceptional advancements in therapeutics and medical devices since the WHO published its foundational adherence report in 2003, current clinical data continue to frame a frustrating reality: long-term adherence rates for chronic illnesses in developed nations still hover around 50%.[4] Decades ago, US Surgeon General C Everett Koop emphasised the point in deliberately plain language – drugs do not work in patients who do not take them.

TxSphere's answer to these challenges is to miniaturise a precedented technology rather than introduce a novel one, an approach Jabil found compelling given its vast experience manufacturing device sub-assemblies. At the core of the platform is a linear volumetric peristaltic pump, derived from the company's experience in infusion pump development – a mechanism with a long clinical track record, reduced to a scale that can be worn. The architecture is modular and two-piece: a reusable pump module and a disposable drug container holding the drug reservoir and an automated soft cannula injector.

TxSphere's first on-body injector, introduced late in 2024, delivers at least 10–20 mL from an integrated internal reservoir while remaining not much larger than an insulin patch pump. The company's newer addition retains those innovations but draws medication from standard vials or cartridges rather than an internal reservoir. That change required a moderate increase in size while preserving the compact form factor and, in return, delivers compatibility with established filling, storage and distribution infrastructure. Together, the two devices offer developers a genuine choice: one prioritises the patient experience with a slightly less efficient filling process, while the other prioritises efficiency in filling, storage and distribution (Figure 1).

The automated soft cannula is concealed from view and inserted gently, and is more comfortable than a needle over an extended wear period. Preparation takes only a few steps – insert the vial or cartridge into the disposable drug container, connect the pump, adhere it to the skin and press "Run" (Figure 2) – with sensors verifying each action before delivery begins, reducing the risk of user error and the wasted doses that follow from it. Delivery is hands-free, so normal activity can continue during the infusion.

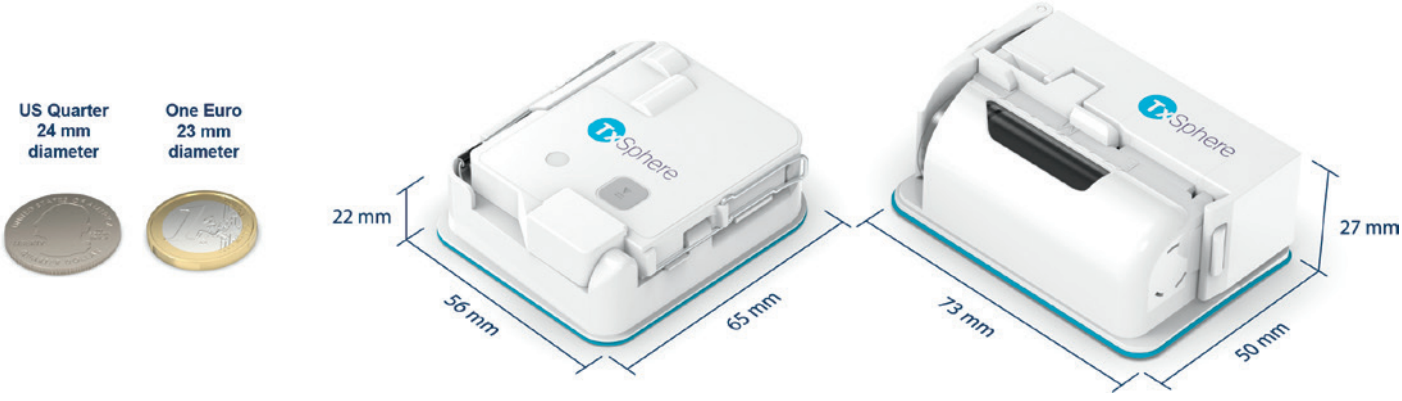

Figure 1: Left – TxSphere's wearable injector with internal reservoir. Right – TxSphere's wearable injector for standard vial/cartridges. Both depicted in 10 mL configurations.

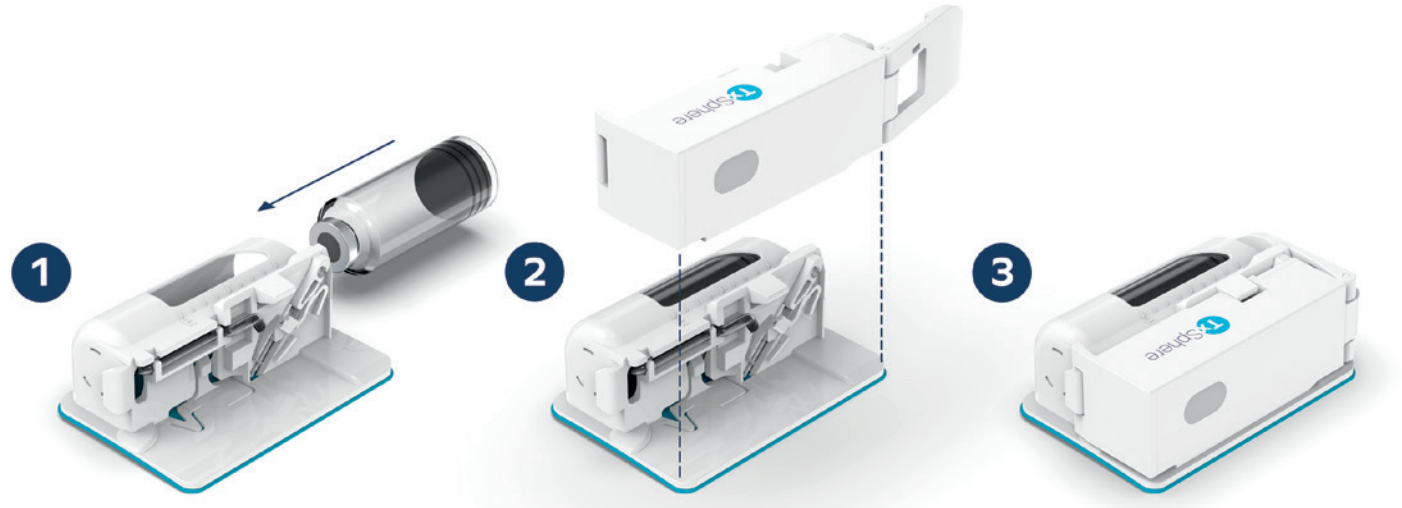

Figure 2: The two-piece modular platform of TxSphere's wearable injectors consist consists of a reusable pump and a disposable drug container for standard vials and cartridges. Three steps are all that is needed to deliver an injection.

"PROVEN MANUFACTURING AND COMMERCIALISATION EXPERTISE EFFECTIVELY SERVE AS A BARRIER TO ENTRY AND, WHERE IT CANNOT BE BUILT ORGANICALLY, THE PRACTICAL ROUTE TO ACHIEVE IT IS PARTNERSHIP."

Because TxSphere wearables draw medication from the reservoir rather than forcing it under high pressure, neither the drug product nor its primary container is subjected to the stresses associated with high-force mechanical delivery. This reduces the need for robust, specialised container solutions while accommodating a broad range of dose volumes, delivery rates and viscosities. It also gives developers greater flexibility to work with lower-concentration formulations, including those using permeation enhancers. By addressing formulation, container and delivery considerations together, the platform simplifies development and helps accelerate the path to commercialisation.

The platform's modular architecture also reflects the industry's growing emphasis on sustainability. Many wearables and autoinjectors require disposal of the entire unit after each use. Reusing the electromechanical components while discarding only the sterile fluid path reduces waste and lowers the cost per dose across long-term treatment programmes – an economic plus as much as an environmental one.

COMBINING PROVEN TECHNOLOGY WITH PROVEN MANUFACTURING

As pharmaceutical companies expand investment in large-volume SC therapies, their success will depend on how effectively device engineering, primary packaging, fill-finish and manufacturing are developed together. Device performance, supply chain resilience and commercial scalability all become part of the evaluation for drug manufacturers who are, by nature, risk averse. Proven manufacturing and commercialisation expertise effectively serve as a barrier to entry and, where it cannot be built organically, the practical route to achieve it is partnership.

This is the basis of the manufacturing collaboration between TxSphere and Jabil, under which Jabil will manufacture TxSphere's reusable on-body injector technology, with the option to integrate fill-finish services for the device's primary drug pack within the same manufacturing ecosystem. The collaboration reflects Jabil's broader strategy to meet the needs of a changing market by expanding offerings across the combination product lifecycle. In the past two years, Jabil has completed the strategic acquisition of Pii (Hunt Valley, MD, US) for drug development and sterile fill-finish and expanded its collaboration with Kymanox (Morrisville, NC, US) for design and regulatory consultation. Today, Jabil offers total system design and manufacturing, from drug development through aseptic fill-finish and secondary packaging.

Traditionally, formulation development, device selection, primary packaging, fill-finish and commercial manufacturing have progressed as sequential workstreams managed across multiple organisations. Each discipline contributes important expertise, but co-ordination between them frequently occurs only after significant design decisions have already been made. In addition, each hand-off or transition between suppliers can introduce risk and cause delays.

As injectable therapies grow more complex, this sequential model constrains flexibility precisely when a programme would most benefit from preserving it; an integrated model, on the other hand, approaches these disciplines as elements of a single engineering system. Design engineering informs manufacturability; primary packaging decisions shape delivery platform selection; fill-finish strategy develops alongside the device architecture; and supply chain planning begins during development rather than after approval.

TxSphere contributes the delivery platform and device design expertise. Jabil contributes design-for-manufacturability, advanced healthcare manufacturing at global scale and sterile fill-finish for the primary drug pack. The platform accommodates multiple primary pack configurations across a dosing range of 3–50 mL on a reusable drive unit, so a single architecture can serve a broad portfolio rather than requiring a new device programme for each asset.

Jabil has applied this systems-thinking approach across multiple drug-delivery programmes, including development of the Qfinity™ reusable autoinjector platform, where design-for-manufacturability, modularity and sustainability have been treated as engineering requirements from the outset rather than as later refinements. Applied to on-body delivery, the same discipline speaks to what pharmaceutical companies weigh most heavily when selecting a large-volume device – confidence that it can be made consistently, at volume, to the standards a combination product requires.

FROM CONCEPT TO COMMERCIALISATION, PARTNERSHIP DELIVERS

For the next generation of injectable therapies, the combination product itself is increasingly becoming the innovation. Engineering-led collaboration between pharma technology development teams and manufacturing solutions partners will play

"AS INJECTABLE THERAPIES GROW MORE COMPLEX, THIS SEQUENTIAL MODEL CONSTRAINS FLEXIBILITY PRECISELY WHEN A PROGRAMME WOULD MOST BENEFIT FROM PRESERVING IT; AN INTEGRATED MODEL, ON THE OTHER HAND, APPROACHES THESE DISCIPLINES AS ELEMENTS OF A SINGLE ENGINEERING SYSTEM."

an important role in translating promising molecules into practical, patient-centric therapies that can be delivered confidently, consistently and at scale.

The pipeline continues to move towards larger dose volumes, higher viscosities and care delivered outside traditional clinical settings. No single delivery technology will serve every development programme, but the opportunities for on-body delivery continue to expand as pharmaceutical pipelines evolve. The platforms that succeed will be those that combine thoughtful engineering with the industrial capability required to translate innovation into commercial reality.

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Oliver Eden, PhD, is a Senior Business Unit Director at Jabil for its Pharmaceutical Solutions division. Dr Eden brings experience from previous roles at Nypro (now Jabil) and Catalent Pharma Solutions. He holds a PhD in Biomaterials Engineering and Master's in Mechanical Engineering from the University of Exeter (UK). Dr Eden possesses a robust skill set that includes pharmaceuticals, forecasting, new business development, product development, biotechnology and more.

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Mike Stout, 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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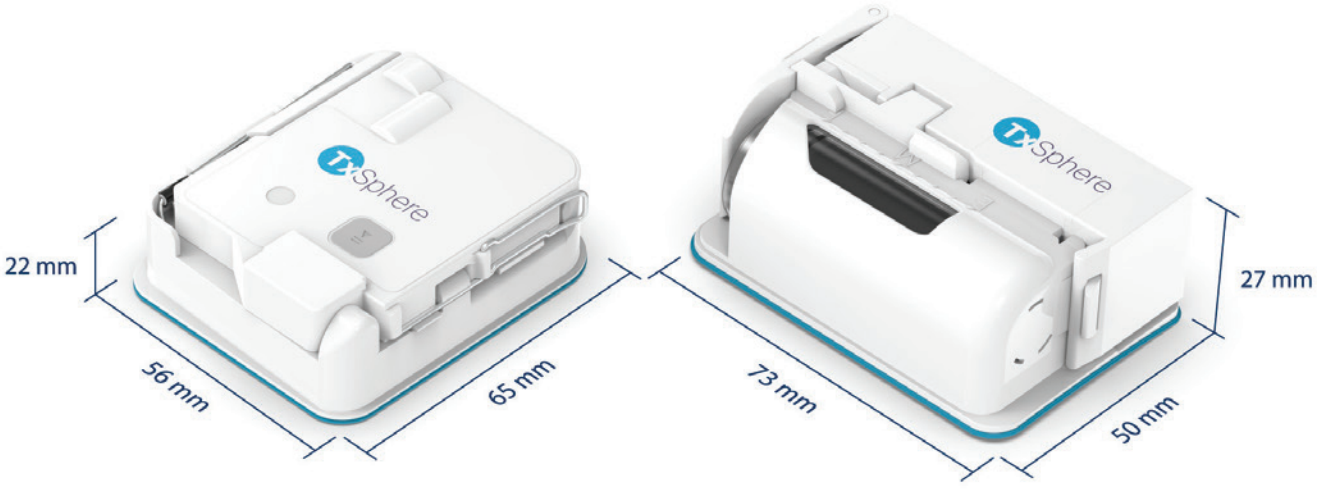

Precision-Manufactured for Commercial Scale

TxSphere's innovative on-body injector platforms are developed and manufactured in partnership with Jabil — combining device innovation with drug product development, aseptic fill/finish, and global manufacturing scale. One partnership, from first-in-human through commercial launch.

Contact us to find the right platform for your combination product program.
TxSphere LLC | Natick, MA
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TxSphere

LIMITS SHATTERED: ENDING THE AUTOINJECTOR AND WEARABLE INJECTOR DIVIDE

Dr Scott Russo of **Synolus Medical**

questions the distinction between wearable injectors and autoinjectors, making the case that it is not fundamental to device design, rather it is an outdated segmentation that results in unnecessary design trade-offs. He introduces MiniGo, a next-generation platform device that aims to overcome this false dichotomy.

For decades, the drug delivery industry has treated autoinjectors and wearable injectors as two distinct categories, each with its own strengths, limitations and trade-offs. Autoinjectors have traditionally offered simplicity and convenience but have been constrained by volume limitations, whereas wearable injectors have enabled larger-volume delivery but often at the cost of increased size, complexity, user burden and expense.

Ultimately, every engineering decision made during the development of a delivery device for a biologic is reflected in the patient's treatment experience. The simpler and more intuitive that experience becomes, the greater the opportunity to empower patients to confidently self-administer their therapy. The delivery of a biologic should not be about choosing between an autoinjector or wearable injector – it should be about choosing a platform that redefines both.

A MATTER OF THINKING, NOT A DELIVERY PROBLEM

For years, drug delivery systems have been developed around the limitations of legacy architectures. Device categories emerged as engineering solutions to solve specific constraints and, over time, those categories have become accepted as fixed realities. A hidden challenge in biologic development is the classic chicken-and-egg scenario, where delivery architecture decisions are often needed while the therapy itself is still evolving.

This situation does not arise because of anything fundamentally demanded by the therapy, but rather because existing delivery technologies require these parameters to be defined before the device development process can progress confidently. The result is a landscape built around compromise. Formulation scientists work to balance dose level, concentration, viscosity and injected volume, while delivery system teams concurrently work to lock in these parameters to select a delivery architecture direction.

A volley of questions between formulation and delivery system teams therefore ensues, as the question becomes "How can a programme confidently select a delivery architecture when the final formulation profile is still evolving?" Conversely, "How can the formulation be finalised if delivery architecture selection is still evolving as well?" This unfortunate dynamic has become so familiar that it goes unquestioned. Historically, this is because delivery limitations have forced developers to work within boundaries defined by legacy systems and outdated thinking, sometimes requiring additional formulation optimisation to make the therapy compatible with the selected delivery approach.

As a result of this dynamic, the therapy often gets adjusted around the limitations of the delivery system, rather than the delivery system accommodating the formulation and dose that would provide the optimal therapeutic outcome. Furthermore, the division between autoinjectors and wearable injectors is not biologically dictated, it has become disjointed from biological or clinical need and is a consequence of historical engineering limitations and entrenched assumptions.

> "THE DIVISION BETWEEN AUTOINJECTORS AND WEARABLE INJECTORS HAS BECOME DISJOINTED FROM BIOLOGICAL OR CLINICAL NEED AND IS A CONSEQUENCE OF HISTORICAL ENGINEERING LIMITATIONS AND ENTRENCHED ASSUMPTIONS."

THE FALSE TRADE-OFF

Today's drug delivery landscape forces pharmaceutical companies to make unnecessary compromises. Autoinjectors provide simplicity in some areas but are limiting when it comes to delivering large doses, often imposing heavy constraints and demanding increasingly complex formulations or administration concessions. Although the industry has come to accept these compromises as unavoidable, they are largely the consequence of historical delivery architectures, rather than any fundamental technical or therapeutic barriers.

Unnecessary trade-offs not only hamper the patient experience but also extend development timelines, add manufacturing complexity and delay commercialisation. As biologic and other injectable therapy requirements continue to advance, such trade-offs become progressively more restrictive. Over time, the industry has largely normalised these inefficiencies. The opportunity now is not to simply optimise around those compromises but to eliminate them.

FROM DEVICE SELECTION TO PLATFORM STRATEGY

Drug delivery architecture should no longer be viewed as a project-specific device selection activity, but as a portfolio strategy. The traditional approach often requires multiple delivery systems across a pipeline, creating additional development work, regulatory complexity, manufacturing variability and supply chain inefficiency.

A true platform approach can change the equation. Rather than force development programmes to transition between different device categories as dose, concentration, viscosity or volume requirements evolve, a true platform approach can provide a continuous delivery architecture designed to support the therapy throughout development and commercialisation, creating operational consistency, reducing risk and preserving flexibility throughout the product lifecycle. Importantly, a platform approach can allow pharmaceutical companies to focus on optimising the therapy rather than yield to device constraints.

WHAT WOULD A TRUE PLATFORM LOOK LIKE?

The term "platform" is used widely throughout the drug delivery industry. However, many so-called platforms still require programme-specific adaptation or molecule-specific customisation. A true biologic delivery platform would remove the historical boundaries that have constrained formulation and delivery decisions – it would not be defined by traditional categories of low-volume or high-volume delivery, but by its ability to support a therapy as it evolves.

A true drug delivery platform would, therefore, provide formulation scientists with greater freedom by supporting a broad range of dose volumes and viscosities without requiring fundamental changes to the device architecture or molecule-specific redesigns. It would also need to integrate naturally into pharmaceutical development, established manufacturing processes and existing fill-finish infrastructure. Most importantly, it would provide a simple and intuitive experience for the patient, regardless of the final formulation strategy. In other words, it would eliminate the traditional trade-offs that have defined the market for decades.

INTRODUCING A NEW APPROACH

MiniGo by Synolus Medical was developed from a simple first principle – what would the ideal patient experience look like? Everything else, from engineering and pharmaceutical development to manufacturing and commercialisation, followed from that question. The result is not just another autoinjector or wearable injector; it is the first standardised crossover delivery platform designed to support

broad formulation flexibility, including a practical delivery range from 1 to 15 mL and high-viscosity capability, without a special configuration for each new molecule or changing dose.

Enabled by its OmniDrive self-regulating flow technology, MiniGo manages changing delivery conditions by adapting to the requirements of the formulation and the patient. In drug delivery, mechanical resistance arises from both tissue and drug attributes, demanding significant changes in working pressures (both in magnitude and direction) to manage. MiniGo responds to this using self-adjusting forces and thus self-regulates delivery. This is not multiple architectures with multiple configurations; this is one power-pack – one device.

Figures 1 and 2 focus on 1–5 mL and 1–10 mL MiniGo configurations, which encompass much of the immediate interest in the platform. MiniGo's ultra-high-viscosity capability can enable more concentrated formulations to remain within compact dose volumes, reducing the need for dilution or migration to larger-volume delivery devices where the molecule permits. For programmes requiring larger doses, the same scalable OmniDrive self-regulating flow architecture extends across the full 1–15 mL MiniGo platform.

Rather than developing a new delivery solution for each therapeutic opportunity, MiniGo enables pharmaceutical companies to evaluate and commercialise a full range

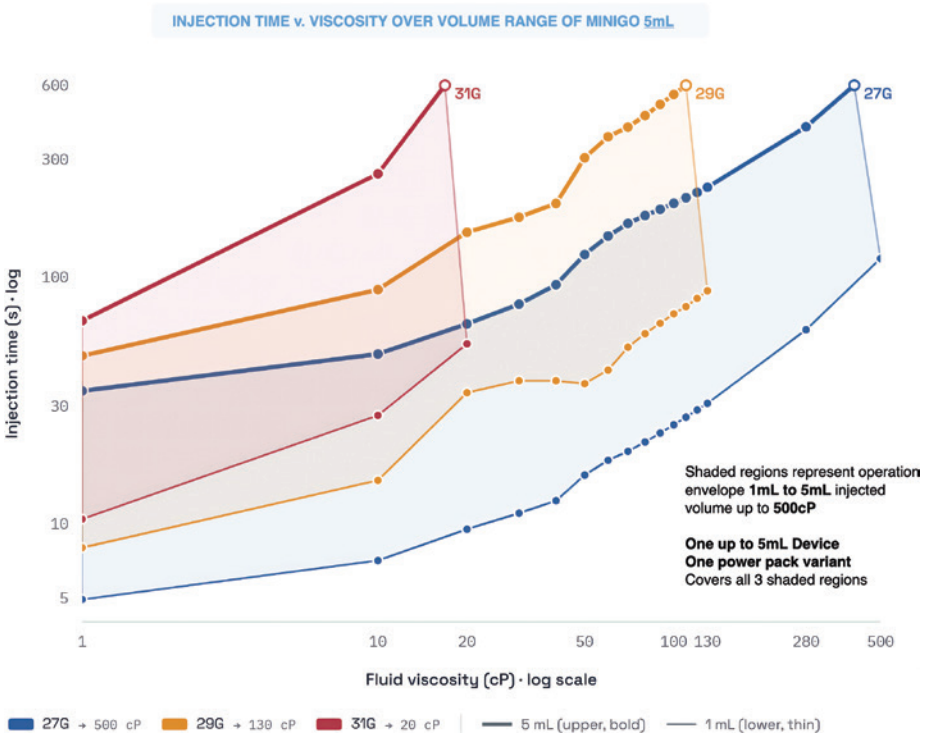

Figure 1: MiniGo 5 capabilities range. The shaded regions represent the 1–5 mL operating envelope supported by a single MiniGo 5 drive configuration.

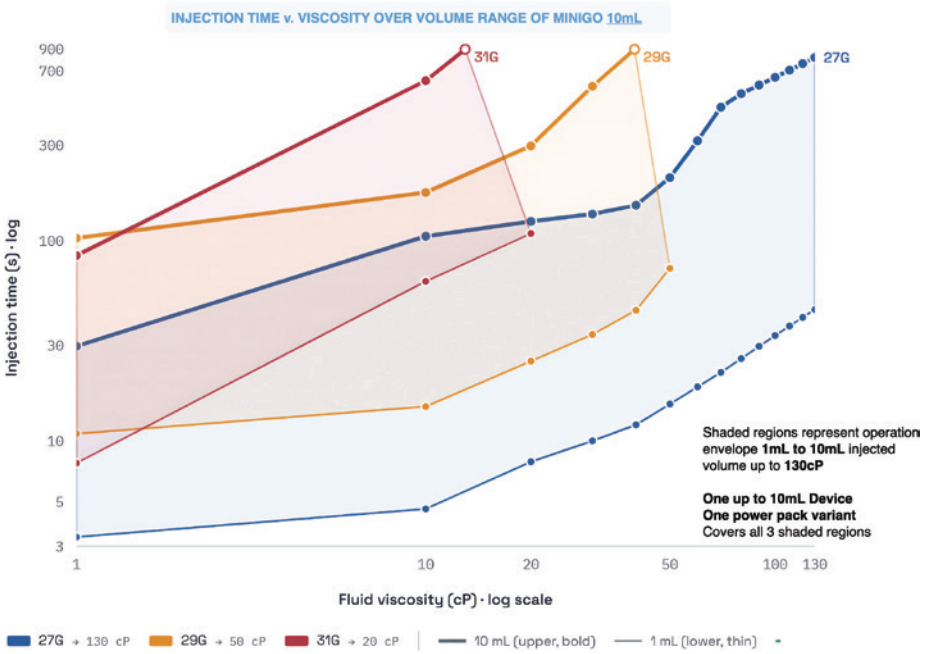

Figure 2: MiniGo 10 capabilities range, shown through 130 cP, the highest viscosity data point currently available at the full 10 mL injected volume. The shaded regions represent the 1–10 mL operating envelope supported by a single MiniGo 10 drive configuration.

"RATHER THAN DEVELOPING A NEW DELIVERY SOLUTION FOR EACH THERAPEUTIC OPPORTUNITY, MINIGO ENABLES PHARMACEUTICAL COMPANIES TO EVALUATE AND COMMERCIALISE A FULL RANGE OF THERAPIES USING THE SAME STANDARDISED PLATFORM, REPLACING THE FRAGMENTED LEGACY MODEL WITH ONE COMMON APPROACH."

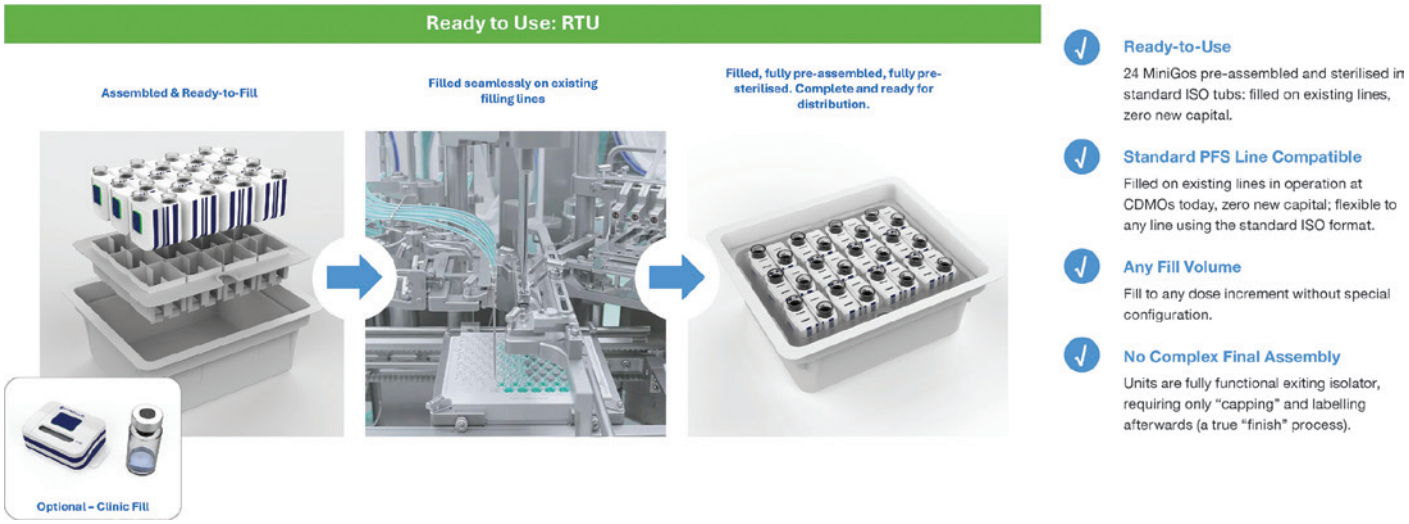

Figure 3: A revolutionary approach – MiniGo ready-to-use for seamless integration into existing prefilled syringe operations with clinic-fill optionality on the same device.

of therapies using the same standardised platform, replacing the fragmented legacy model with one common approach. MiniGo is the first embodiment of this platform philosophy, translating first-principles thinking into practical, industry-redefining delivery solutions.

MiniGo was engineered from the outset with manufacturability, scalability and commercial competitiveness in mind. By simplifying platform architecture and reducing unnecessary complexity, it not only delivers technical and patient advantages but also achieves unit-cost economics that compete with conventional autoinjector technologies (Figure 3).

The true economics of drug delivery systems extend well beyond the cost of the delivery device itself. Manufacturing efficiency, packaging, logistics, patient preference, persistence and commercial differentiation all contribute to what might be described as "autoinjector economics". A standardised platform has the potential to improve value across the entire product lifecycle, not simply reduce the cost of the delivery device.

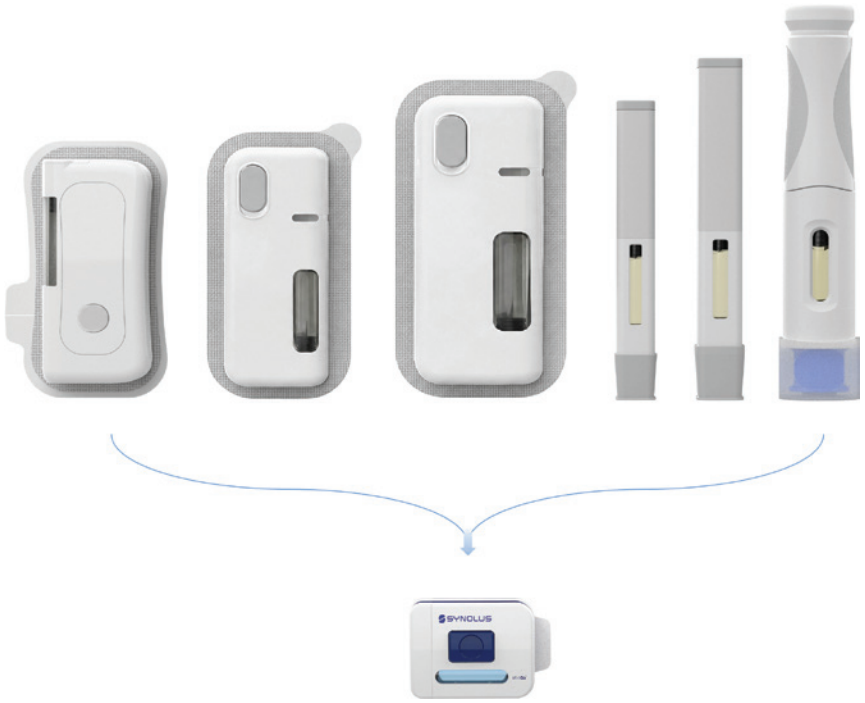

Figure 4: Multiple conventional injection-device architectures converge into one compact MiniGo platform, providing broader delivery flexibility while using standard ISO tubs and existing filling lines with no complex final assembly.

DESIGNED FOR PATIENTS, BUILT FOR PHARMA

While platform efficiency is critical, whether or not the delivery is successful is ultimately decided by patients. Complexity creates friction. Friction reduces confidence. Reduced confidence can negatively impact adherence. Conversely, simplicity builds confidence, and greater confidence has the potential to support stronger adoption, improved persistence and greater resilience throughout a product's commercial life. MiniGo was designed to remove friction throughout the product lifecycle, from pharmaceutical development to point of care (Figure 4).

The design journey of MiniGo began with a grounding philosophy of simplifying patient experience through a prefilled, pre-assembled architecture, requiring only three simple actions – peel, stick, click. By boiling down the patient interaction to its simplest form, the MiniGo platform supports confident, intuitive and independent self-administration.

The impetus to achieve such simplicity is more than just a design objective –

it is a need directly voiced by patients. A formal user preference study conducted by Bold Insight (Chicago, IL, US), involving 400 current autoinjector users, reinforced that philosophy. A total of 83% of participants stated that they would be likely to switch from their current injection therapy to MiniGo, while 94% of current autoinjector or wearable users rated MiniGo as more convenient because of its hands-free administration. While engineering makes the platform possible, it is the patient experience that ultimately determines its success. For pharmaceutical companies, that simplicity creates value far beyond the patient experience, supporting stronger adoption, greater persistence and more consistent real-world outcomes.

Furthermore, MiniGo offers patients something that is rarely considered in biologic delivery – freedom of choice. For longer administrations, the platform can be comfortably worn hands-free, removing the burden of long hold times from patients. For shorter administrations, it can simply be held comfortably in place throughout the injection. The platform adapts to both the therapy and the patient, not the other way around.

Figure 5: Synolus MiniGo device platform.

THE NEXT ERA OF BIOLOGIC DELIVERY

The next era of biologic delivery will not be defined by larger and more complex devices – it will be defined by smarter platforms that remove historical constraints between the therapy, the manufacturer and the patient. Today, the biologics market is being shaped by two powerful trends that are both moving towards the same point. Firstly, native subcutaneous therapies are advancing towards higher therapeutic doses. Secondly, traditional intravenous biologics are increasingly being reformulated for subcutaneous administration.

Both trends create similar delivery challenges, requiring greater flexibility across dose, concentration, viscosity and volume. This convergence requires a new type of delivery architecture, one capable of supporting the evolving needs of biologic therapies, without being vulnerable to forced transitions between device categories as formulations develop.

Furthermore, these trends are exposing the limitations of legacy device categories. The historical division between autoinjectors and wearable injectors was created by engineering constraints, not by the needs of the biologics themselves. The next generation of biologic delivery should not require choosing between those categories; it should eliminate the need for that distinction altogether.

> "THE NEXT ERA OF BIOLOGIC DELIVERY WILL NOT BE DEFINED BY LARGER AND MORE COMPLEX DEVICES – IT WILL BE DEFINED BY SMARTER PLATFORMS THAT REMOVE HISTORICAL CONSTRAINTS BETWEEN THE THERAPY, THE MANUFACTURER AND THE PATIENT."

CONCLUSION

For decades, the industry has accepted a fundamental trade-off between simplicity and capability. Autoinjectors represented one side of that equation and wearable injectors represented the other. The next generation of biologic delivery demands something different – a crossover platform that removes compromise, simplifies development, improves the patient experience and supports the future of biologics (Figure 5). The end of autoinjectors and wearable injectors as we know them is not a prediction; it is the logical outcome of better design.

MiniGo is a platform currently under development. It has not received FDA clearance or approval.

Dr Scott Russo

Scott Russo, PhD, is Founder and Chief Executive Officer of Synolus Medical. A mechanical engineer with a focus in biomechanics, Dr Russo founded Synolus in 2020 after leading the development and commercialisation of more than 10 medical devices across orthopaedics, drug delivery and ophthalmology, spanning diagnostic, surgical and therapeutic applications. Prior to Synolus, he held senior leadership positions at Unilife and AstraZeneca, and served as Chief Technology Officer at Volk Optical (Halma).

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Company Showcase

GRAND RIVER ASEPTIC MANUFACTURING

Grand River Aseptic Manufacturing's (GRAM's) operations are focused on a strong commitment to sterile filling. GRAM prioritises patient safety by adhering to strict aseptic standards and collaborating closely with each client, using its extensive expertise to generate optimal outcomes.

GRAM's Sterile Filling Facility One opened in 2020 and features production lines approved by both the EU and the US FDA. The facility has the capacity to produce over 80 million vials as well as more than 10 million syringes and cartridges per year.

"FOR PHARMACEUTICAL COMPANIES, CHOOSING A CDMO GOES BEYOND ASSESSING CAPACITY; IT IS ABOUT FINDING A PARTNER COMMITTED TO QUALITY AND INNOVATION."

Sterile Filling Facility Two is the company's newest sterile filling facility, equipped to provide over 50 million units of syringe and cartridge filling capacity annually, starting with Line 5 (Table 1). This facility includes the infrastructure needed for future expansion to support client needs and meet market demand.

Line 1: Liquid & Lyophilised Vials	Line 2: Liquid Vials	Line 3: Prefilled Syringes & Cartridges
• Bausch+Ströbel • SKAN isolator • 4-head • IMA lyophiliser • 2R, 6R, 10R, 20R, 50R • 20 million units/yr • 6,200 lyo hr/yr • EU/FDA approved	• Bausch+Ströbel • SKAN isolator • 4-head • 2R, 6R, 10R, 20R, 25R • Up to 12,000 units/hr • 20–25 million units/yr • Identical to Line 1 • EU/FDA approved	• Bausch+Ströbel • SKAN isolator • 1/2-head • PFS: 1, 2.25, 3 mL • Cartridges: 3, 5, 10, 20 mL • 1,000–3,000 units/hr • 8–10 million units/yr • EU/FDA approved
Line 4: Liquid Vials	**Line 5: Prefilled Syringes & Cartridges**	**Available Future Space**
• Bausch+Ströbel • SKAN isolator • 8-head • 2R, 6R, 10R • External vial washer • 24,000 units/hr • 40–50 million units/yr	• Groninger • SKAN isolator • 10-head • PFS: 1, 2.25, 3 mL • Cartridges: 5, 10 mL • 24,000 units/hr • 40–50 million units/yr • Media Runs Q1 2027	Space and utilities to support three additional fill lines and client-dedicated projects 

Table 1: GRAM's fill-finish lines.

For pharmaceutical companies, choosing a CDMO goes beyond assessing capacity; it is about finding a partner committed to quality and innovation. GRAM is dedicated to delivering consistent, high-quality sterile fill-finish services that empower pharmaceutical companies in their mission to improve patient outcomes. Specialising in biologics, GRAM's five filling lines serve pharma's liquid or lyophilised vial, syringe and cartridge products.

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Image of the new sterile filling platform taken during the FAT. Source: groninger

DESIGN VERIFICATION FOR THE REAL WORLD: COMPLEX DRUG DELIVERY IN UNCONTROLLED ENVIRONMENTS

Dr Matthew Roberts and **Andrew Fiorini**, both of Cambridge Design Partnership, explore the key steps involved in building a successful design verification programme for ambulatory electromechanical infusion systems and share the lessons they have learned along the way.

Large-volume drug delivery is a rapidly growing industry, as more biologics, oncology therapies and treatments for chronic conditions move from hospital-administered infusion into home and self-administered settings. Many of these drug products require a subcutaneous infusion pump, changing the way infusion pumps are being used. This has resulted in increased regulatory scrutiny of how these devices perform once they leave controlled testing conditions (Figure 1).

DESIGN VERIFICATION TESTING OF AMBULATORY INFUSION PUMPS

For electromechanical ambulatory infusion pumps, design verification (DV) typically begins with the International Electrotechnical Commission (IEC) standard IEC 60601-2-24. However, demonstrating safe and effective drug delivery in real-world use extends beyond the standard's scope. The Association for the Advancement of Medical Instrumentation (AAMI)'s Technical Information Report (TIR) 101:2021 addresses this gap, with particular relevance to ambulatory, self-administered systems, where the gap is widest.

It is noteworthy that, although this report provides extensive guidance as to how to test and report system performance, it leaves manufacturers responsible for defining the conditions under which performance should be verified. Self-administration conditions introduce additional complexities, and success depends on understanding the delivery system before testing begins.

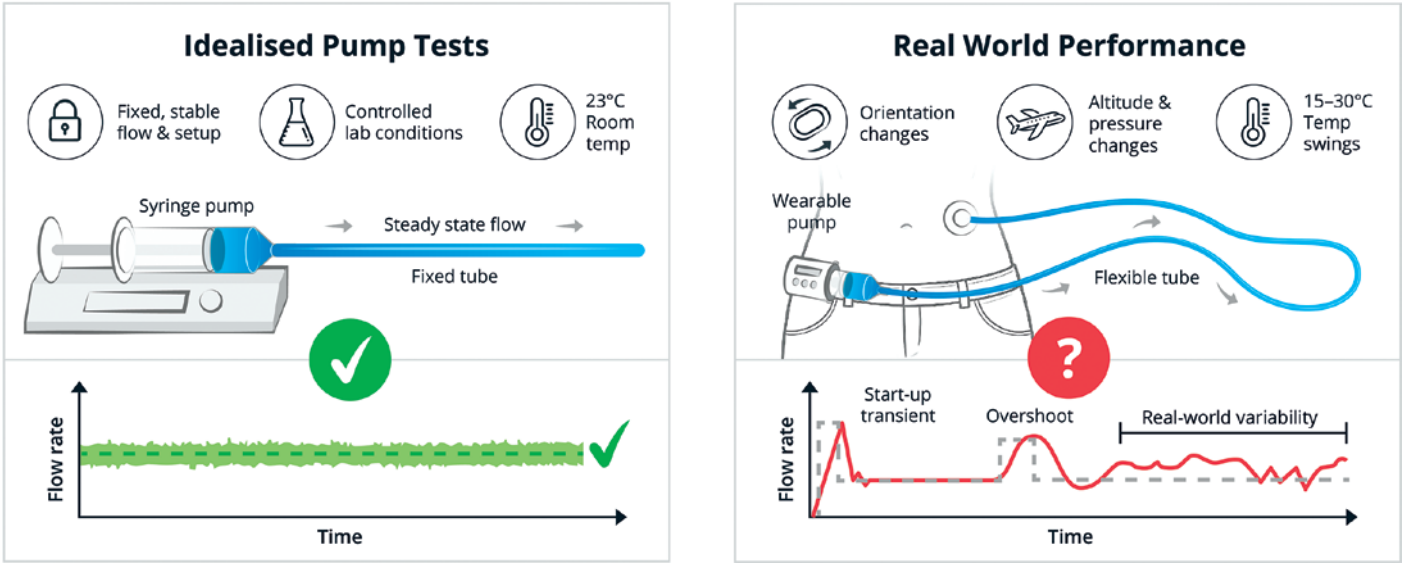

Figure 1: The real-world performance of modern, complex drug delivery systems can differ significantly from that indicated by standard laboratory pump tests.

BEYOND IEC 60601-2-24

IEC 60601-2-24 is the internationally recognised standard for electromechanical infusion pumps, syringe pumps and volumetric infusion controllers, providing a well-established framework for accurate and consistent drug delivery in both clinical and ambulatory settings.

The most complex pumps that the standard defines are Type 5 profile pumps that can combine basal and bolus delivery of drug products to manage symptoms that can fluctuate through the day. Insulin pumps for diabetes and apomorphine pumps for the management of Parkinson's disease are two such products, delivering a basal rate for most of the day and patient-controlled boluses to manage mealtimes (for diabetics) or "off" episodes for patients with Parkinson's disease. Whereas most pump testing described in IEC 60601-2-24 should be conducted with Class III water, pumps intended for use with a specific drug should be tested with that drug.

Water for injection behaves differently from many modern drug products, which may be highly viscous or exhibit non-Newtonian behaviour. At-home use introduces further variables that can affect performance and the dose received by patients:

- Pronounced temperature swings that, compared with clinical settings, can affect both formulation properties and catheter behaviour
- Delivery profiles often include patient-triggered bolus doses or variable flow rates, making transient performance important
- Pumps may be worn at different heights, orientations and locations on the body throughout the day.

To address the gap between IEC 60601-2-24 and real-world conditions, the AAMI published TIR101 in 2021, introducing test methods and reporting metrics that better reflect ambulatory and self-administered use conditions.

The sponsor is expected to define, justify and execute a statistically robust DV programme that demonstrates that the system performs as intended and the level of risk presented to patients is within acceptable limits. This flexibility is valuable but creates challenges: sponsors must consider which variables matter most for their drug-device combination and ensure that their testing strategy is both scientifically justified and regulatorily defensible.

DV testing of complex drug products using the AAMI TIR101 guidance can appear daunting, but it can be effectively managed by following three key steps:

1. Define the test matrix and reporting metrics
2. Design and de-risk the testing programme
3. Execute the DV testing.

From experience, more than 80% of the work lies in designing and de-risking the test programme itself – this is particularly true under AAMI TIR101. Unlike many traditional standards, with tightly defined test conditions, AAMI TIR101 leaves sponsors responsible for the test matrix, environmental conditions and acceptance criteria. Success depends heavily on the characterisation work performed before formal testing begins. Failure to prepare adequately can jeopardise a programme, resulting in repeated testing and delaying submissions by several months. However, with the right planning and a risk-based approach, even highly complex systems can be verified efficiently and with confidence.

ESTABLISH THE TEST MATRIX AND REPORTING METRICS

Despite provision of details on how to measure, what to report and how to structure the data, TIR101:2021 does not contain acceptance criteria. It is up to the sponsor to justify which tests are applicable, what results are acceptable and how confidently those results can be trusted.

Establishing acceptance criteria starts with understanding patient dosage sensitivity, including minimum effective dose and clinically meaningful dose variation. Unlike IEC 60601-2-24, which focuses on pump performance, TIR101 views this through the lens of patient self-administration, evaluating drug concentration fluctuations using pharmacokinetic coefficient of short-term variation (PK-CV) methods. This should also drive the pump specification. TIR101:2021 requires testing at the lower and upper limits of pump flow rates – allowing the pump to operate outside clinically useful windows can significantly increase the complexity and timescales of DV (Figure 2).

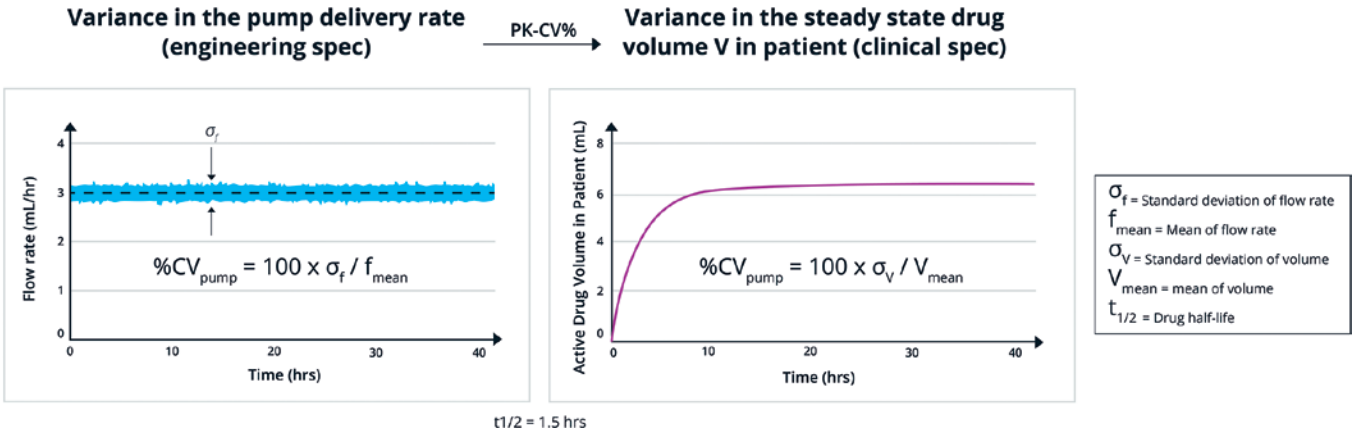

Figure 2: In the PK-CV mode, drugs with a longer half-life will have a higher active volume in the patient and will be less sensitive to variance in pump flow rate.

"A PUMP WITH AN ESTABLISHED PERFORMANCE HISTORY AND EXISTING APPROVALS CAN CARRY A SMALLER, BETTER-UNDERSTOOD TEST MATRIX THAN A NEWLY DEVELOPED PLATFORM, IF ITS SPECIFICATIONS ARE UPDATED TO MEET THE SPECIFIC USE CASE."

The test matrix should reflect all clinically relevant operating conditions. Every claimed operating environment increases the DV burden; therefore, unnecessarily broad specifications can lead to significant additional testing. A pump with an established performance history and existing approvals can carry a smaller, better-understood test matrix than a newly developed platform, if its specifications are updated to meet the specific use case.

DESIGN AND DE-RISK THE TEST PROCESS

As with all DV processes, characterisation (or pre-DV) directly influences the efficiency of formal test execution. For ambulatory infusion devices dealing with complex formulations, unexpected behaviours arising during test execution can derail the entire programme. The following steps detail how to efficiently design and de-risk the DV protocol:

1. Risk identification
2. Risk elimination and mitigation
3. Define data analysis and integrity.

Risk Identification

For complex infusion systems, risks may often not be visible in product requirements or design documentation, so pre-DV activities should focus on uncovering underlying physical properties that may influence measurement performance (Figure 3).

Examples encountered during infusion pump verification programmes can include:

- Trapped air bubbles created during cartridge assembly, including their presence and migration with pump orientation
- Air bubbles becoming dispersed into catheters during fluid transfer
- Non-Newtonian formulation properties (e.g. shear thinning) behaving drastically differently during infusion versus bolus delivery
- Fluid evaporation through catheters and beakers.

These effects risk being misinterpreted as pump performance issues if the root causes are not fully understood. Flow-rate instability and end-of-dose issues could be incorrectly attributed to a pump's drive mechanism, when the true causes are formulation – rather than pump-limited. For example, different air bubble locations along a catheter can produce distinct, repeatable flow signatures that closely mimic a mechanical fault, and separating the two typically requires careful analysis. Pre-DV activities should focus on identifying and understanding such mechanisms before they appear during formal verification.

Risk Elimination and Mitigation

Once identified, risks should be eliminated, controlled or characterised using targeted experimentation and engineering judgement. Effects such as balance drift, fixture design problems and temperature gradients can introduce significant measurement errors. For ambulatory pumps, this includes ensuring gravimetric balances have settling times long enough to resolve genuine flow transients without mistaking balance noise for a delivery event. Effective mitigation activities are those that eliminate sources of uncertainty.

Ambulatory pumps operate across broad parameter spaces, including temperature, viscosity, backpressure, orientation and start-up conditions, all of which affect performance. Design of experiments is an effective tool for systematically exploring these spaces, identifying interactions and sensitivities, and determining whether behaviour remains within acceptable limits across the intended operating range, thereby ensuring that an appropriate subset of testing conditions, representing potential worst-case scenarios, are chosen for the formal DV testing.

A recurring challenge in infusion pump verification is that the root cause can be misidentified. Formulation behaviour

"FORMULATION BEHAVIOUR REQUIRES CLOSE ATTENTION AND VERIFICATION, AS MATERIAL PROPERTIES ON A CERTIFICATE OF ANALYSIS MAY BE INSUFFICIENT FOR PREDICTING HOW A FORMULATION BEHAVES INSIDE AN INFUSION SYSTEM."

Figure 3: Efficient testing begins before execution, with extensive pre-DV planning and preparation work.

requires close attention and verification, as material properties on a certificate of analysis may be insufficient for predicting how a formulation behaves inside an infusion system. Shear rates and residence time can differ substantially from the conditions under which such data were generated – for example, density versus temperature.

As a result of investigations such as these, the mitigation strategy for a programme shifts towards understanding the physical mechanisms responsible and quantifying their impact. By the time formal DV commences, experimental signatures observed during the pre-DV phase can be accounted for and correctly assessed, reducing the risk of inefficient post-event root cause investigations and repeat testing.

Define Data Analysis and Integrity

During a DV programme, the characteristics of the data generated and how they are analysed are equally as important as the design of the physical test step. For example, a transient flow-rate disturbance may appear dramatic in raw data but have negligible impact on delivered dose, while a seemingly insignificant disturbance may accumulate into a clinically meaningful error over time. Distinguishing between the two requires careful analysis to identify clinically relevant issues from avoidable experimental artefacts.

This becomes particularly important with automated analysis workflows. Automation improves repeatability and processes large datasets efficiently, but introduces risks of incorrect data manipulation and interpretation. Validation should focus not only on software calculations but also on checks to ensure that the correct data are selected and analysed. Defining analysis, acceptance criteria and anomaly classification rules during characterisation ensure that formal DV answers meaningful questions about device performance as opposed to asking new questions of the data.

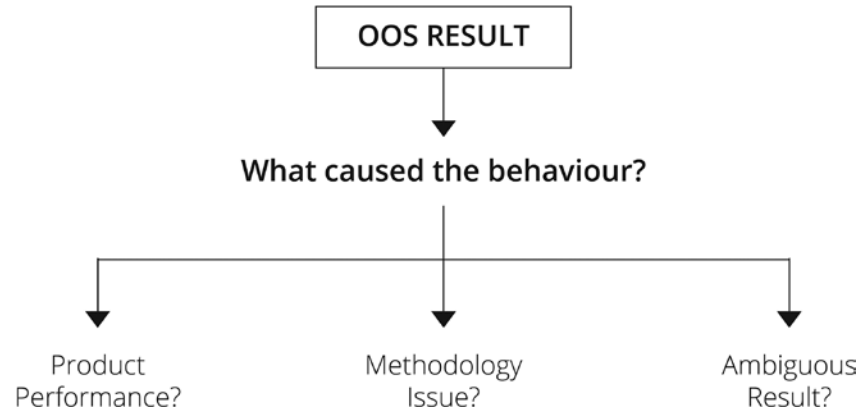

Figure 4: Decision framework illustrating the primary categories of causes considered during investigation of an OOS result.

EXECUTE THE DV TESTING

Before executing the full DV matrix, teams must be trained, confident in procedures and clear on how to respond to unexpected results. Training should be documented, with the lab operating under a vigilance-driven, blame-free culture focused on catching issues early.

Planning how to respond to an out-of-specification (OOS) result beforehand is a key part of this culture, signalling to the reviewer that the process is robust and root cause analysis procedures are followed (Figure 4). OOS investigations all follow a simple logic:

- If the behaviour reflects the real drug delivery performance, the failure must be accepted and included in the statistical analysis
- If the behaviour reflects some aspect of the methodology, careful argument may justify the exclusion and retest of an erroneous result, if it can be proven as such
- If the behaviour is ambiguous, capture evidence (e.g. environmental data, balance data, photographs), learn as much as possible and document it for further investigation. This will ultimately allocate the result to one of the first two categories.

Following these guidelines significantly reduces the burden of root cause analysis and reporting, and, even where acceptance criteria are not met, the resulting understanding will support strong, evidence-based recommendations for product improvement.

A genuine product failure and a system effect may only be distinguishable after careful investigation, demonstrating why agreeing the OOS logic in advance is so important. The objective of characterisation is to ensure that formal DV contains no unexpected lessons so that execution focuses on demonstrating device performance rather than investigating previously unknown phenomena.

CONCLUSION

For ambulatory infusion systems, successful DV may not be limited by the ability to execute the required tests but by how well the underlying system is understood before testing begins. Modern delivery systems combine electromechanical pumps, consumables, complex formulations and patient-driven use conditions, meaning that performance is frequently governed by interactions between these elements rather than the pump mechanism alone. Trapped air bubbles, formulation rheology, start-up

"DEFINING ANALYSIS, ACCEPTANCE CRITERIA AND ANOMALY CLASSIFICATION RULES DURING CHARACTERISATION ENSURE THAT FORMAL DV ANSWERS MEANINGFUL QUESTIONS ABOUT DEVICE PERFORMANCE AS OPPOSED TO ASKING NEW QUESTIONS OF THE DATA."

transients and fluid-path compliance can all generate behaviours that resemble pump failures, which, through characterisation work, can be correctly classified.

Successful programmes treat DV as a confirmation exercise by defining clinically meaningful metrics, identifying hidden sources of variability and establishing robust interpretation methods before commencing formal testing. By following these principles, sponsors can reduce programme risk while generating evidence that is both scientifically robust and regulatorily defensible.

ACKNOWLEDGEMENT

With special thanks to Manuel Acha for his assistance with the article.

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THE PERCEPTION PROBLEM WITH SC VOLUME LIMITS AND ITS DRUG DEVELOPMENT COST

Dr Haydon DuMond and **Dr Mehul Desai** of **Enable Injections**, along with **Dr Shirish Ingawale** of **Takeda**, examine survey evidence and regulatory precedent showing that the widely cited 2–3 mL limit on subcutaneous delivery reflects device history and information habits rather than tissue biology, and consider the consequences for formulation strategy, device selection and the growing pipeline of large-volume subcutaneous therapies.

Ask a cross-functional drug development team how much fluid can be delivered under the skin and a specific range tends to come back: 2–3 mL. It appears in target product profiles, frames early formulation decisions and is used to rule delivery routes in or out before a drug candidate is too far into development. This quantity is treated as a fixed property of subcutaneous (SC) tissue delivery. It is not. The SC space accommodates far larger volumes, and approved products have delivered well beyond 3 mL for years. The limit that circulates is really a property of the standard prefilled syringe and autoinjector, not of the tissue, and conflating the two has turned a device constraint into an assumed biological limit. Treating this constraint as a biological fact narrows the options that reach patients.

Recent survey work across the industry, together with a run of regulatory approvals, now make the gap between belief and evidence measurable. This article follows that gap in four stages: where the belief came from and why it persists; what it costs in formulation strategy, device selection and abandoned programmes, including claims that lack evidence for permeation enhancers; the regulatory record that increasingly argues against this ceiling;

"THE LITERATURE HAS OFTEN COMPOUNDED THE CONFUSION, STATING THAT SC DELIVERY IS LIMITED TO AROUND 2 mL WITH NO REFERENCE TO INJECTION DURATION, DELIVERY METHOD OR DEVICE, CAUSING A DEVICE CONSTRAINT TO TAKE ON THE APPEARANCE OF A BIOLOGICAL PRINCIPLE."

and what would actually close the distance between belief and evidence. Most respondents revised their view simply after being shown a table of products already approved to deliver large volumes, suggesting that the gap can close by putting forward the existing evidence and regulatory record in front of the people making the call.

A DEVICE LIMIT MISTAKEN FOR A BIOLOGICAL ONE

The 3 mL limit has a traceable origin. For most of the period in which SC biologics have become common, the dominant hardware was the prefilled syringe and the autoinjector, formats historically constrained to roughly 1–2.25 mL delivered in seconds.[1,2] By contrast, current on-body injectors approved as combination products can deliver up to 25 mL from a single device over longer periods. Furthermore, syringe pumps can deliver similarly large volumes without a permeation enhancer and with only mild pain scores.[3] The deliverable volume has always been set by the platform in hand rather than by the tissue capacity. The products that reached the market, such as those in 2.25 mL autoinjectors, reflected those constraints and clustered at low volumes, so over time the capability of the devices was misattributed to the tissue.

Two distinctions get lost in that misattribution. The first is between an all-at-once bolus and an infusion delivered over several minutes, which gives the tissue time to accommodate and disperse a much larger volume.[4] The second is between device capability and biological capacity. The literature has often compounded the confusion, stating that SC delivery is limited to around 2 mL with no reference to injection duration, delivery method or device, causing a device constraint to take on the appearance of a biological principle.[5,6]

The following counterexamples are neither rare nor new. SC immunoglobulin has been self-administered for almost two decades at volumes far above 3 mL, with products delivering greater than 30 mL per site without any permeation enhancer.[2] Pegcetacoplan is delivered at 20 mL via an on-body injector[2] and SC isatuximab delivers 10 mL via an on-body injector, both without a permeation enhancer.[7,8] A separate group of larger-volume products have reached the market with hyaluronidase, including SC daratumumab, trastuzumab, rituximab, ocrelizumab and efgartigimod.[2,9] Device capability has moved well past this misperceived limit.

Survey population (ref)	N	Bolus ≤3 mL	Infusion ≤3 mL
Drug development / R&D[13]	88	65%	33%
Formulation, permeation-enhancer focus[12]	100	65%	42%
Formulation, high-concentration focus[11]	100	62%	40%
Cross-functional (clinical development, medical affairs, commercial)[10]	90	68%	39%
Combined	**378**	**65%**	**39%**

Table 1: Perceived SC volume limits across four industry surveys (combined N = 378, 2024–2025).

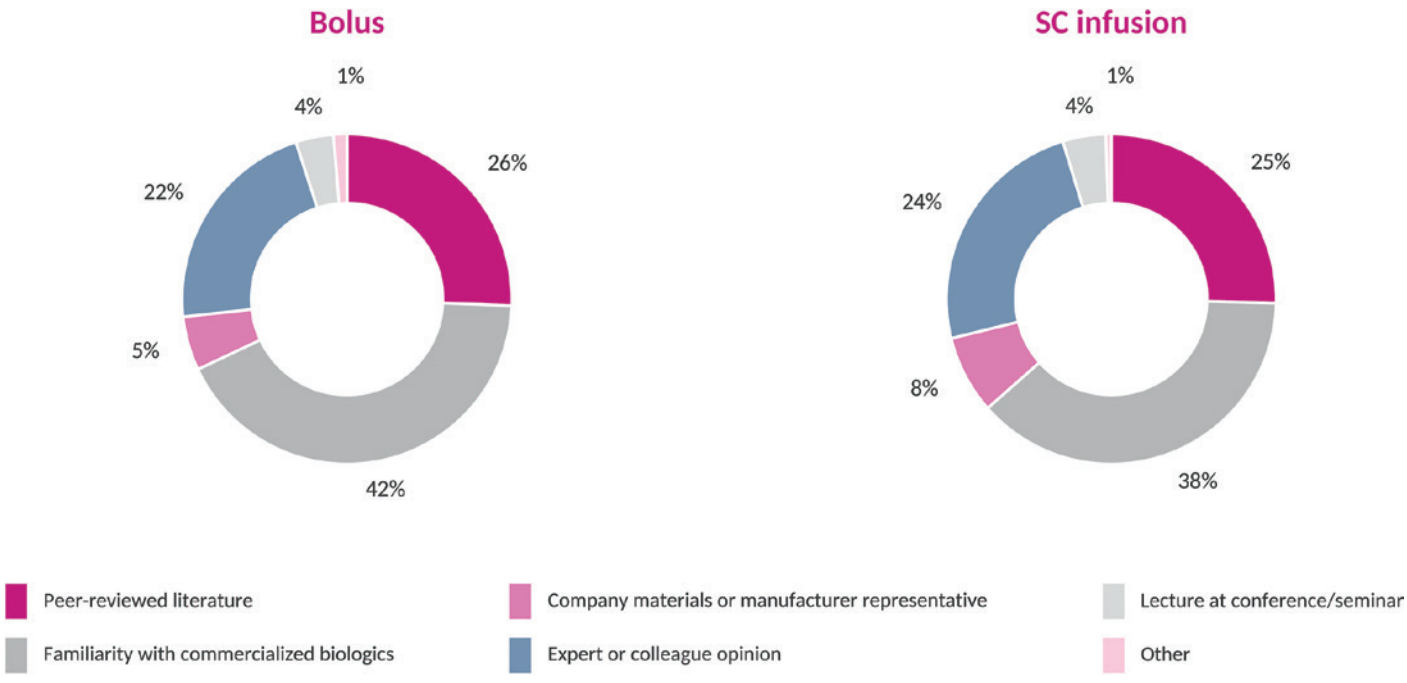
WHAT DECISION-MAKERS BELIEVE AND WHY

To measure the perception directly, four industry surveys conducted across 2024 and 2025 put the volume question to a total of 378 experienced professionals.[10–13] The surveys sampled distinct populations: portfolio decision-making functions (R&D; new product planning/portfolio management; chemistry, manufacturing and controls; combination products), two separate groups of formulation scientists, and a cross-functional group spanning clinical development, medical affairs and commercial roles. The mean experience was around 14 years, so this was not a novice group. The belief was nonetheless replicated closely across all four samples. Between 62% and 68% of respondents in each survey placed the maximum bolus volume deliverable over a few seconds without a permeation enhancer at 3 mL or less (Table 1). When the question was reframed as an infusion over several minutes, 33% to 42% of respondents still held to 3 mL or less.

More telling was when respondents explained where their belief came from, and here too the four surveys corresponded. In all four groups and both framings, familiarity with marketed biologics was the leading basis. Pooled across the surveys, this reasoning accounted for 42% of responses for a bolus and 38% for an infusion, ahead of peer-reviewed literature, expert or colleague opinion and company materials or conference lectures (Figure 1).

As most approved biologics are dosed in small volumes, these products shape expectations about the practical upper limit, rather than data on tolerability or pharmacokinetics, and the vast

"BETWEEN 62% AND 68% OF RESPONDENTS IN EACH SURVEY PLACED THE MAXIMUM BOLUS VOLUME DELIVERABLE OVER A FEW SECONDS WITHOUT A PERMEATION ENHANCER AT 3 mL OR LESS."



n = 378 for each panel. Percentages are rounded to the nearest whole number. Other: n = 5 (bolus), n = 2 (SC infusion).

Figure 1: Stated sources of knowledge of perceived SC volume limits across four industry surveys, shown separately for a bolus and for an infusion over several minutes (compiled from references 10–13).

majority of literature rarely distinguishes a bolus over seconds from an infusion over several minutes.[6] As most respondents were unaware of approved large-volume products delivered without a permeation enhancer,[10] the result is a self-reinforcing loop in which familiarity with small-volume biologics feeds a peer consensus that then shapes future decisions.

THE COST LANDS ON THE PIPELINE

A perceived limit treated as a real one causes damage early on. In a survey of drug development experts, 90.9% had been directly involved in a mean of approximately four SC programmes that were either deprioritised or abandoned because they could not meet a small drug volume target.[13] When a therapeutic dose will not fit under the assumed ceiling, teams reach for familiar workarounds. They raise concentration, which increases viscosity, aggregation risk and manufacturing complexity.[11] They co-formulate with a permeation enhancer. Or they shelve the large-volume SC asset altogether, removing an option before anyone has tested whether the tissue would accept the volume.

The choice is often framed as high-concentration, small-volume versus low-concentration, large-volume, and the perceived volume ceiling systematically biases teams towards the former.[11,14] In a survey of 100 formulation scientists asked about high-concentration development, increasing concentration to reduce injection volume and changing the primary container were both perceived as riskier, more time-consuming and more costly strategies for converting an intravenous (IV) formulation to SC administration over keeping the formulation concentration unchanged and delivering the larger volume with an on-body injector.[11] A larger deliverable volume would

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allow some molecules to remain at a lower, more stable concentration and avoid the formulation burden entirely, but that path is closed off if the volume is wrongly assumed to be undeliverable. Therefore, the assumption does more than just remove candidates – it steers the survivors towards the more difficult formulation problem by default.

The bias is compounded by inertia in device choices. Legacy formats, meaning the needle and syringe, the autoinjector and the prefilled pen, accounted for 78% of respondents' historical device experience, while on-body injectors accounted for under 10%.[10] Asked how strongly past device use influences future selection, 81% rated it high or very high, and the leading driver of device choice was development cost and timeline.[10] Familiar pathways may seem less risky, so they persist even where they may not best serve the drug or the patient, a pattern well described in the behavioural literature on status quo and anchoring bias in development decisions.[15]

The stakes are highest for the drug classes now moving towards SC delivery. Antibody-drug conjugates (ADCs) are a fast-growing example, still administered almost entirely by IV infusion, with

SC delivery now being explored as they enter earlier treatment lines.[16] Most are weight-based and lyophilised,[17] and their linked hydrophobic payloads make high-concentration formulation especially difficult,[16] placing them squarely in the large-volume space where the volume misconception does the most damage.

THE PERMEATION ENHANCER EVIDENCE GAP

The same survey exposed a second, related gap. Among respondents familiar with permeation enhancers, enhanced bioavailability was ranked as the single most valuable attribute, above safety, speed and patient preference.[10] However, the published evidence for a bioavailability benefit with permeation enhancers is extremely thin. Across analyses of biologics co-administered with hyaluronidase, only one product, a pooled polyclonal immunoglobulin whose absorption kinetics differ from a monoclonal antibody, has shown a clear improvement in permeation.[12]

Nearly all of the remaining data on monoclonal antibodies supporting increased bioavailability with permeation enhancers is modelled or unpublished.[12,18] When shown comparisons of bioavailability with and without permeation enhancers, 40% of respondents declined to change their view and pointed directly to insufficient or unpublished evidence.[10] That scepticism is reasonable, and it defines the kind of evidence that would change expert opinion: published, controlled comparisons rather than modelled or unpublished data. Incentives are not lacking here either. When a permeation enhancer is positioned as the technology that unlocks large-volume delivery, the parties best placed to correct the misconception have little commercial reason to do so, and a belief that overstates the need for a permeation enhancer can quietly persist as a result.

A parallel misattribution appears on safety. When asked which factors contribute to the better tolerability of some SC products versus their IV counterparts, 65.6% of respondents selected change of route, 47.8% selected reformulation or excipient changes and 25.6% selected the permeation enhancer itself, on a question allowing multiple selections.[10] The lower or delayed peak concentration and the reduced infusion-related reactions of SC delivery are largely route effects, present with or without a permeation enhancer,[19] and hyaluronidase may in fact raise the rate of absorption and peak exposure.[9] A Phase III study of isatuximab delivered via an on-body injector without a permeation enhancer reported an approximately 17-fold reduction in systemic infusion-related reactions versus IV administration, consistent with the benefit arising from the route and low pressure delivery rather than the additive.[20] Attributing bioavailability and safety advantages to hyaluronidase may encourage its broader adoption despite evidence suggesting that these benefits are not necessarily attributable to the permeation enhancer itself.

"ATTRIBUTING BIOAVAILABILITY AND SAFETY ADVANTAGES TO HYALURONIDASE MAY ENCOURAGE ITS BROADER ADOPTION DESPITE EVIDENCE SUGGESTING THAT THESE BENEFITS ARE NOT NECESSARILY ATTRIBUTABLE TO THE PERMEATION ENHANCER ITSELF."

WHAT THE APPROVALS ESTABLISH

The most direct argument against the volume limit is regulatory and increasingly global. An on-body injector, part of the enFuse® On-Body Delivery System manufactured by Enable Injections, Inc, delivering 20 mL of pegcetacoplan (EMPAVELI®, Biogen, Cambridge, MA, US) without a permeation enhancer, was approved by the US FDA in October 2023 for paroxysmal nocturnal haemoglobinuria (PNH).[21] The same platform has since gained further clearance from regulators in Saudi Arabia, Brazil, South Korea and Canada, and in May 2026 received CE certification in Europe for the pegcetacoplan combination Aspaveli® (SOBI, Stockholm, Sweden) across PNH and complement-mediated kidney disease.[22] In June 2026 the European Commission approved SC-delivered isatuximab (Sarclisa, Sanofi, Paris, France), delivered by CirCLIQ®, an on-body injector built on the same enFuse platform, across its IV multiple myeloma indications (Figure 2).[7] The FDA followed in July 2026 across the drug's IV indications in the US, where the SC product is branded as Sarclisa Escena.[8]

The pattern of regulators clearing large-volume SC delivery without a permeation enhancer, across drugs, devices and geographies, continues.

CLOSING THE GAP

The same surveys also show that the belief can be undone. After simply reviewing a table of approved large-volume products, 55.6% of respondents revised their view of the maximum volume deliverable without an enhancer.[10] What reverses this misconception is credible, published, grounded evidence, not

Figure 2: The enFuse On-Body Delivery System is the technology platform used for the EMPAVELI Injector and CirCLIQ Injector, both of which have received regulatory clearance in global markets.

unpublished or anecdotal claims. That points to a clear agenda for teams that communicate SC delivery information. Distinguish bolus (over seconds) tolerability from infusion (over minutes) tolerability explicitly, since conflating the two sustains much of the residual scepticism. Evaluate device platforms using current clinical evidence, not with the format a team has used before. Hold permeation-enhancer value propositions, and bioavailability claims in particular, to the same evidentiary standard applied to the molecule. And treat regulatory precedent as what it is: proof that the volume question has already been answered in practice.

The 2–3 mL range was only ever an aspect of the devices that dominated the last decade, not a limit of the SC tissue. Large-volume SC delivery was never biologically out of reach; it has simply become more routine as on-body injectors and large-volume devices have matured. The SC tissue, the delivery devices and the regulatory record now point in the same direction. Closing the distance between what has been approved and what the industry believes is now largely a matter of evidence and communication, and the data suggest it can be done.

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*Sanofi: Sanofi's Sarclisa subcutaneous approved in the EU as the first anticancer treatment administered via an on-body injector. News release. Published June 8, 2026.

CONSISTENCY IN LARGE-VOLUME BIOLOGIC DRUG DELIVERY: WHY TISSUE BACKPRESSURE MATTERS

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Andrew Moore of **Gerresheimer** discusses the importance of backpressure and its variance across the patient population when designing an infusion system for large-volume biologics, including how the company's Gx InPuls and Gx InPuls Flex infusors are able to adapt to this variance dynamically to ensure a consistent patient experience.

Until recently, on-body infusion pumps were primarily used for small-volume subcutaneous (SC) basal infusions, but today they are increasingly being seen as a self-administration solution for rapid large-volume SC infusions of biologic drugs. This has led to many innovative drug delivery solutions being developed to address the new needs associated with this growing category of drugs.

One challenge that has not been given enough attention is the impact that backpressure from the patient's SC tissue can have on the drug delivery solution and user experience. Published studies have characterised backpressure in human and animal models, revealing its broad range. These studies have shown that backpressure is affected by both intrinsic factors within the device developer's control, such as flow rate and volume,

> "THESE STUDIES HAVE SHOWN THAT BACKPRESSURE IS AFFECTED BY BOTH INTRINSIC FACTORS WITHIN THE DEVICE DEVELOPER'S CONTROL, SUCH AS FLOW RATE AND VOLUME, AND EXTRINSIC FACTORS RELATING TO THE PATIENT AND INJECTION SITE."

and extrinsic factors relating to the patient and injection site. As a result, predicting backpressure precisely prior to each infusion is not possible.

Understanding backpressure provides important insights for companies when developing a device for SC on-body infusion. At Gerresheimer, expected backpressure ranges have been assessed for the SensCore micropump technology employed in the Gx InPuls and Gx InPuls Flex infusion pumps, demonstrating consistent infusion performance despite backpressure variability.

WHAT IS BACKPRESSURE?

Backpressure is an inherent characteristic of SC infusion. It arises when the tissue resists fluid entering the SC space and is typically assessed by measuring the difference in pressure between comparable infusions into tissue and into air (Figure 1).

Intrinsic drug and device design factors, such as flow rate, volume and viscosity, are each positively correlated with backpressure. Higher backpressures caused by increases in these factors can be either controlled or accommodated for through device design. With increased demand for high-flow-rate infusions for large volume and viscous biologic drugs, backpressure will have a non-negligible impact on infusion performance and device developers should ensure that the device generates a compensating pressure to deliver the drug at an expected flow rate.

An additional and possibly more challenging dynamic for device developers to accommodate is the broad variability of backpressure, ranging from 4 to 100 kPa, across possible injections and infusion rates.[1–4] This variability is caused by extrinsic factors outside of the control of the device developer. The exact source of these extrinsic effects is not well understood but may relate to physiological factors such as injection site location, tissue hydration and local vascularity.

Given the combined contribution of intrinsic and extrinsic factors, backpressure should not be treated as a fixed value. Instead, an on-body infusion device should be designed to accommodate the full range likely to be encountered, including substantial interpatient variability.

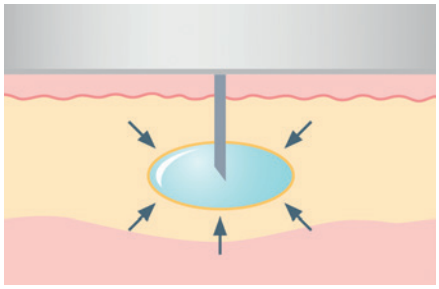

Figure 1: Illustration of backpressure in subcutaneous infusion.

This can be demonstrated through infusion rate accuracy testing with a simulated backpressure testing platform.

HOW IS BACKPRESSURE CHARACTERISED?

By using studies that characterise backpressure in human and animal models, device developers can proactively design for a range of expected backpressures. Large-volume SC infusion was evaluated by Doughty *et al* in Yorkshire swine, and mean backpressures were reported, ranging from approximately 3.7±1.4 kPa for a 5 mL infusion delivered over 5 minutes, to 24.0±3.4 kPa for a 1 mL injection delivered over 10 seconds.[2] In one particular test, a 10 mL infusion delivered over 10 minutes, backpressure was measured at 7.4±7.8 kPa. In this instance the standard deviation exceeded the mean, indicating that physiological variability can exceed 100% of the average pressure recorded, even where infusion conditions are identical across subjects.

In another study, Thomson evaluated backpressure in 11 patients with Type 2 diabetes. Backpressure during SC insulin injection was estimated using changes in injection flow rate as the basis for measurement. Measurable counterpressure was detected in 8 of the 11 patients ranging from approximately 164 to 998 mbar (16.4 to 99.8 kPa).[3,4] These findings revealed substantial interpatient variability in backpressure and a more than sixfold difference in tissue resistance between individuals.

Overall, a range of 4–100 kPa is possible across the full range of potential infusions. However, the exact range of backpressures expected for a given application is highly affected by controllable factors such as flow rate, volume and viscosity.[3] As an example, an infusion with a non-viscous drug with a flow rate below 100 mL/hr might produce a maximum backpressure of only 20 kPa. While device developers may target a broad range up to 100 kPa, the expected backpressure range should be assessed for the anticipated performance range of the device (Figure 2).

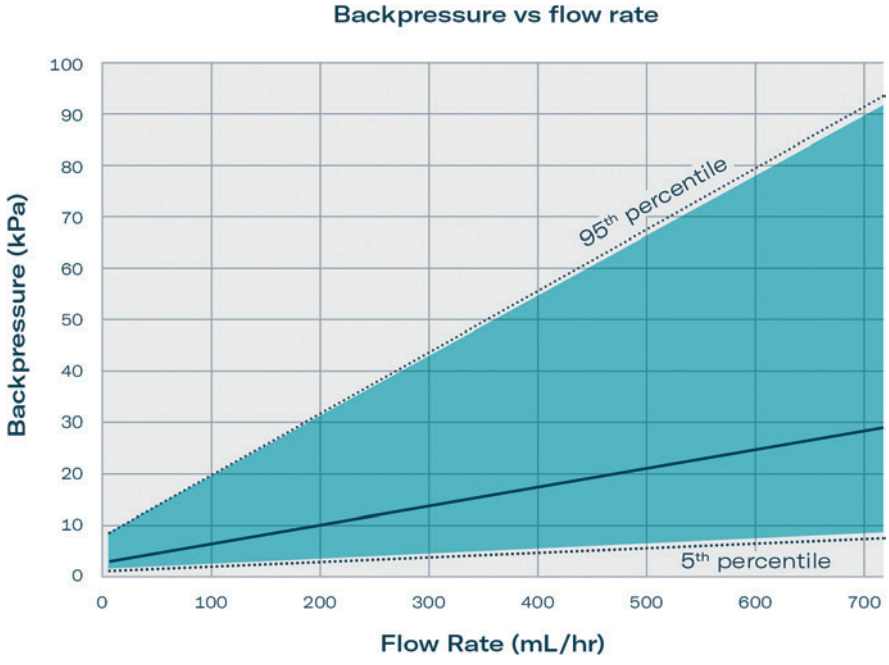

Figure 2: Backpressure measurements versus flow rate.

IMPLICATIONS FOR DEVICE DEVELOPMENT

Drug delivery devices are already designed to overcome internal resistance, such as friction within the primary container and fluid dynamic resistance in the fluid path. In this context, backpressure can be treated as an additional fluid path pressure, with the expected flow rate as a function of the difference between the pressure produced by the device and the external backpressure. From a design perspective, this can make use of existing methodologies for modelling infusion rate while integrating a new variable of backpressure.

The greater design challenge is dynamically adapting to backpressure variability. Without this dynamic adaptation, an on-body infusion device cannot maintain a consistent infusion rate and user experience. Inconsistency in infusion rates may be acceptable from a pharmacokinetic perspective for large-molecule monoclonal antibodies, which typically take several days to reach maximum serum concentration (T_{max} ~2–8 days).[5] On that timescale, the difference between a 30-minute and a one-hour infusion is expected to be pharmacokinetically minor. However, the successful self-administration of a drug relies heavily on a consistent user experience – an uncontrolled infusion rate may lead to use errors.

"THE GREATER DESIGN CHALLENGE IS DYNAMICALLY ADAPTING TO BACKPRESSURE VARIABILITY. WITHOUT THIS DYNAMIC ADAPTATION, AN ON-BODY INFUSION DEVICE CANNOT MAINTAIN A CONSISTENT INFUSION RATE AND USER EXPERIENCE."

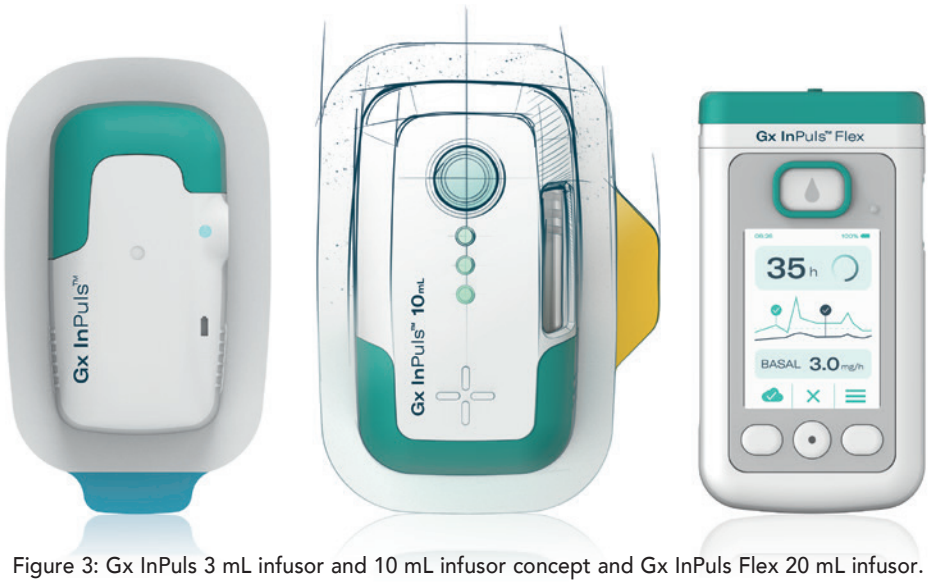

Figure 3: Gx InPuls 3 mL infusor and 10 mL infusor concept and Gx InPuls Flex 20 mL infusor.

When presented with an unexpectedly long infusion, patients may interpret the slower delivery as an occlusion or other device malfunction and remove or replace the infusor before the dose has been fully delivered. Such variability can introduce uncertainty and increase the likelihood of use errors or use-related harm. Designing a device to accommodate the expected range of backpressures, and providing clear indications of dosing status, is important not only for device performance but also to support safe and reliable patient use.

Various on-body infusion device solutions address both backpressure and occlusion detection in different ways. Electromechanical devices typically use electronic dynamic controls which adjust power output to increase or decrease the pressure produced by a device. Dynamic pressure regulation is also feasible for mechanical systems.

INFUSOR DESIGN THAT RESPONDS TO VARIABLE BACKPRESSURE

The Gx InPuls from Gerresheimer is an on-body infusor platform for SC infusion, incorporating a built-in automatic needle insertion and retraction mechanism. Gx InPuls Flex is an off-body infusor platform for SC infusion that uses an infusion set to transport the drug from the device to the patient (Figure 3). Both are electromechanical devices that integrate the unique Gerresheimer SensCore linear-rotary micropump to precisely control flow rate in microlitre increments.

"GX INPULS AND GX INPULS FLEX AUTOMATICALLY POWER-COMPENSATE FOR BACKPRESSURE IN ORDER TO ENSURE CONSISTENT INFUSION RATES."

The pulsatile wetted pump technology has specific benefits related to backpressure. The piston design of the pump acts as a valve and prevents backflow even when backpressure increases dynamically during an infusion. The wetted pump technology also simplifies infusion rate control. The system must ensure that each pulse or stroke of the pump is completed within a certain timeframe and that the pump seals can withstand the backpressure. Additionally, the control system does not require a complex chain of elastomeric or frictional components downstream of the pump.

Gx InPuls and Gx InPuls Flex automatically compensate for backpressure in order to ensure consistent infusion rates. They also incorporate Hall effect sensors to detect an occlusion, indicated by incomplete pump strokes. The sensors are designed to trigger at a pressure greater than 200 kPa to ensure that normal backpressure is not misidentified as an occlusion. Both devices also include alarms as well as visual and

audible indications to inform patients of the infusion status and alert them to any occlusion event.

To understand the performance of Gx InPuls and Gx InPuls Flex, laboratory testing was performed on the 10 µL SensCore micropump subsystems to simulate infusion under backpressure. The testing was performed by infusing at a rate of 360 mL/hr into a pressurised vessel and incrementally increasing and then decreasing the pressure. Delivery volume accuracy (DVA) was measured at each backpressure setting and assessed against acceptance criteria of 100±5%. Samples were first preconditioned by simulating the full lifecycle of the pump to assess if performance degrades over its foreseeable use life (Figure 4).

Testing demonstrated that DVA can be maintained within the acceptance criteria for a wide range of backpressures from 0 to 150 kPa, exceeding the range of expected backpressure by a significant margin. A backpressure greater than 200 kPa is used as a threshold to trigger an occlusion detection alarm because this lies significantly above the expected backpressure range. The test confirmed that the Gx InPuls and Gx InPuls Flex infusors can achieve target infusion rates across the full range of expected backpressure variability.

If the predictability of the patient experience can be improved by consistent delivery times, instructions for use are simplified as a result and variability in the time required to complete therapy is reduced across the patient population. By designing for the full physiological range of backpressures, rather than for a nominal operating condition, reliable performance across a broad range of clinical scenarios can be delivered by the Gx InPuls and Gx InPuls Flex infusors.

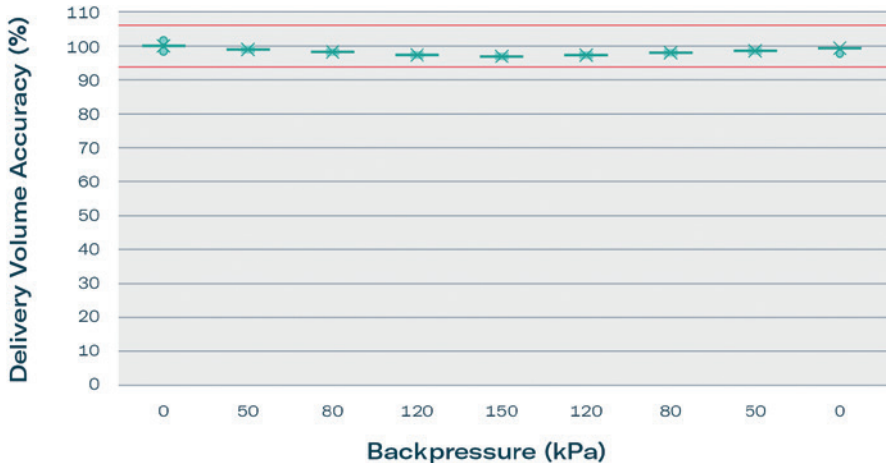

Figure 4: Delivery volume accuracy at 360 mL/hr for backpressure from 0 to 150 kPa.

CONCLUSION

With the increasing interest in using on-body infusion devices for large-volume, high-flow-rate infusions, backpressure becomes a critical attribute to understand and account for in product design. Adapting to backpressure variability is essential for maintaining a consistent and reliable user experience. Future research may provide more insights into extrinsic effects on backpressure and how they can be controlled through administration workflows. In addition, absorption enhancers such as hyaluronidase may be co-formulated with drugs to affect tissue permeability and reduce backpressure. However, current device developers should ensure that variability can be managed by the device until these factors are fully understood and without relying entirely on absorption enhancers, which are not part of all infusion formulations.

Many drug delivery solutions, including Gx InPuls and Gx InPuls Flex, are designed to accommodate a broad range of backpressures and have demonstrated this capability under testing. By designing to adapt to a range of backpressures, rather than for a nominal operating condition, a predictable and reliable experience can be provided across a diversity of patient physiologies and therapeutic properties. As on-body infusion continues to expand into these higher-volume, higher-viscosity and higher-flow-rate applications, backpressure should be treated not as a peripheral engineering consideration, but as a core design input from the earliest stages of device development, on the same footing as dose accuracy and occlusion detection.

"IF THE PREDICTABILITY OF THE PATIENT EXPERIENCE CAN BE IMPROVED BY CONSISTENT DELIVERY TIMES, INSTRUCTIONS FOR USE ARE SIMPLIFIED AS A RESULT AND VARIABILITY IN THE TIME REQUIRED TO COMPLETE THERAPY IS REDUCED ACROSS THE PATIENT POPULATION."

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Andrew Moore

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Expert View

DESIGNING A WEARABLE DRUG DELIVERY PUMP

Dr Sammy Hassan of Sanner delves into the measures required to ensure safe and reliable use of wearable drug delivery pumps, explaining the difficulties and benefits of incorporating such standards into a device.

Wearable drug delivery pumps are reshaping how therapy is delivered. By moving controlled, continuous and personalised dosing out of the clinic and onto the patient, wearable pumps can help to improve mobility, support home-based treatment, reduce hospital visits and enable precise regimens over extended periods.

However, a wearable pump is not a miniature pump strapped to the body. It is a safety-critical, medical, electrical system that must deliver the right dose, at the right rate, under shifting environmental, mechanical, electrical and user conditions. Over-infusion, under-infusion, occlusion, unintended activation, software malfunction, battery failure or a single mishandled interaction can all cause serious harm.

Therefore, safety must be a core design requirement from day one rather than a layer added just before submission. A small group of standards frames this work: IEC 60601-1 sets the general requirements for basic safety and essential performance of medical electrical equipment; IEC 62304 defines the software lifecycle; IEC 60601-2-24 addresses infusion pumps and controllers specifically; and ISO 14971 provides the risk management process that ties them together.

Figure 1: A person wearing an insulin pump.

> "SAFETY MUST BE A CORE DESIGN REQUIREMENT FROM DAY ONE RATHER THAN A LAYER ADDED JUST BEFORE SUBMISSION."

THE OPPORTUNITY

The central opportunity is to bring essential treatments into everyday life. Ambulatory therapy lets patients receive medication while remaining mobile, which is valuable across chronic conditions, oncology, insulin delivery, pain management, hormone therapy and subcutaneous biologics.

Embedded electronics are what make accurate infusion possible. Sensors and closed-loop control support precise flow profiles, with bolus and basal delivery, programmable schedules and lockout periods tuned to the individual. Bluetooth, near-field communication or cellular links can add configuration, adherence tracking and remote diagnostics; designed well, they also give earlier warning of faults or misuse. As the device is worn by the patient, it must also be compact, light, discreet and intuitive (Figure 1). Meeting all these requirements at once pulls electronics, firmware, mechanical design and human factors into a single co-ordinated effort.

Figure 2: The safety measures that an insulin pump should contain.

SAFETY AS THE PRIMARY DESIGN DRIVER

The core challenge is in keeping the pump safe under normal use, foreseeable misuse and single-fault conditions – what IEC 60601 calls maintaining basic safety and essential performance. For an infusion device, essential performance typically means an accurate delivery rate, prevention of unintended delivery, occlusion detection, alarm generation and safe shutdown.

A safety-centred process starts with hazard identification and risk analysis under ISO 14971. Typical hazards for a wearable pump include:

- Over-delivery, under-delivery or a missed dose
- Downstream or upstream occlusion, or free flow
- Air ingress
- Liquid leakage
- Incorrect cartridge installation or patient set-up
- Accidental use of incorrect drug
- Battery depletion mid-therapy
- Software lock-up or timing failure
- Wireless interference or cybersecurity vulnerabilities
- Mechanical damage from impact, moisture or body movement.

> "INTERLOCKS ARE NOT FEATURES FOR CONVENIENCE. THEY ARE RISK CONTROLS, WHICH MEANS THEY MUST BE SPECIFIED, VERIFIED, VALIDATED AND TRACEABLE TO THE HAZARDS THEY ADDRESS."

Each hazard must be traced to a specific risk control – mechanical, electrical, software, procedural or, most often, several interlinked controls.

INTERLOCKS: A KEY SAFETY MECHANISM

An interlock prevents the device from entering a hazardous state unless defined safety conditions are met. In a pump these can be incorporated in hardware, software, mechanical design or the user workflow. They can include cartridge-presence detection, reservoir-door closure, cannula-insertion confirmation, priming and bolus lockouts, occlusion-triggered stops, battery undervoltage lockout and drug-container authentication (Figure 2).

A cartridge interlock, for instance, can block device operation until the drug cartridge is correctly seated, using a switch, Hall-effect sensor, optical sensor, radio frequency identification (RFID) tag or coded mechanical feature. A door interlock can prevent pumping while a reservoir or access panel is open; a priming interlock can stop delivery to the patient while the device is still priming.

Interlocks are not features for convenience. They are risk controls, which means that they must be specified, verified, validated and traceable to the hazards they address. IEC 62304 requires relevant software to be developed through a controlled lifecycle, with the software safety classification setting the level of rigour.

REDUNDANCY AND DUAL-PROCESSOR ARCHITECTURES

For high-risk delivery functions, a single microcontroller controlling the pump, reading sensors, managing alarms and supervising its own safety may not be enough. One software fault, timing error, memory corruption or lock-up could drive unsafe delivery.

"IF THE PRIMARY PROCESSOR MISBEHAVES, THE SAFETY PROCESSOR CAN DISABLE THE ACTUATOR, RAISE AN ALARM, FORCE A SAFE STATE AND LOG THE FAULT, CREATING AN INDEPENDENT LAYER OF SAFETY THAT DOES NOT DEPEND ON THE MAIN CONTROL PATH."

A redundant architecture can mitigate single points of failure. A primary processor runs pump operation and the user interface (UI); an independent safety processor monitors the critical parameters – motor activity, delivery timing, pressure readings, battery voltage, watchdog signals and state transitions. If the primary processor misbehaves, the safety processor can disable the actuator, raise an alarm, force a safe state and log the fault, creating an independent layer of safety that does not depend on the main control path.

A robust dual-processor design typically includes:

- Independent watchdog monitoring between processors
- Separate clock sources for timing supervision
- Independent measurement of motor actuation or flow-related signals
- Hardware-controlled pump-enabled lines
- Safety-processor authority to disable delivery
- Cross-checking of dose counters and therapy state
- Non-volatile fault logging and a defined safe state after a fault.

Redundancy is not free – a second processor adds communication, synchronisation, power, verification, printed circuit board area and test burdens. It should be justified by risk analysis, not added by reflex.

SOFTWARE SAFETY UNDER IEC 62304

Software sits at the centre of pump safety by providing dosing algorithms, motor actuation, alarms, user input, connectivity, logging and fault detection. IEC 62304 calls for a structured lifecycle: planning, architecture, detailed design, implementation, verification, integration testing, release, maintenance, configuration management and problem resolution.

Safety-related behaviours should be captured as explicit requirements, for example:

- Stop delivery when occlusion pressure exceeds the defined threshold
- Prevent bolus delivery during lockout periods
- Detect motor stall and enter a safe state
- Alarm before remaining battery capacity is insufficient for therapy
- Prevent therapy start if the cartridge is missing or misfitted
- Record safety-critical faults with timestamps
- Transition to a predefined safe state after watchdog timeout.

The architecture should isolate safety-critical functions within the device. Wireless and mobile-app features must never command delivery without passing through safety checks, and the therapy-control layer should be insulated from faults in the UI or communication layers.

"REDUNDANCY IS NOT FREE – A SECOND PROCESSOR ADDS COMMUNICATION, SYNCHRONISATION, POWER, VERIFICATION, PRINTED CIRCUIT BOARD AREA AND TEST BURDENS. IT SHOULD BE JUSTIFIED BY RISK ANALYSIS, NOT ADDED BY REFLEX."

IEC 60601 CONSIDERATIONS

As a medical electrical device, a wearable pump falls under IEC 60601-1 for protection against electrical and mechanical hazards, excessive temperature, abnormal operation and single faults. Three collateral standards matter especially here:

- IEC 60601-1-11 covers equipment used in the home environment, which is relevant because patients or carers, not clinicians, operate the device.
- IEC 60601-1-2 covers electromagnetic compatibility, which matters because a wearable device sits in the vicinity of phones, chargers, wireless networks and security systems all day.
- For infusion-specific requirements, IEC 60601-2-24 covers ambulatory, syringe, volumetric and controller pumps.

KEY ENGINEERING CHALLENGES

Dose Accuracy

Pump mechanism, motor control, reservoir design, tubing compliance, pressure variation, fluid viscosity, temperature and body position all influence delivery. The design needs calibration, verification and fault detection that keep dosing within acceptable limits.

Occlusion Detection

Low flow rates and small volumes make occlusions hard to catch. Pressure sensing, motor-current monitoring, flow estimation or displacement sensing may all be required – the real difficulty is detecting genuine occlusions quickly without flooding the user with false alarms.

Power Management

The device must be small and battery-powered, yet watchdogs, alarms, clock accuracy, memory integrity and fault monitoring must stay alive throughout delivery of the therapy. Low-power design must never quietly disable a safety function, and under-voltage behaviour must be predictable and safe.

Human Factors

Users may have limited training, impaired vision, reduced dexterity or anxiety about treatment. The device should minimise setup

errors, give clear feedback and make unsafe actions difficult – through interlocks, guided workflows, alarms and physical keying.

Environmental Robustness

Sweat, moisture, vibration, impact, temperature swings and constant movement all act on a wearable device. Therefore, enclosure design, ingress protection, connector reliability, adhesive performance and mechanical retention all need deliberate attention.

Recommended Safety Architecture

A safety-focused wearable pump should layer its risk controls: a primary control processor, an independent safety processor, motor-driver-enabled control, cartridge and door interlocks, pressure sensing, motor feedback, battery monitoring, audible and visual alarms, non-volatile fault logging and a secure communication interface.

The primary processor handles scheduling, UI, connectivity and normal pump control. The safety processor independently checks that the primary processor is behaving and that critical outputs, such as the motor-enabled signal, pass through a safety gate that the safety processor or fault logic hardware can control. Crucially, safety should not rest on software alone. Wherever possible, hardware interlocks and independent monitoring should be incorporated to stop a single fault from reaching the patient.

"WHEREVER POSSIBLE, HARDWARE INTERLOCKS AND INDEPENDENT MONITORING SHOULD BE INCORPORATED TO STOP A SINGLE FAULT FROM REACHING THE PATIENT."

CONCLUSION

Wearable pumps open real opportunities for patient-centric, remote and personalised care. However, because the device controls medication directly, safety must be designed into the architecture from the outset. IEC 60601 frames basic safety and essential performance, IEC 62304 governs the software lifecycle, IEC 60601-2-24 covers infusion specifics and ISO 14971 ties the risk picture together.

The safest designs do not lean on one perfect component or one flawless routine. They are layered systems in which foreseeable failures are detected, controlled and stopped before they reach the patient. Fundamentally, building those layers well is an electronics and embedded-systems problem as much as a clinical one.

Dr Sammy Hassan

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WEAR IT WELL: HOW ON-BODY DELIVERY SYSTEMS HAVE EVOLVED TO EMPOWER PATIENTS AND EMBOLDEN INNOVATORS

Dan Yates of **West Pharmaceutical Services** considers how wearables have increased their value for both patients and pharma partners through intentional design optimisation, highlighting how insights from real-world use have led to intentional design directions that satisfy the needs of these critical stakeholder groups, further building confidence in a configurable platform that maintains significant potential for future innovation.

In the pharmaceutical industry, far from the world of fast fashion, "ready to wear" takes on a whole new meaning. Here, it applies to wearable medical devices that, over the past decade, have rapidly transitioned from promising concept to patient-ready product. Today, momentum continues to build in this segment of the market, which is helping to fuel a transformational shift in patient care by filling a gap between intravenous infusions and subcutaneous (SC) autoinjectors. With a projected compound annual growth of 11% taking the global value of on-body injectors to an estimated US$29.36 billion (£21.75 billion) by 2034, wearables are definitely not a passing trend.[1]

The success of wearables and on-body delivery systems (OBDSs) can largely be attributed to confidence. This can be seen in patients through their ability to safely facilitate the controlled delivery of ever-increasing volumes of injectable therapies beyond the confines of healthcare facilities and without oversight from a healthcare professional. For those managing chronic conditions, who might face the burden of frequent injections or infusions of high-dose and potentially viscous biologic treatments, this aspect of wearables undoubtedly provides various important benefits.

At the same time, innovation in device design has provided pharma partners with greater confidence in the feasibility and future potential of wearable platforms. Advances in areas such as manufacturing agility, component compatibility, reliability and dose deliverability have lowered

"IN A FAST-MOVING SPACE, THE SMARTDOSE OBDS DESIGN TEAM AT WEST CAREFULLY AND INTENTIONALLY GUIDED THE PLATFORM'S DEVELOPMENT ON A TRAJECTORY OF CONTINUOUS IMPROVEMENT."

development risk while enabling timeframes to be reduced. As such, wearable devices have opened new commercial opportunities for market share and sales growth, addressing unmet patient needs via novel treatments and differentiated delivery.

DESIGNING FOR REAL PEOPLE WITH REAL NEEDS

Alongside pen injectors and autoinjectors, wearables have answered a growing call for greater flexibility in the delivery of injectable therapies, providing greater autonomy and convenience for patients while also easing the demand on healthcare professionals and clinical facilities. Specifically, wearables answer this call where the combination of drug concentration and viscosity result in therapies of larger volumes and/or longer injection durations. By exceeding the traditionally accepted 1–2 mL limitation of SC injections for self-administration with an autoinjector, wearables aim to support maximal patient convenience with minimal injection discomfort. Over time, these devices have evolved to accommodate larger drug formulation volumes and a wider range of therapies, further extending their potential to reduce injection frequency and reliance on infusion-based delivery.

West's SmartDose® 10 OBDS is the product of an optimisation strategy integrated into the device from its inception. An earlier, lower-volume version of the OBDS was selected for SC delivery of a biologic medication for lowering cholesterol and protecting against major cardiovascular events.[2] The in-market experience and real-world feedback gained from this application fed directly into a design-enhancement process, with the platform subsequently being revised, adapted and extended to accommodate dose volumes of up to 10 mL. This updated platform was employed in the FUROSCIX (furosemide) On-Body Infusor launched by scPharmaceuticals (Burlington, MA, US) in 2022 as the first at-home SC diuretic for patients with heart failure or chronic kidney disease.

In a fast-moving space, the SmartDose OBDS design team at West carefully and intentionally guided the platform's development on a trajectory of continuous improvement. While strong foundations were laid with the original platform, device design is very rarely a "one and done" process. More typically, it is based on a sequence of optimisation cycles, allowing for vital iteration of discrete variables in search of even better answers.

COMBINING CONTAINMENT AND DELIVERY CONSIDERATIONS

Enhancing the patient experience was always a key priority to meet both their high-level treatment requirements and their everyday practical needs based on human factors insights. In a regulatory context, this approach of iterative product development is aligned with the US FDA's Patient-Focused Drug Development initiative.[3] From an engineering perspective, it fits with the philosophy of patient-centric design, where innovation is rooted in a clear definition of user pain points.

In this case, the key questions concerned how the usability of the SmartDose OBDS could be further enhanced or refined in the interests of a better experience and improved therapeutic outcomes. The increase in capacity from 3.5 to 10 mL, for example, enabled a wider range of high-dose biologics to be administered in a single treatment, but this benefit could only be realised if both elements of containment and delivery could be successfully addressed and answered – both in isolation and as part of an integrated system.

Here, there is no "chicken or egg" conundrum regarding which should be tackled first, as secure containment of the drug product over its lifecycle will always be the primary concern. Indeed, robust verification of attributes such as container closure integrity and the mitigation of unwanted interactions between drug and packaging component are absolute prerequisites that must be prioritised early in development.

In the case of West's SmartDose 10 OBDS, the two distinct elements of drug container and delivery mechanism combine to form a user-loaded wearable system. This differs from some systems where the primary container is incorporated into a self-contained, preloaded device. While the act of loading a cartridge represents an additional step in the injection process for the patient, this is counterbalanced by a series of important benefits.

First among these benefits is the fact that user-loading gives patients a valuable opportunity to visually inspect the dose prior to administration, providing them with a level of assurance that "blind" closed mechanisms cannot. The potential to enhance patient confidence in dosing is further boosted with SmartDose 10 OBDS through the use of visual, tactile and audible feedback triggers that make the process of user-loading more intuitive and support error reduction. Furthermore, with a user-loaded device, if any electromechanical issues arise at initiation, they can be addressed separately while the container element is preserved, avoiding costly drug wastage.

"THE POTENTIAL TO ENHANCE PATIENT CONFIDENCE IN DOSING IS FURTHER BOOSTED WITH SMARTDOSE 10 OBDS THROUGH THE USE OF VISUAL, TACTILE AND AUDIBLE FEEDBACK TRIGGERS THAT MAKE THE PROCESS OF USER-LOADING MORE INTUITIVE AND SUPPORT ERROR REDUCTION."

A FULLY INTEGRATED APPROACH – FULL CONFIDENCE IN DELIVERY

Such benefits highlight the many advantages of separating dose and delivery. At the same time, however, they accentuate the importance of guaranteeing complete compatibility between these two elements when they combine to form a delivery system. Simply put, the interface between the container and the delivery component must be flawless to ensure the required levels of performance, reliability and error prevention. Having mastery over both container and device design makes it possible to optimise key interfacing features. In the case of SmartDose, these include making loading only possible if the drug container is correctly oriented; requiring the drug container to be loaded to facilitate locking of the drug-container compartment and enabling the activation button, as well as preventing patients from piercing the container on insertion.

Any risk that the two elements of container and device do not seamlessly dovetail together introduces the potential for usability problems, loading errors and a lack of confidence in full delivery of the injectable dose. Such compatibility risks are typically prompted by supply chain inconsistencies, where container and delivery mechanism are sourced from different providers. Even with extensive due diligence, the tight tolerances involved in such precision-engineered components can mean compatibility is not fully optimised between the container profile and the electromechanical component. This issue is mitigated with the SmartDose 10 OBDS because all key elements of the device and container system are sourced from West. This integrated approach both strengthens and simplifies the potentially complex development pathway for a combination device, enabling manufacturing and regulatory requirements to be met alongside patient needs.

> "THE SMARTDOSE OBDS WAS CONCEIVED TO DELIVER A BETTER EXPERIENCE FOR PATIENTS REQUIRING INJECTABLE TREATMENTS, AND THIS PROMISE HAS DRIVEN ITS EVOLUTION, ALONG WITH THE OPTIMISATION OF KEY DEVICE ATTRIBUTES."

Sitting within this philosophy is the Crystal Zenith® cyclo-olefin polymer cartridge officially licensed from Daikyo Seiko (Tochigi, Japan), a strategic partner of West's since 1973. The decision to employ a polymer rather than glass cartridge within the SmartDose 10 OBDS was driven by a series of containment benefits, many of which are particularly pertinent for the complex, sensitive biologics that are suited to wearable delivery but prone to interaction and degradation when in contact with packaging-related compounds.

Polymer containers are lightweight and feature a much stronger breakage profile than glass. This not only safeguards against production line issues but also, crucially, underpins the superior strength needed for the delivery of highly viscous drug products. In addition, tighter dimensional tolerances and no added silicone oil make for highly consistent break-free and extrusion forces, ensuring reliable performance.

SOLVING PATIENT NEEDS, ANSWERING PARTNER CHALLENGES

The SmartDose OBDS was conceived to deliver a better experience for patients requiring injectable treatments, and this promise has driven its evolution, along with the optimisation of key device attributes. These include the ability to

carry out preloading checks of the drug container; the use of a high-performance polymer container to safeguard dose integrity and deliverability; and the adoption of a single-source component strategy to guarantee compatibility between drug container and injector mechanism, thus promoting overall system integrity.

However, solving patient challenges has not been the only aspect of the intentional iteration of the platform's design. West has also been able to deliver complementary advantages for pharmaceutical companies that de-risk and accelerate development, reducing cost and time to market. For example, maintaining adherence to the user-loading model not only introduces the ability for a patient to check the dose, it also reduces complexity in manufacturing, storage and distribution. Standard filling processes can be employed because the containers are engineered to standard dimensions. In addition, because the drug doses and device are not integrated into a unified unit, there is no requirement to manage the co-ordination of primary container and device assembly, potentially with a validated manufacturing partner, which would introduce associated quality assurance processes, incurring further time and cost requirements.

ENGINEERING A DEVICE TO DELIVER PERFECT FIT

Clearly, these are valuable benefits for pharma partners, but they are rooted in a patient-centric design framework that prioritises the needs of the patient first and foremost. After all, it is only when guided by a systematic assessment of users' problems that solutions that truly fit can be engineered; and it is only by understanding users' real-world intentions that intentionality can be applied to the design to deliver a device with real-world appeal.

In the case of SmartDose 10 OBDS, patients are not just provided with a wearable device but with the confidence to autonomously administer injections of higher volumes at lower frequencies. It was not long ago that such approaches were aspirational, but advances in user-centric technology are writing the next chapter of the wearable injector story and redefining what is possible for at-home patient care. West believes that, far from being a fashionable trend, such devices are set to further embed themselves in the drug delivery landscape based on a clear strategic intent – when patients wear West's device, they need to wear it well.

West's SmartDose® on-body delivery system is not independently cleared or approved by any Regulatory Body for general healthcare professional or patient use, nor is it available for general commercial purchase. Its distribution and use are subject to applicable regulatory requirements for clinical investigation and for marketing authorization, as used in combination with a specific drug or biological product. Each component of a combination product is subject to the requirements established by the Regulatory Body for that component (drug, biologic or device). The regulatory process can be more complicated for combination products including an evaluation of the product characteristics, delivery system and its functionality, intended users and use environment(s), as well as the potential for undesirable interactions between the drug or biologic and the delivery system. As a result, we note that the SmartDose® on-body delivery system's compatibility with any particular drug or biologic must be confirmed, and its ability to achieve the desired patient benefits must also be confirmed, on a case-by-case basis in a manner sufficient to meet Regulatory Body requirements. Failure to follow product instructions for use may result in compromised sterility; contamination; leakage (including possible exposure to medication); and/or underdosing. Product misuse could potentially lead to needlestick injury, user and/or patient exposure to pathogens or infection, and/or suboptimal or delayed therapy. Products are shown for information purposes only. Important product and safety information and warnings available online.

SmartDose® is a registered trademark of West Pharma. Services IL, Ltd., a subsidiary of West Pharmaceutical Services, Inc.

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BEYOND DRUG DELIVERY: THREE LENSES FOR SELECTING AN ON-BODY PLATFORM

YPSOMED SELFCARE SOLUTIONS

Reto Jost, **Nadine Kaufmann** and **Shawn James**, all of **Ypsomed**, discuss three complementary decision lenses and explain how they offer a practical framework for evaluating early platform decisions that can shape outcomes across the entire product lifecycle.

On-body delivery is being reshaped by three converging trends. Biologic therapies are moving from intravenous (IV) infusion to subcutaneous (SC) administration in growing numbers: a systematic review of more than 1,300 biologics identified 182 that require SC doses above 2 mL, roughly two-thirds of which are in the 2–10 mL range[1] (Figure 1). A new generation of biologics is also being developed specifically for large-volume, high-viscosity SC delivery. That shift alone changes what a delivery platform needs to be capable of. At the same time, self-administration is expanding further outside of the clinic – into homes – driven by both healthcare systems and patients. Alongside this, expectations around circularity and resource efficiency are increasingly shaping design decisions from the outset.

Together, these pressures are testing previous assumptions about on-body device design. Selecting the right on-body platform therefore requires a balanced assessment across multiple dimensions, not a single pass–fail test as to whether a device can deliver a given drug. Ypsomed have devised three complementary decision lenses: technical and therapeutic fit, usability and programme readiness, and end-of-life considerations, which, combined,

"EVERY ON-BODY DEVICE SELECTION BEGINS WITH THE THERAPY, NOT THE DEVICE."

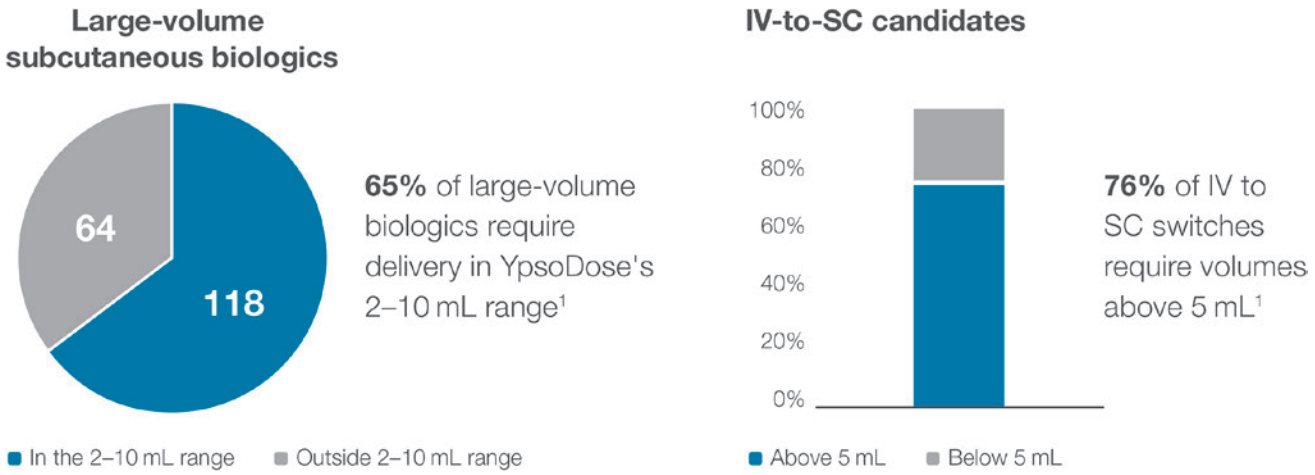

Figure 1: Large-volume biologics and IV-to-SC conversion candidates relative to YpsoDose's 2–10 mL operating range.

offer a practical framework to evaluate how early platform decisions can shape outcomes across the entire product lifecycle.

THROUGH THICK AND THIN: ENGINEERING FOR VISCOSITY, VOLUME AND BEYOND

Every on-body device selection begins with the therapy, not the device. Ask a device development or combination product lead how they assess a new on-body delivery programme, and the conversation rarely starts with the platform's features; it starts with questions about the drug itself. How viscous is the formulation? What volume must be delivered? How long can the injection reasonably take? Is the drug product compatible with the primary container and fluid path? These questions come first because the answers determine which platforms are even viable candidates.

A platform capable of serving many different biologics needs range, not a single fixed point of performance. Volume and viscosity vary considerably from one therapy to the next, and a platform limited to either attribute restricts which programmes it can actually support. This is why operating range matters as much as raw capability: the same underlying platform should be able to serve a given programme's specific requirements, rather than requiring a new device architecture for every new molecule. In practice, this range is what defines YpsoDose, Ypsomed's prefilled and ready-to-use patch injector. Its specifications include: a fill volume of 2.0–10.0 mL, an injection flow rate of 0.3–3.0 mL/min and a motor-driven system supporting a broad viscosity range, for example, 10 mL of a 50 cP formulation delivered in 10 minutes (Figure 2).

Only once those requirements are met can a meaningful assessment of platform quality begin. At that point, the focus shifts from what the therapy requires to how well the engineering behind the platform holds up. Built-in sterility, for example, allows for final assembly outside of a cleanroom and reduces the complexity of aseptic assembly, simplifying manufacturing without compromising safety. An optimised fluid path can reduce the waste of high-value biologics. Designs that allow for component separation can open up recycling opportunities. Here, good engineering decisions reach further than delivery performance alone. They can shape development efficiency, patient usability, manufacturability at commercial scale and what is ultimately possible at end of life.

Meeting these technical demands draws on expertise well beyond the delivery mechanism itself, spanning fluid management, sterile systems, electronics, software and human factors. For Ypsomed, this multidisciplinary base was built over decades rather than being assembled for a single programme. In 1986, the company (then Disetronic) launched one of the world's first microprocessor-controlled insulin pumps, and the fluid management, sterile systems and reliability engineering developed for continuous insulin therapy continue to inform how YpsoDose and other on-body platforms are built today.

Technical fit is the foundation, but it is not the whole picture. A platform must also support intuitive, confident use by the patient administering it, which is where the next dimension of platform selection comes in.

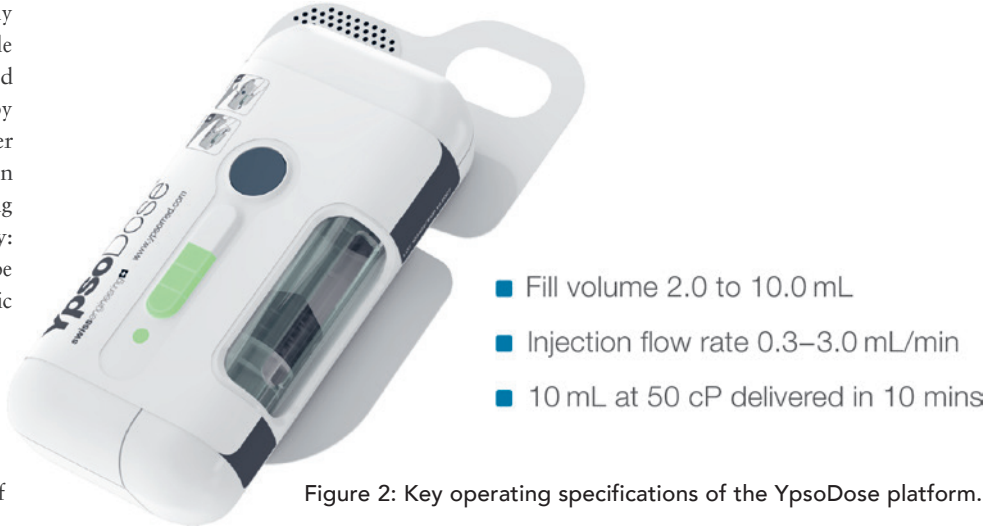

Figure 2: Key operating specifications of the YpsoDose platform.

IN SAFE HANDS: USER CONFIDENCE AND PLATFORM MATURITY

A technically sound platform is only valuable if people can use it correctly, consistently and confidently. Human factors engineering focuses on how patients interact with a device in real-world settings, with the aim of minimising uncertainty, reducing opportunities for user errors and building confidence throughout the injection process.

That confidence cannot be added at the end of development. It has to be engineered in from the start. Human factors activities begin long before the final product design is set – using iterative user research and formative studies to understand how patients think, behave and interact with the device – with the goal of identifying and eliminating barriers before the product ever reaches patients. For example, an eye-tracking study conducted with ETH Zurich (Zurich, Switzerland) led to refinements of YpsoDose's progress bar and status light, optimising their size, position, brightness and segmentation to ensure that patients could interpret device status quickly and confidently.

This attention to confidence matters most for therapies that are administered infrequently, as is typical for larger-volume biologics delivered by on-body devices. For autoimmune disease and cancer treatments, for example, dosing frequency can range from every week up to every six months. Unlike daily injections, infrequent administration gives patients fewer opportunities to become familiar with a device and therefore increases the chance of errors, which makes simple, intuitive handling essential for confident, long-term use.

This approach is directly highlighted in YpsoDose's design. Its ready-to-use configuration removes cartridge and drug-handling steps, reducing opportunities for user error before the injection even begins. Skin-contact detection sensors confirm correct application before, during and after injection, while clear audio and visual feedback guides patients throughout use. The device is also designed to perform reliably across varying temperatures, orientations and injection sites, as patients rarely inject under identical conditions each time. Together, these features are built to reduce uncertainty and support confident self-administration outside clinical supervision.

For pharmaceutical companies, however, confidence in the patient experience is only part of programme readiness. A qualified manufacturing process, completed verification activities, an established primary container and an experienced partner network all help to reduce development risk and support a smoother path to commercialisation. These elements matter because design changes that surface late in development, after verification work is already underway, can delay regulatory submissions and add significant cost. Starting from a platform with established qualification data and a proven partner network avoids much of that risk before a programme even begins. For YpsoDose, this includes partnerships with SCHOTT Pharma (Mainz, Germany) for primary containment using the 10 mL cartriQ® cartridge and ten23 health (Basel, Switzerland) for fill-finish and final assembly, bringing expertise across the value chain as programmes move towards commercialisation (Figure 3).

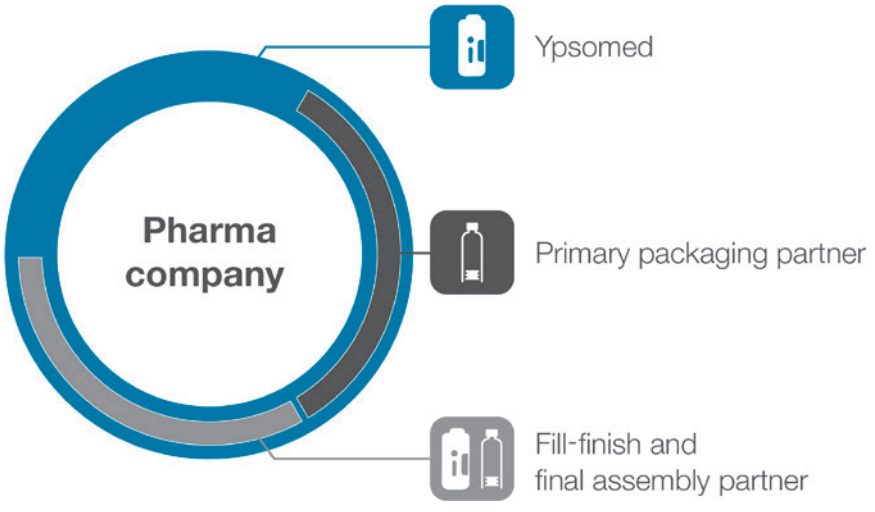

Figure 3: YpsoDose is a complete, clinic- and market-ready solution, supported by expert partners in primary packaging (SCHOTT Pharma) and final assembly (ten23 health).

"SELECTING AN ON-BODY PLATFORM THEREFORE MEANS SELECTING THE ENGINEERING KNOWLEDGE, MANUFACTURING CAPABILITY AND PARTNER ECOSYSTEM THAT SURROUND IT, NOT JUST THE DEVICE ITSELF."

Selecting an on-body platform therefore means selecting the engineering knowledge, manufacturing capability and partner ecosystem that surround it, not just the device itself. A mature platform can remove complexity throughout development, allowing pharmaceutical companies to focus more of their effort on the therapy itself. Confidence in use and confidence in execution go hand in hand, and for many programmes, that confidence now must also apply to end-of-life considerations.

LIFE AFTER DOSE: LCAs AND COMPONENT REUSE

The final injection should not mark the end of the engineering conversation. Decisions made during platform development shape what becomes possible once a device has fulfilled its intended purpose, and expectations around circularity, resource efficiency and product stewardship are becoming a more visible part of platform selection.

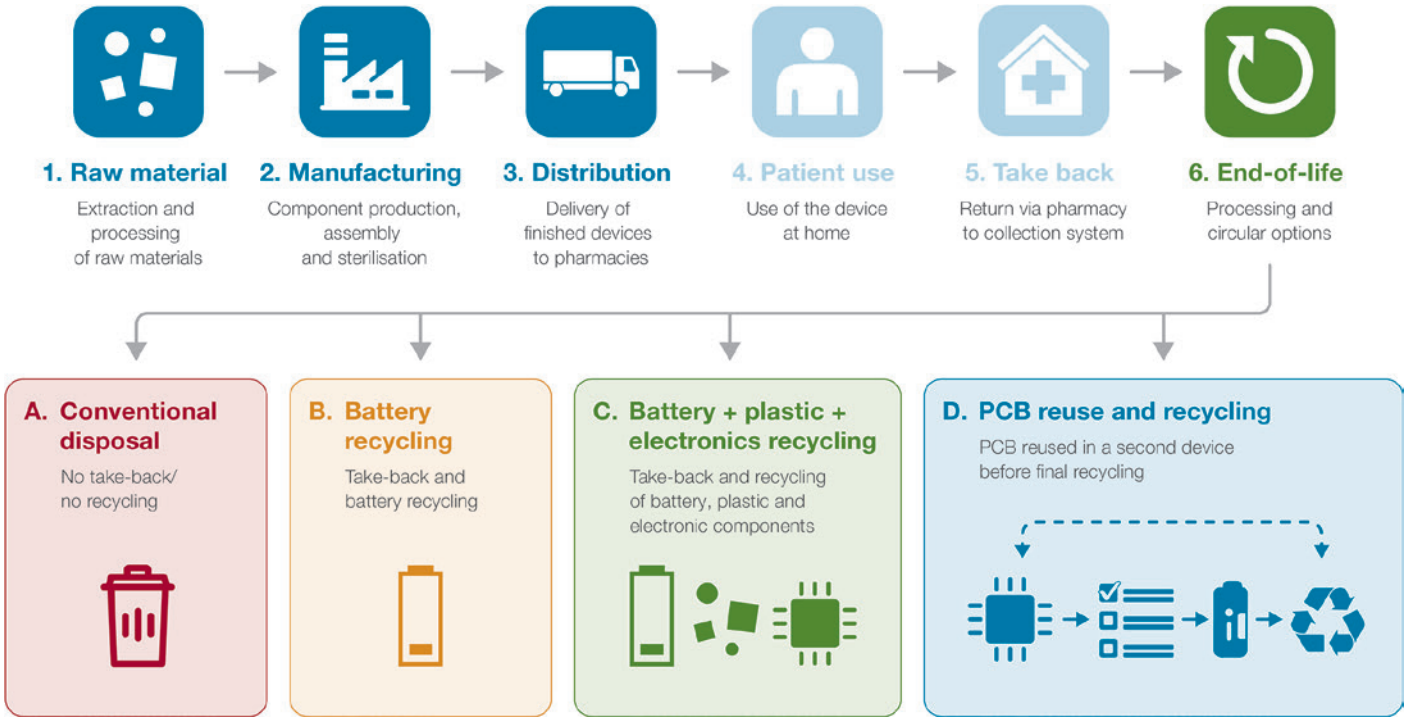

Figure 4: Lifecycle and end-of-life options for YpsoDose. Ypsomed's LCA used a conservative assumption of one reuse per PCB, though more reuses are feasible.

Like technical performance or usability, end-of-life performance cannot simply be added later. It is the result of engineering decisions made throughout product development. Choices around material selection, product architecture and component integration determine whether a device can support take-back, disassembly, recycling or component reuse. These same engineering decisions can also influence other aspects of lifecycle performance. With high-value biologics, even small amounts of residual drug left in the fluid path add up to meaningful cost and waste at scale, and manual filling steps can introduce further losses on top of that. YpsoDose addresses this through a prefilled cartridge and a simplified fluid path consisting of two cannulas and a short connecting tube. The device's own fluid path contributes less than 0.015 mL of residual volume, bringing the total system residual, including the cartridge, to under 0.262 mL, while eliminating manual filling from the process entirely.

Lifecycle assessment (LCA) provides a way to move discussions from aspiration to evidence. Rather than relying on broad sustainability claims, pharmaceutical companies need to understand which decisions deliver measurable outcomes. To support this, Ypsomed has undertaken an LCA of YpsoDose in accordance with internationally recognised ISO 14040 and ISO 14044 standards. The assessment compares multiple end-of-life scenarios, including baseline disposal, battery removal and take-back, printed circuit board recycling and plastics recycling combined with printed circuit board (PCB) reuse. The assessment identified PCB reuse and recycling of battery and plastic components as the scenario with the greatest CO_2 reduction potential, shrinking the product's carbon footprint by over 23% compared with the LCA's baseline scenario of only recycling the battery (Figure 4).

Ypsomed is constantly evaluating practical take-back concepts and engaging with recycling partners across its entire platform portfolio. For YpsoDose specifically, Ypsomed is also designing disassembly tools, and even actively testing the reuse of PCBs, going well beyond mere compliance. PCB reuse in particular offers significant potential to reduce CO_2 emissions and conserve valuable materials, especially as the PCB is one of the main contributors to the device's environmental footprint. These activities also help Ypsomed to prepare for evolving regulatory requirements for electronic medical devices, particularly in Europe (e.g. the new EU Batteries Regulation). Ultimately, selecting an on-body delivery platform means considering the entire product lifecycle, from the earliest engineering decisions through commercialisation and beyond the final injection. Platforms developed with this broader perspective can help pharmaceutical companies to meet today's technical and commercial requirements while remaining prepared for tomorrow's.

A WIDE ANGLE: THREE LENSES, ONE DECISION

Selecting an on-body delivery platform has become a broader engineering and strategic decision than it once was. Technical capability remains fundamental, but it is no longer the only criterion that determines long-term success. Platform maturity, patient confidence, development efficiency, commercial readiness and lifecycle considerations all influence how effectively a therapy can move from concept to commercial reality.

These factors do not operate independently. Engineering decisions that improve technical performance can also

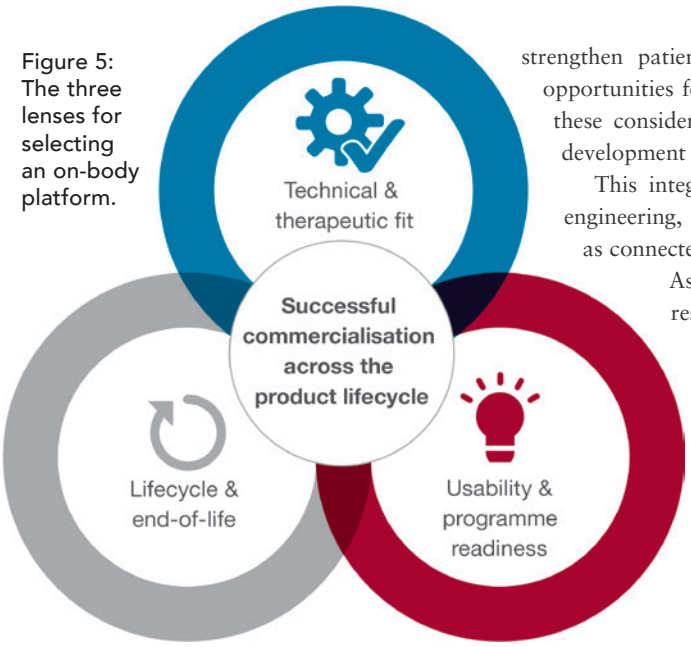

Figure 5: The three lenses for selecting an on-body platform.

strengthen patient usability, simplify development, reduce drug waste or create new opportunities for circularity. The strongest platforms are those that are built to balance these considerations from the outset, rather than addressing them one at a time as development progresses.

This integrated philosophy is reflected in the development of YpsoDose, where engineering, human factors, industrialisation and lifecycle design have been treated as connected parts of the same effort rather than separate workstreams.

As biologics, self-administration and sustainability expectations continue to reshape on-body delivery, the questions pharmaceutical companies ask when selecting a platform will also keep evolving. The platforms best positioned to meet them will be the ones designed to deliver value from the earliest engineering decisions to well beyond the final injection (Figure 5).

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Interview:
Off The Critical Path: Bringing Device Strategy Forward In Combination Product Development

While emerging biotech and small-to-mid-sized pharmaceutical companies often possess strong molecules, they have limited in-house device and combination product infrastructure, meaning that, if they treat the delivery system as a late-stage procurement decision, it can frequently land squarely on the critical path. Considering this situation, **David Karvani** of **Ventura Solutions** and **Dr Greg Moakes** of **LTS Lohmann Device Technologies** discuss how, to navigate the complex technical and regulatory hurdles inherent to device development efficiently, pharma sponsors increasingly need to enter into a collaborative ecosystem early in the development lifecycle.

Q Emerging biotech and small-to-mid pharma often have a strong molecule but limited device and combination product infrastructure – where do these companies struggle most, and how do your respective roles make it easier?

DK The pattern across the industry is fairly consistent: a company spends years de-risking its molecule and the device gets treated as something to solve later, until a clinical or regulatory milestone forces the issue and it suddenly lands on the critical path. By then, the team is making device decisions under time pressure, often without the in-house design controls, human factors or combination-product regulatory experience to give them the confidence they need.

As an integrated device partner, taking that work off the critical path before it becomes a crisis is exactly what we do, serving as a complete device organisation for our pharma clients. Early on, that means translating the target product profile – dose, volume, viscosity, patient setting and dosing frequency – into a concrete set of device requirements so that the pharma company can choose a delivery approach against defined criteria rather than simply reacting to whatever is in front of it. After that, we do the feasibility work that connects the formulation to a real device and primary container so that the development team does not lock in a formulation that no available device can actually deliver.

"THE TROUBLE SHOWS UP AT THE INTERFACES – WHO OWNS THE USE-RELATED RISK ANALYSIS, WHOSE DOCUMENT IS THE SOURCE OF TRUTH FOR A GIVEN REQUIREMENT AND HOW DO DESIGN CHANGES FLOW BACK INTO DRUG STABILITY?"

GM Based on what I have seen, this is where the synergy between a proven platform manufacturer and an integrated device partner creates value. At LTS, for example, we bring significant electroanalytical and biomechanical engineering depth, validated on-body delivery system platforms, extensive device master file data and active clinical and regulatory support. In so doing, we help translate complex formulation realities into reliable, validated device inputs.

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David Karvani is Senior Director of Business Development and Strategic Partnerships at Ventura Solutions. His career has focused on the development and commercialisation of drug-device combination products, particularly parenteral drug delivery systems, including prefilled syringes, autoinjectors and on-body injectors. His experience spans clinical-, early- and late-stage product development, as well as regulatory strategy, market access and commercialisation planning.

On the other side, integrated device partners can provide the flexible execution support that many emerging sponsors lack, including establishing the design control framework, risk management, human factors planning, as well as a combination product regulatory strategy that is decided deliberately rather than defaulted into. Underneath all of that is programme management that keeps the device workstream aligned with the clinical and chemistry, manufacturing and controls (CMC) timelines so that they arrive together. This way, the sponsor's team can stay focused on its molecule while an experienced device infrastructure runs the programme in parallel. What changes is that decisions are made earlier, with better information and with fewer expensive reversals later.

Q **Once a company decides to move forwards, how do you actually divide the work, and where are the handoffs between an integrated device partner and a platform manufacturer?**

DK The honest answer starts with how it usually goes wrong. A sponsor typically contracts a device manufacturer and a fill-finish CDMO separately and then tries to co-ordinate them itself while running clinical programmes. The trouble shows up at the interfaces – who owns the use-related risk analysis, whose document is the source of truth for a given requirement and how do design changes flow back into drug stability?

The cleanest way to think about the division is by constituent parts (Figure 1). First, the device platform manufacturer owns the platform design, device level design history file, device master record and validated manufacturing processes. Secondly, the integrated device partner sits on the sponsor side to help manage system-level requirements, creation and management of the combination product-level design history file and risk management file, human factors execution, quality system updates and regulatory strategy, along with managing the device manufacturers and vendors. Finally, the pharma sponsor owns the molecule, the clinical programme, the overall combination product design history file (DHF) and the final regulatory submission.

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GM The point worth emphasising is that, while external partners can bridge resource gaps, the sponsor always retains ultimate ownership of the full combination product system and the DHF. In practice, the device team defines the system requirements from the target product profile and passes on the device-relevant ones to the platform manufacturer, who confirms what the platform can achieve and feeds back its design inputs and constraints.

The important point is that the sponsor builds and owns its own combination product DHF, and that work sits with the sponsor device team, whether it is internal or external. The combination product DHF incorporates that device design information, but it remains the sponsor's document, created on the sponsor side, not inherited. Design reviews are the sponsor's own internal process, run by the sponsor's device team, not a joint exercise with the platform manufacturer. Furthermore, change control is led by the sponsor, with the platform manufacturer brought in as needed based on what a given change actually touches, so any device-relevant change gets the manufacturer's input while the sponsor stays accountable for the combination product as a whole.

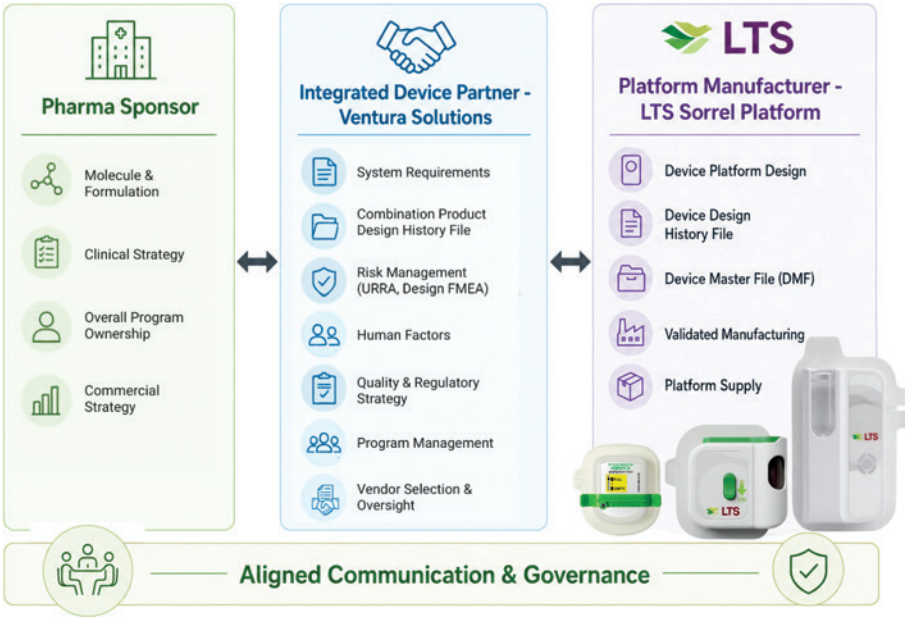

Figure 1: Collaborative model and ownership across the pharma sponsor, integrated device partner and platform manufacturer.

"THE BREAKDOWN WE SEE MOST OFTEN IS THE LATE HANDOFF, WHEN A SPONSOR HANDS A FINISHED FORMULATION TO A PLATFORM MANUFACTURER, OR A FINISHED DEVICE TO A FILL-FINISH PROVIDER, WITH NO INTEGRATING PARTY, AND THE INTERFACES GET DISCOVERED DURING VERIFICATION OR, WORSE, DURING A REGULATORY REVIEW."

This only works if that split is agreed at the start. The breakdown we see most often is the late handoff, when a sponsor hands a finished formulation to a platform manufacturer, or a finished device to a fill-finish provider, with no integrating party, and the interfaces get discovered during verification or, worse, during a regulatory review. Defining the division early is not bureaucracy – it is what prevents the need for rework down the line.

This approach also lets the device platform manufacturer do what it does best. When the requirements arriving at its door are clear and the regulatory path is already chosen, a validated platform can be quickly configured against those requirements, rather than absorbing requirement churn.

Figure 2: The delivery device sits at the intersection of the molecule, primary container, manufacturing, human factors, design and regulatory workstreams.

"ENGAGING A DEVICE TEAM AND DEVICE PLATFORM MANUFACTURER EARLY HELPS TO IDENTIFY THESE ISSUES SOONER. THE SAME QUESTIONS ARE ADDRESSED AT THE START, WHEN ANSWERS ARE EASIER AND LESS COSTLY TO ACT ON, RATHER THAN DURING VERIFICATION OR REGULATORY REVIEW."

Q For the sponsor, what actually changes when both a device team and a platform manufacturer are engaged early? What does it mean for project risk, timelines and decision-making?

DK The benefits are easiest to see by looking at where combination-product programmes usually lose time and money, which is late in development. Costly failures include reopening a design freeze to address previously unidentified human factors issues, reworking formulations due to primary container compatibility issues or revising regulatory pathways that do not support the intended product presentation or labelling.

Engaging a device team and device platform manufacturer early helps to identify these issues sooner. The same questions are addressed at the start, when answers are easier and less costly to act on, rather than during verification or regulatory review. For the sponsor, this reduces development risk in practical terms – fewer late design changes, fewer human factors surprises and a regulatory strategy selected deliberately rather than discovered by default (Figure 2).

Taking this approach also improves the quality of decision-making. A lot of the device missteps we see come from a narrow view of what is available. A company defaults to the modality it has seen before and either overengineers a problem or picks an approach the molecule does not actually need. Mapping the solution space up front, with people in the room who have run these programmes before, means that choices are made against defined criteria rather than by habit. The sponsor is not guessing.

GM There is a capital efficiency angle too, and it applies to both halves of the collaboration. On the device platform side, a validated platform avoids paying to design and qualify a device architecture from scratch – a substantial investment for a capability the sponsor may only need intensively during specific phases. The same logic then applies on the development side; standing up a full design control, human factors and combination product regulatory team in-house is a large investment to make right at the start of a programme.

Most sponsors will grow into these capabilities in time – they tend to need them for lifecycle management and as their portfolio expands, and many build out their own device teams as they scale. The real question is timing. An external device team can provide that capability in the early phase, when building it internally would be premature, and the internal function gets built later, when the timing is right rather than under pressure. Between the two, the money stays pointed at the molecule and the clinic.

The honest caveat is that most of this upside depends on engaging early. The same two parties can still help a programme when brought in late, but by then the work is mitigation rather than prevention, and the savings are smaller. If there is one benefit that the sponsor feels most directly, it is the speed of reaching clinic.

Q If you could give an emerging biotech one piece of guidance before they start their device programme, what would it be? And what does getting it right look like?

DK If there is one thing worth changing, it is not only the timing but also the resources brought into the programme. Many teams treat the device as a procurement decision to be made near the end of development, once the molecule has been de-risked and the formulation largely finalised. This instinct is understandable because no sponsor wants to commit significant resources to a device for an asset that may not progress through early clinical development. However, waiting too long, or proceeding without the appropriate device engineering, human factors, quality and regulatory expertise can allow critical decisions to be made without fully considering their implications for the combination product.

Engaging early does not mean launching a full device development programme or committing significant capital before the asset is ready, it means establishing the appropriate foundation. A sponsor can define the target product profile, assess technical feasibility, identify potential platform and primary container options, and develop an initial regulatory strategy while meaningful flexibility still exists.

This early work may also include determining whether engagement with the US FDA or another regulatory authority would help clarify the proposed development pathway, intended presentation or combination product requirements. In parallel, the sponsor can begin assessing whether its pharmaceutical quality system requires additional procedures or updates to support applicable combination product requirements, including the integration of device-related quality system requirements.

At the product level, the team can establish the initial design control framework, begin building the sponsor-owned DHF, develop preliminary system and device requirements, initiate risk management and define how responsibilities will be divided among the sponsor, platform manufacturer, primary container supplier, fill-finish partner and other development providers. The cost of this foundational work is generally modest relative to the overall programme. More importantly, it allows subsequent platform selection, development planning and capital commitments to be made using technical evidence and a defined regulatory and quality framework, rather than under deadline pressure.

GM I would add that a sponsor should treat the device as a system-level development decision rather than as a component purchased at the end. The questions that matter are development questions, not procurement ones. Can the formulation be delivered at the intended volume and viscosity? Does the use scenario introduce risks that must be addressed through design, labelling or training? Does the proposed regulatory pathway support the intended product presentation and labelling? These questions are less costly and less disruptive to answer before the platform and formulation are locked.

What "good" looks like is often fairly unglamorous. It is the kind of work that may go unnoticed precisely because it prevents a problem from occurring. Consider, for example, a mid-sized biopharmaceutical company developing a high-volume, high-viscosity biologic. In a late-engagement scenario, the team may finalise the formulation without sufficient input from the device and primary container workstreams. It could then discover during later development that delivery forces, container performance, delivery duration or other system constraints are incompatible with the intended presentation. Addressing those issues at that stage may require changes to the formulation, primary container, device strategy or clinical plan.

Conversely, when the sponsor engages a device platform manufacturer and an experienced combination product device partner during initial product profiling, feasibility can be assessed before the formulation and primary container configuration are finalised. The team can evaluate established platform parameters, including deliverable volume, viscosity, flow rate, delivery duration, container compatibility and intended use conditions.

For example, the LTS Sorrel platform has been characterised using primary container configurations supporting delivery volumes of up to 25 mL and formulations with viscosities exceeding 170 cP. Its software-controlled delivery profile also allows delivery parameters to be adjusted within the platform's operating range based on the characteristics of the drug product and the intended administration profile.

Using these platform-specific data early allows the sponsor to determine whether the formulation, primary container and delivery requirements are compatible before key product decisions are locked. Where constraints are identified, the formulation or delivery strategy can be adjusted while options remain available, reducing the likelihood that device feasibility becomes a critical-path issue later in development.

"ENGAGING EARLY DOES NOT MEAN LAUNCHING A FULL DEVICE DEVELOPMENT PROGRAMME OR COMMITTING SIGNIFICANT CAPITAL BEFORE THE ASSET IS READY, IT MEANS ESTABLISHING THE APPROPRIATE FOUNDATION."

By the time the molecule reaches its next key clinical milestone, the sponsor can already have a defined device strategy, preliminary requirements, informed regulatory pathway and feasible platform direction. This helps keep the device workstream aligned with the clinical and CMC programmes rather than allowing it to become a source of delay.

This is also why the entry point matters. A sponsor does not need to commit immediately to a full device development programme to benefit from early engagement. A focused feasibility effort can answer the questions that matter most, including rheological feasibility, primary container compatibility, delivery profile, intended use and platform fit. This targeted work represents a relatively small investment compared with the overall programme and allows the sponsor to make critical decisions using real data before significant capital is committed.

Q **Any final thoughts for a team about to start?**

DK If I had to leave a sponsor with one thought, it is this – the device is not a late-stage purchase, it is an early development decision. Emerging companies rarely run into trouble because they lack ambition; more often, the device question simply gets asked too late, after the formulation, the primary container, the clinical strategy or the intended use has already narrowed the options. Bringing a platform manufacturer and a device partner into the conversation early, before the formulation is locked and while the regulatory path is still open, does not add cost or complexity, it removes the reversals that quietly consume both. For a lean team with a promising molecule, that is often the difference between a device workstream that supports the development programme and one that ends up holding it back.

"EMERGING COMPANIES RARELY RUN INTO TROUBLE BECAUSE THEY LACK AMBITION; MORE OFTEN, THE DEVICE QUESTION SIMPLY GETS ASKED TOO LATE, AFTER THE FORMULATION, THE PRIMARY CONTAINER, THE CLINICAL STRATEGY OR THE INTENDED USE HAS ALREADY NARROWED THE OPTIONS."

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Expert View

INDUSTRIAL ARCHITECTURE: THE NEXT COMPETITIVE ADVANTAGE IN WEARABLE INJECTORS

Andy Wertheim of Quvara Medical puts forward the case that wearable drug delivery devices comprise two separate architectures – therapeutic and industrial – that must be developed and implemented in tandem if a development programme is to achieve long-term commercial success.

Every wearable injector has two interconnected architectures (Figure 1). The first of these, the "therapeutic architecture", defines how the product safely and effectively delivers the therapy – a sophisticated combination of formulation science, device engineering, human factors and digital connectivity, designed to move complex biologics out of the clinic and into the patient's home. The second, the "industrial architecture", determines whether or not that product can be manufactured consistently, verified efficiently, supplied reliably and sustained profitably throughout its commercial life.

While the therapeutic architecture is well understood and heavily funded, its industrial counterpart receives far less explicit attention. Yet, history across the drug delivery landscape demonstrates that technical innovation alone rarely guarantees market dominance. The recent boom in the glucagon-like peptide-1 (GLP-1) market provides perhaps the clearest example – extraordinary therapeutic innovation and unprecedented patient demand for semaglutide and tirzepatide were nevertheless constrained by the ability of their manufacturers to expand manufacturing capacity at sufficient speed. Novo Nordisk has subsequently committed US$4.1 billion (£3 billion) to expanding US manufacturing capacity, including additional aseptic manufacturing and fill-finish capacity,[1] while Eli Lilly has committed a further $5.3 billion to its Lebanon (IN, US) site to expand API capacity for Mounjaro® (tirzepatide, Eli Lilly) and Zepbound® (tirzepatide, Eli Lilly).[2]

Products succeed not simply because the therapy or device is innovative, but because the industrial systems supporting

"WHILE THE THERAPEUTIC ARCHITECTURE IS WELL UNDERSTOOD AND HEAVILY FUNDED, ITS INDUSTRIAL COUNTERPART RECEIVES FAR LESS EXPLICIT ATTENTION. YET, HISTORY ACROSS THE DRUG DELIVERY LANDSCAPE DEMONSTRATES THAT TECHNICAL INNOVATION ALONE RARELY GUARANTEES MARKET DOMINANCE."

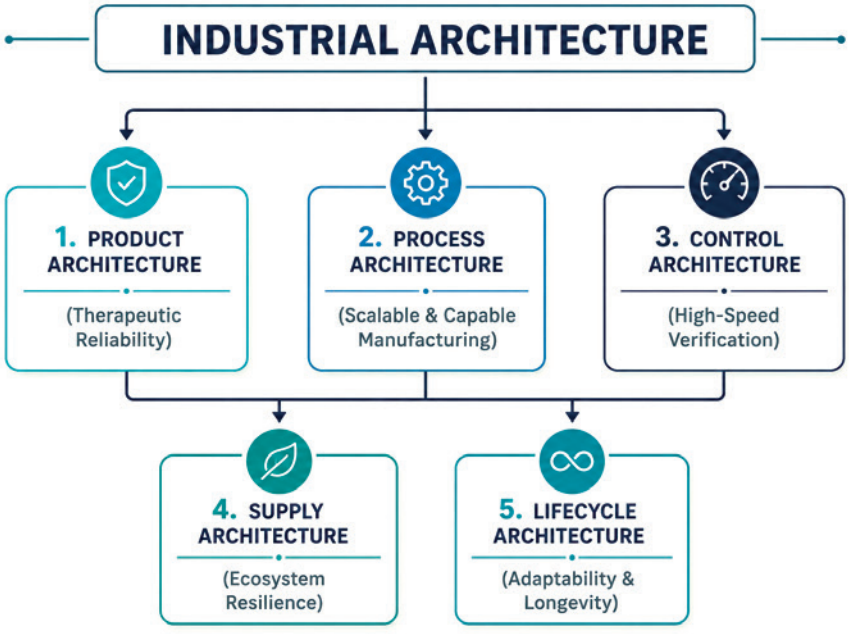

Figure 1: The therapeutic and industrial architectures of a wearable device.

them can deliver that innovation reliably at commercial scale. As such, the current industry-wide shift towards home-based, high-volume subcutaneous delivery has heightened scrutiny on supply reliability.[3,4] Regulators have moved rapidly to address these industrial complexities. For example, ISO 11608-6:2022 sets explicit standards for on-body systems, and the US FDA's 2024 draft guidance on Essential Drug Delivery Outputs reinforces the need to manage manufacturing variation across the entire product lifecycle.

Wearable injectors are no longer just medical devices; they are integrated drug, engineering and manufacturing ecosystems. To realise their full commercial potential, organisations must stop treating device design, manufacturing, quality and supply as isolated workstreams. They must consciously engineer both architectures simultaneously.

FROM INNOVATION TO INTEGRATION

The wearable injector industry has achieved remarkable technical milestones over the past decade. Sophisticated mechanical and electromechanical platforms now routinely handle complex delivery profiles outside traditional healthcare settings. However, the industry's primary vulnerability is no longer a lack of engineering capability; it is a lack of disciplinary integration.

Wearable injector programmes are traditionally managed in functional silos – formulation scientists optimise the drug, device engineers refine the fluid path, quality teams map compliance and manufacturing engineers build the assembly lines. Each discipline executes its role exceptionally well, but commercial failure routinely occurs in the blind spots between them. Programmatic decisions that seem entirely logical from a single technical perspective frequently create catastrophic downstream consequences when the design is frozen and changes become cost-prohibitive.

The GLP-1 supply crisis has offered a stark lesson in this dynamic. Demand for therapies such as Wegovy® (semaglutide, Novo Nordisk), Mounjaro® and Zepbound® expanded faster than the industrial infrastructure supporting them. Novo Nordisk responded with multibillion-dollar investment in additional manufacturing and fill-finish capacity, while Eli Lilly similarly embarked on major capacity expansion. This lesson extends well beyond GLP-1s – commercial demand is only valuable when the industrial ecosystem can translate it into product available to patients.

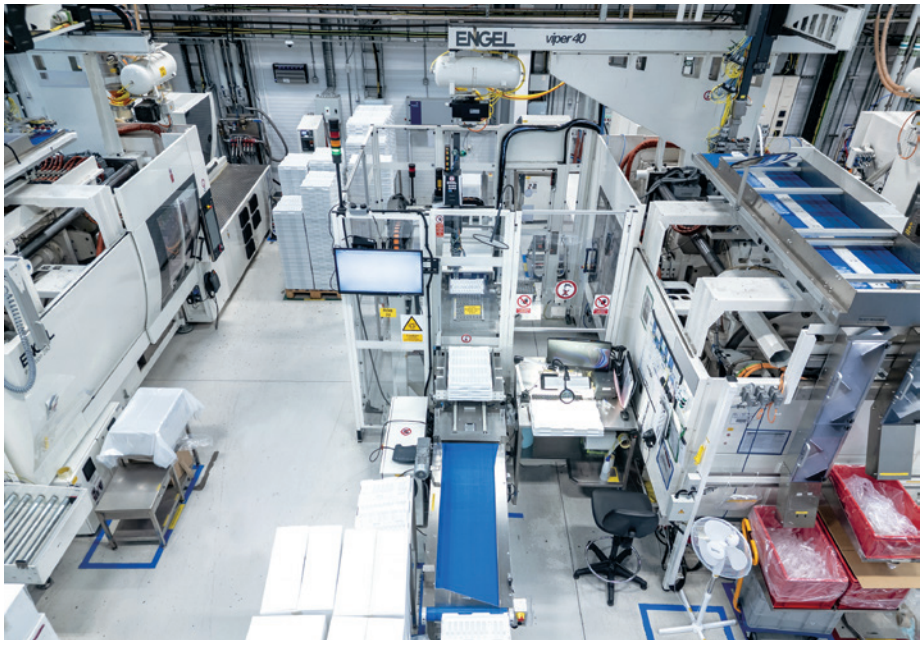

Figure 2: Industrial architecture considers five dimensions – product, process, control, supply and lifecycle – that ask whether a development programme is prepared for industrial-scale production and commercialisation.

The importance of industrialisation is increasingly visible within the wearable injector market itself. For example, BD's (Franklin Lakes, NJ, US) Libertas™ platform has been engineered not only around drug delivery performance and patient usability but also around compatibility with established prefillable syringe filling processes and commercial equipment. BD also highlights validated filling and assembly processes as part of the platform's development proposition. This illustrates an important evolution in device development – manufacturability and industrial integration are becoming attributes of the platform itself, rather than activities deferred until after device design.

As devices expand into highly complex biologic territories, such as the on-body presentation of Sarclisa® (isatuximab-irfc, Sanofi), the intersection of advanced formulations, micro-electronics and high-volume assembly demands even tighter integration. As devices become more capable, the industrial systems required to build them become exponentially more complex. Competitive advantage will belong to the companies that design better industrial systems, not just better devices.

THE FIVE DIMENSIONS OF INDUSTRIAL ARCHITECTURE

This holistic perspective can be defined as "industrial architecture". It does not replace established frameworks such as systems engineering, quality by design, or design for manufacture and assembly. Instead, it focuses on a broader commercial question: "Has the entire industrial system been engineered to deliver the required product performance consistently, efficiently and sustainably throughout its market life?" To answer this, multidisciplinary teams must evaluate five interconnected dimensions of industrial architecture early in the development lifecycle, ensuring that clinical choices do not inadvertently break the commercial model (Figure 2).

Product: Can the Product Design Support its Own Industrialisation?

The "product" dimension spans the formulation, primary container, fluid path, drive mechanism, electronics,

primary adhesive and user interface. While traditionally evaluated against clinical safety and usability, the product dimension also dictates the industrial constraints that follow. Choosing a specific primary container modifies automated handling line requirements – opting for an electromechanical drive over a mechanical spring alters verification protocols and component sourcing. Product design and industrial design must evolve in unison; a device designed in a vacuum will inevitably struggle on the factory floor.

Cost reduction and sustainability are not late-stage procurement exercises; they are architectural design objectives. Component count, material selection, tolerances, testability, automation complexity, scrap risk and supplier strategy all determine the cost base and environmental footprint long before commercial launch. Industrial architecture enables teams to reduce cost and environmental impact by design while protecting performance, quality, supply resilience and regulatory confidence.

Process: Can the Manufacturing Process Naturally Deliver Critical Performance Outputs at Scale?

Commercial viability hinges on process capability, not raw capacity. A manufacturing line capable of producing millions of units is a liability if the process cannot repeatedly hit the narrow window of characteristics required for therapeutic performance. Wearable delivery involves a highly volatile mix of component tolerances, assembly forces, material behaviours and electronic calibrations.

Modern process validation is not a pre-launch checkbox. The FDA's process-validation guidance explicitly frames validation as a lifecycle activity built on scientific understanding and control of manufacturing variation.[5] For wearable injectors, that means engineering a manufacturing process in which natural, statistical variation does not compromise the device's essential outputs.

Control: Is the Device Designed to be Verified at High Speed, or Will Inspection Strangle the Supply Chain?

Quality cannot be inspected into a product; it must be designed into it. The "control" dimension identifies the specific variables that dictate therapeutic success and determines the most efficient way to assure them, whether through raw material specifications, in-line vision systems, statistical process control or end-of-line functional testing. Because wearables fuse mechanical, fluidic, electronic and software systems into one combination product, testability must be treated as a core design requirement. If demonstrating compliance requires slow, overly complex or destructive end-of-line testing, the commercial model will buckle under the cost of verification.

Supply: Can the Broader Industrial Ecosystem Withstand Commercial Shocks?

A wearable injector is only as resilient as its weakest sub-tier supplier. Electronics, specialised elastomers, high-performance adhesives, moulded components and batteries each bring distinct supply chain risks. The "supply" dimension maps these dependencies early. Questions surrounding multicavity tooling ownership, second-sourcing, technology transfer protocols and geographic manufacturing footprints must be resolved during the design phase, not after launch, transforming supply chain vulnerabilities into conscious, managed strategic choices. The value of redundancy is measurable – modelling of pharmaceutical supply-chain reliability has found that, under baseline assumptions, adding a backup supplier to a lean configuration reduced expected shortages from 10% to 4%.[6]

Lifecycle: Can the Industrial System Adapt as the Product and Market Evolve?

Launch is not the finish line; it is the baseline. Over a product's commercial lifespan, production volumes scale up, new clinical indications are approved, electronic components face obsolescence, software requires patching and manufacturing lines are transferred to new sites. The "lifecycle" dimension treats post-launch changes as active design inputs rather than operational emergencies. The goal is to design a flexible product and manufacturing framework that can absorb inevitable lifecycle changes without triggering disruptive regulatory refiling or supply interruptions.

The evolution of West Pharmaceutical Services' (Exton, PA, US) SmartDose® platform (see page 52) illustrates this lifecycle reality. Developed across multiple delivery-volume configurations, the platform has continued to evolve as market requirements have changed. In 2026, West transferred the manufacturing and supply rights and associated facilities for its 3.5 mL system while continuing to develop and manufacture other SmartDose® configurations, including its 10 mL platform.[7] Industrial architecture must therefore accommodate not only scale-up but technology evolution, portfolio changes and manufacturing transfer throughout a platform's commercial life.

> "CHOOSING A SPECIFIC PRIMARY CONTAINER MODIFIES AUTOMATED HANDLING LINE REQUIREMENTS – OPTING FOR AN ELECTROMECHANICAL DRIVE OVER A MECHANICAL SPRING ALTERS VERIFICATION PROTOCOLS AND COMPONENT SOURCING."

INDUSTRIAL ARCHITECTURE IN PRACTICE

To see the interplay of the dimensions of industrial architecture, consider a common scenario: a development team decides to increase a formulation's concentration to reduce the overall injection volume, aiming to improve patient convenience. Clinically and commercially, the choice appears flawless. However, the cascading industrial consequences are profound:

- **Product & Process:** Higher concentration increases fluid viscosity, requiring a significantly higher delivery force. This forces a shift from a standard mechanical spring to a high-force drive system, altering component tolerances and increasing required assembly forces.

- **Control & Supply:** The increased assembly forces require more stringent in-line automated inspection to prevent cosmetic and structural component damage. Meanwhile, the high-force mechanism requires specialised materials, narrowing the supply base to a handful of tier-one vendors.

What began as a straightforward pharmaceutical optimisation ripples through the entire system, ultimately dictating production yields, capital expenditure and long-term gross margins. Industrial architecture does not stifle this type of clinical innovation; it eliminates the surprises, allowing teams to balance these trade-offs consciously while design changes are still viable.

FIVE QUESTIONS BEFORE DESIGN FREEZE

Before committing to major capital investment and freezing a device design, a combination product programme must answer five questions with absolute clarity:

1. **Essential Outputs:** Have the essential drug delivery outputs been clearly isolated from non-critical metrics and structurally protected?
2. **Process Capability:** Does the manufacturing process naturally deliver the essential outputs via statistical capability, or does it rely on excessive end-of-line inspection?
3. **Verification Efficiency:** Is the control strategy balanced, combining material specifications, automated in-line metrics and functional testing without creating a production bottleneck?
4. **Ecosystem Resilience:** Have sub-tier dependencies – including tooling capacity, electronic components and material single-sources – been mapped, stressed and explicitly accepted?
5. **Lifecycle Flexibility:** Can the device design and the manufacturing line absorb a component swap, a software update or a site transfer without halting commercial supply?

CONCLUSION

The future of wearable injectors will undoubtedly be driven by breakthrough science, such as ultra-high-volume delivery, advanced digital connectivity and deeply intuitive patient-centric design – technical innovation remains the entry ticket. However, as devices become more sophisticated, the basis of competition shifts. The ultimate market winners will not necessarily be the companies with the most complex device features, but those that achieve true integration by unifying the device, process, control system, supply chain and lifecycle strategy into a singular, resilient commercial system.

Successful industrialisation is no longer the passive handover of a finished design to a manufacturer. It is a deliberate, upfront integration strategy. Every wearable injector has two architectures, and the organisations that consciously design both are the ones that will dominate the market.

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ULTRASONIC JOINING PROCESS ENSURES RELIABLE ASSEMBLY OF SENSITIVE CGM COMPONENTS

Fabio Weingärtner of **Herrmann Ultraschall** discusses the value of ultrasonic welding for wearable diagnostic and drug delivery devices, using a continuous glucose monitor developed by GlucoModicum as a case study, describing the joining challenges for distinct, delicate components and the innovative solutions produced to overcome complex design requirements.

Wearable devices, such as continuous glucose monitors (CGMs) and on-body injectors, can be challenging when it comes to fabrication. As a case study, a novel needle-free CGM designed by GlucoModicum (Helsinki, Finland), proved to be a particularly demanding application due to factors such as the presence of sensitive electronics, needing to join different plastics and a demand for short production cycles. Facing this stringent set of design requirements, Herrmann Ultraschall was able to meet them by developing a specialised ultrasonic joining process that ensured that the CGM could be fabricated quickly and reliably. In addition to close collaboration between the partners, the decisive success factors proved to be the dedicated design of both the component and the welding tool (Figure 1).

What makes GlucoModicum's wearable CGM unique is its non-invasive operating principle, which differentiates it from conventional CGM systems. Unlike other CGMs on the market, which require a needle to puncture the skin and place a filament beneath it to access interstitial

> "THE DECISIVE SUCCESS FACTORS PROVED TO BE THE DEDICATED DESIGN OF BOTH THE COMPONENT AND THE WELDING TOOL."

Figure 1: Despite the use of different plastics and a complex component design, Herrmann Ultraschall succeeded in developing a safe and reliable joining process for GlucoModicum's new, needle-free CGM.

fluid, GlucoModicum uses its patented magnetohydrodynamics (MHD) technology to draw interstitial fluid through the skin to the sensor without piercing it. The wearable system consists of two components: a rechargeable transmitter and a one-day biosensor. The biosensor is made of a thin multilayer film supported by a plastic ring.

For the automated production of the biosensor, GlucoModicum needed a joining technology capable of dealing with different components within one process. To achieve this, the film must be attached to the plastic ring before the electrical connection pads are connected to the back of the plastic ring.

Figure 2: To ensure the safe, automated manufacturing of the CGM, GlucoModicum decided to use ultrasonics, which produces strong, durable connections without the need for additional bonding agents.

CRITERIA FOR THE RIGHT JOINING TECHNOLOGY

Both components involved demanding requirements that the joining technology had to fulfil. First, an especially gentle process was required for the sensitive film to protect the integrity of the electronics, in order to ensure the reliable functionality of the medical device itself. At the same time, the bond strength had to be sufficiently high to guarantee secure wear during everyday use.

Additionally, the system needed to be designed for high-volume manufacturing, with automated production of tens of millions units per year planned. As a result, the joining process also needed to support automated manufacturing with short cycle times and highly repeatable results (Figure 2).

EARLY DECISION IN FAVOUR OF ULTRASONIC JOINING

Conventional joining technologies, such as adhesive bonding, reached their limits for this wearable application. The extremely small contact area between the film and the housing made it difficult to achieve a reliable bond using traditional methods, while curing times would have further slowed down the production process.

In contrast, initial feasibility tests conducted in Herrmann Ultraschall's ultrasonic laboratory quickly demonstrated that ultrasonic technology could not only deliver the required bond strength but also meet all demands regarding appearance and processing speed.

CHALLENGING PROJECT DEVELOPMENT

In conventional ultrasonic welding of plastics, typically two identical materials are joined together. In this case, however, the film and the housing consisted of two different plastics that did not allow for a conventional weld.

As a result, a related process was used that is primarily applied for embedding membranes or non-wovens into housings. In this process, high-frequency vibrations are transferred to a plastic housing via a welding tool known as a sonotrode.

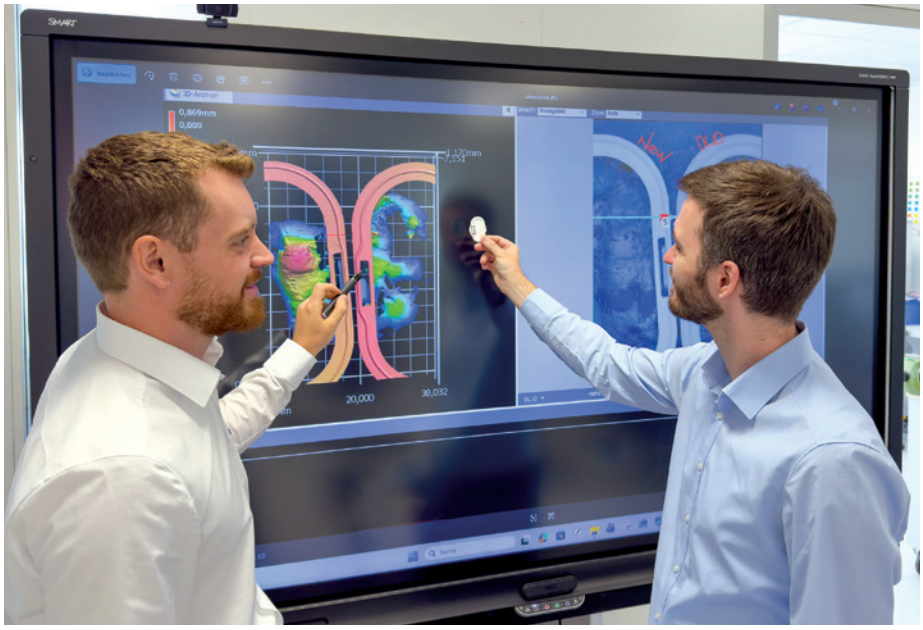

Figure 3: With the consulting provided by Herrmann's application engineers, the product design was slightly adjusted to make it ideal for ultrasonic bonding.

The resulting frictional heat causes the plastic to melt and flow into the pores of the membrane, creating a highly robust mechanical bond.

Unlike membranes, however, the fine plastic film used in the CGM does not contain pores – only microscopic surface roughness. In addition, it incorporates highly sensitive electronic sensors that must not be damaged during the joining process. The solution was a process best described as an interlocking of the materials, implemented through two different technical approaches (Figure 3).

"THE COMBINATION OF A CUSTOMISED SONOTRODE DESIGN AND AN OPTIMISED ENERGY DIRECTOR ULTIMATELY ENABLED THE CREATION OF A ROBUST MECHANICAL INTERLOCK CAPABLE OF WITHSTANDING LARGER FORCES AND MECHANICAL STRESS."

SPECIALISED DESIGN OF COMPONENTS AND WELDING TOOLS

The first step was to adapt the component design itself. In close collaboration between product designers and application engineers, the plastic housing was further optimised to provide an ideal energy director for the process. This ensured that the introduced energy was concentrated locally during joining, protecting the surrounding areas of the component while ensuring that the bond was created only at the intended locations. Unlike conventional ultrasonic welding applications, the energy director in this project was not designed with a sharp geometry, but with rounded edges to protect the film from damage.

Initial trials showed that conventional sonotrodes were not capable of meeting GlucoModicum's requirements regarding bond strength. Therefore, through multiple test series, the application engineers developed a unique sonotrode contour specific to this application. The combination of a customised sonotrode design and an optimised energy director ultimately enabled the creation of a robust mechanical interlock capable of withstanding larger forces and mechanical stress.

In the second joining application within the CGM, where the multilayer film had to be connected to electrical contacts, the primary focus was to protect the electronic components. Since the sonotrode operates directly on the electrical contacts, the contour of the welding tool once again became a critical factor. In this case, a sonotrode with a completely smooth surface and no additional structure proved to be the most suitable solution, enabling uniform and gentle transmission of vibrations into the component (Figure 4).

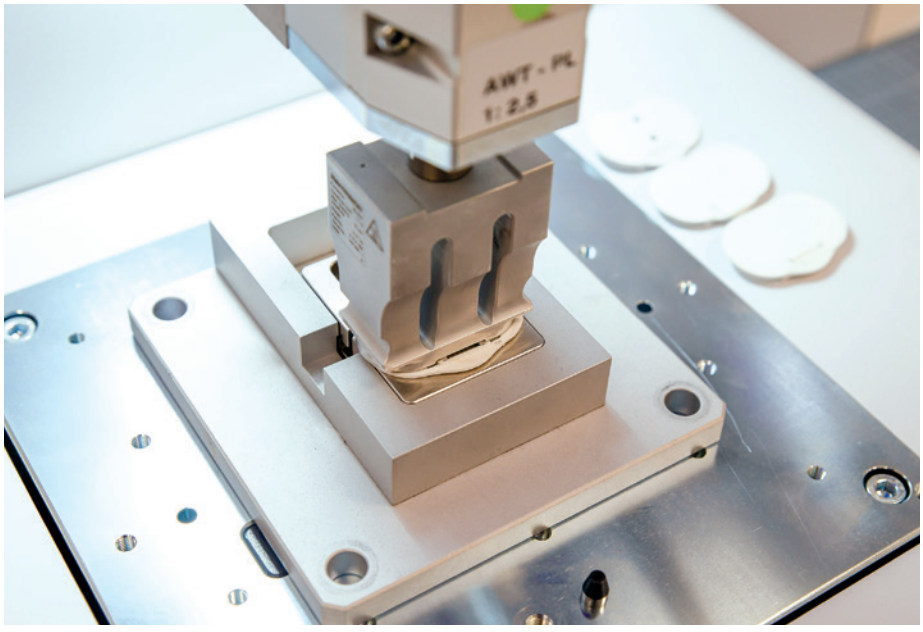

Figure 4: Thanks to a special contour on the welding tool, the delicate film containing the electronics could be gently yet firmly bonded to the plastic ring of the biosensor.

CASTING RESIN PROVIDES ADDITIONAL COMPONENT PROTECTION

To further protect the sensitive components, a dedicated fixture for the welding process was developed, made from a specialised casting resin with a hardness comparable to that of skateboard wheels. This material provides the ideal balance: rigid enough to securely position the component during the process and to protect the sensitive surface from damage. As a result, visual defects on the components could also be reliably avoided.

FINE-TUNING THROUGH PROCESS PARAMETERISATION

After developing the appropriate welding tools, the next phase of the project focused on defining the optimal process parameters. In particular, the adjustment of energy input, force and welding time were essential to ensure a reproducible process that fulfilled all requirements regarding appearance, functionality and safety. When determining the ideal welding parameters, it is always about finding the right balance. Ultrasonic welding can create extremely strong bonds, but this may compromise the visual appearance. Conversely, connections can be optimised for a flawless appearance, but doing so can come at the expense of bond strength. In this case, through multiple rounds of testing in its laboratory, Herrmann Ultraschall was able to identify the ideal parameter set – strong enough to create a reliable bond, yet gentle enough to protect both the sensitive electronics and the visual appearance of the application.

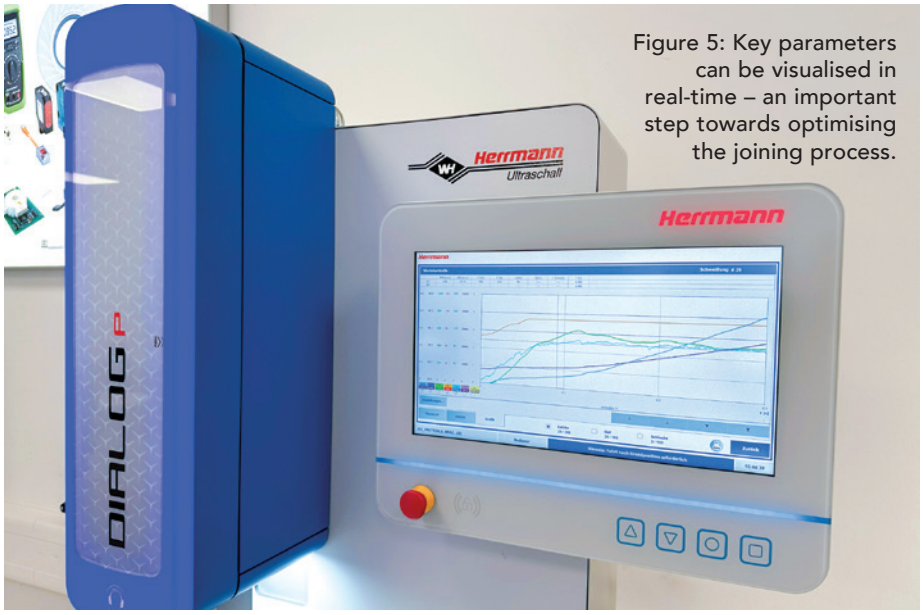

Figure 5: Key parameters can be visualised in real-time – an important step towards optimising the joining process.

With a cycle time of only 200–250 milliseconds, the process was also designed to be exceptionally fast. As is typical for ultrasonic joining, no additional curing times or pre- and post-processing steps were required. This makes the developed process ideally suited for high-volume automated production (Figure 5).

CLOSE COLLABORATION AS THE FOUNDATION FOR SUCCESS

This demanding process development highlights the importance of close collaboration between application engineers and product designers. By involving Herrmann Ultraschall at an early stage of the project, critical design features could be integrated into the component itself. In combination with the specially developed welding tools, these adaptations ultimately enabled the desired results.

At the same time, the project demonstrated the versatility of ultrasonic joining technology, showing that not only identical but also dissimilar plastics can be joined reliably, quickly and with excellent visual quality – even under highly demanding conditions.

> "WITH A CYCLE TIME OF ONLY 200 TO 250 MILLISECONDS, THE PROCESS WAS ALSO DESIGNED TO BE EXCEPTIONALLY FAST. AS IS TYPICAL FOR ULTRASONIC JOINING, NO ADDITIONAL CURING TIMES OR PRE- AND POST-PROCESSING STEPS ARE REQUIRED."

Fabio Weingärtner

Fabio Weingärtner is Account Manager in the Medical team at Herrmann Ultraschall. He advises companies in the medical industry worldwide on ultrasonic welding technologies and supports the development of reliable joining solutions for wearable and healthcare applications.

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Early Insight

FROM SPACE PROPULSION TO DRUG DELIVERY: A NEW SUBCUTANEOUS PLATFORM FROM TORRAMICS

TORRAMICS

David Johnston of **Torramics** introduces the NanoFlow platform, a wearable injector based on semiconductor architecture rather than a traditional mechanical pump, enabling enhanced dosing precision and further miniaturisation than is possible with legacy systems. He goes on to outline the technology's potential to expand beyond insulin to other large-volume subcutaneous drug delivery applications.

SC DELIVERY AS THE PREFERRED ROUTE FOR NEW THERAPIES

Over the past two decades, subcutaneous (SC) drug delivery has emerged as the preferred route for an expanding class of therapeutics. Led by insulin delivery, newer therapeutics, such as glucagon-like peptide-1 (GLP-1) agonists, monoclonal antibodies (mAbs) and other agents have been developed for or moved from intravenous (IV) or intramuscular administration into patient-controlled SC systems. This shift has been enabled by advances in mechanical self-injection technology – autoinjectors, injection pens and wearable pumps – that have brought self-administration and automation to millions of patients.

These mechanical systems represent significant engineering achievements in service of people in need. Insulin pump adoption now accounts for over 50% of insulin therapy in paediatric patients with Type 1 diabetes in the US and 29% among adults. The development of reliable, miniaturised mechanical assemblies has been central to this adoption.

However, mechanical assemblies operate within inherent engineering constraints. Miniaturisation has reached points of diminishing returns, even with advanced designs and precision fabrication. For therapies requiring highly reliable, manageable extended precision delivery and sensing – or for achieving further reductions in device size and energy consumption – an alternative technological foundation is necessary.

Torramics is developing technology to apply semiconductors to produce a nanocompressor with unprecedented reductions in size and energy requirements, as well as more precise delivery and improved sensing capabilities. This platform shift creates new possibilities for wearable drug delivery across the entire range of subcutaneously administered therapies.

"TORRAMICS IS DEVELOPING TECHNOLOGY TO APPLY SEMICONDUCTORS TO PRODUCE A NANOCOMPRESSOR WITH UNPRECEDENTED REDUCTIONS IN SIZE AND ENERGY REQUIREMENTS, AS WELL AS MORE PRECISE DELIVERY AND IMPROVED SENSING CAPABILITIES."

PLATFORM TECHNOLOGY: NANOCOMPRESSOR

The nanocompressor was developed at by Torramics's team at the NASA Ames Research Center (Mountain View, CA, US) with the original aim of developing novel propulsion technology. The basic operating principle of the nanocompressor combines thermoelectrics with thermal diffusion to move air molecules from cold to hot in nanodimensions within a micro-electromechanical systems chip structure, developing compression (Figure 1).

This action is bidirectional, with a change in polarity of the electrical current changing the direction of the temperature gradient. Air compressed this way is transferred to a membrane in Torramics's nanofluidics system, providing push and pull forces for pumping liquid.

The nanocompressor replaces mechanical assemblies pushing on a membrane, valve or piston, enabling device designer to move from designs with many large moving parts to ones with no moving parts. Molecular gas compression actuation by Torramics's technology uses low voltages and currents, little power and produces very small amounts of waste heat, which can help to protect heat-sensitive drug molecules.

PLATFORM TECHNOLOGY: NANOFLUIDICS

The delivery chamber is made up of three sections: an inlet from the drug reservoir, a pumping section for measuring and moving drug solution, and an outlet to the infusion set (Figure 2). This three-chamber architecture provides multiple levels of control and safety, and has been applied in drug delivery systems many times before.

Each compression stroke delivers a precise volume of drug – 500 nL per cycle for the insulin delivery design. This design has been shown to deliver ±2% accuracy in extensive lab testing over a range of fluid viscosities from 1 to 180 cP. The inlet and outlet valves prevent free flow in either direction, protecting against unintended delivery and other issues.

The design provides pressure-sensing with real-time occlusion detection, overcoming problems with delayed detection in mechanical pump designs. Some cases with existing insulin pumps can take many hours to sense occlusions, during which the drug is not being delivered. On occasion, occlusions may actually be sensed by the user's continuous glucose monitor before the pump itself. Furthermore, test results demonstrate low risk for extractables and leachables, along with no loss of drug potency during delivery.

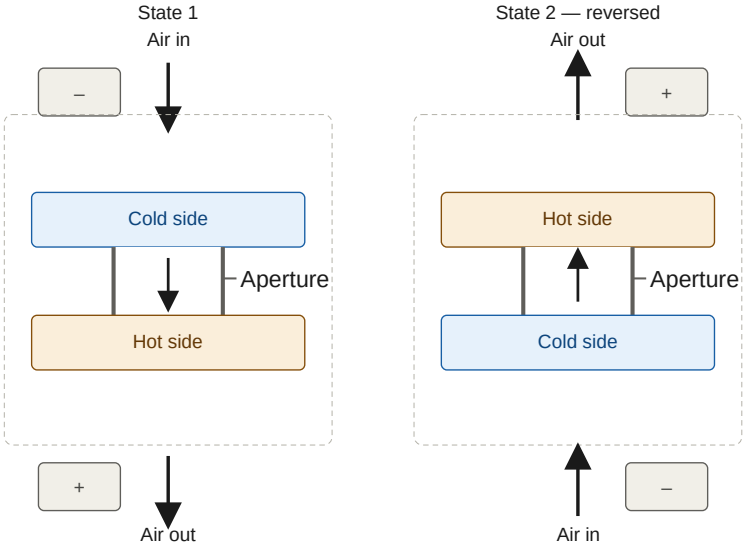

Figure 1: Gas compression through thermoelectrics/thermal diffusion.

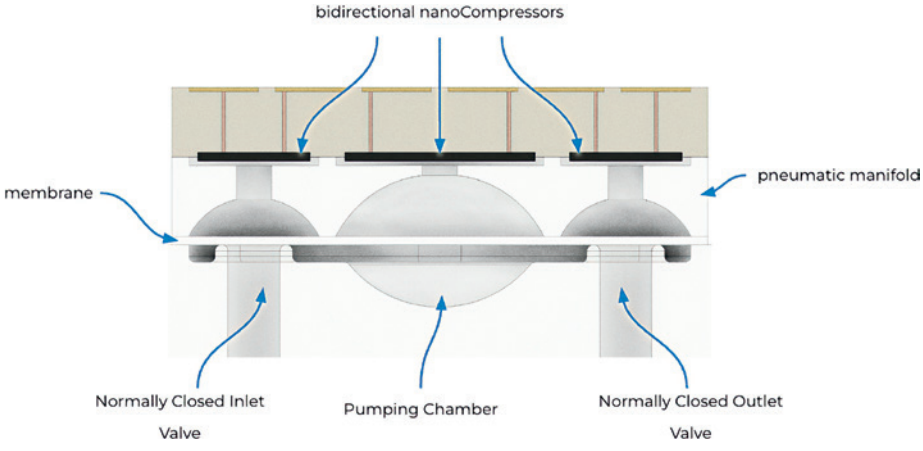

Figure 2: Anatomy of the Torramics nanofluidics system.

INITIAL PRODUCT APPLICATION: NANOFLOW FOR INSULIN DELIVERY

Torramics has selected insulin delivery as the initial target application for this platform, with a fully closed-loop design. The closed-loop controls will replace the bolus deliveries tied to meal announcements in currently marketed devices. The device measures 33 mm in diameter and 7 mm in height above the skin, with a mass of approximately 5 g when filled with 2 mL of aqueous drug. These dimensions are a direct result of the miniaturisation and low-energy requirements made possible by the semiconductor-based platform compared with mechanical alternatives.

Currently marketed systems often deliver insulin via an assembly of mechanical parts. While these systems have substantially expanded the options available for insulin therapy, product size is no longer a competitive advantage among these products, as the size of mechanical pumps has reached a minimum. All new devices have tended to be about the same size as the market growth leader – Omnipod (Insulet, Acton, MA, US).

The substantially smaller form factor of Torramics's NanoFlow offers advantages in profile reduction and operational simplicity, achieved through the underlying shift in technology rather than through a refinement of the mechanical design. NanoFlow's more compact form offers several practical benefits – for example, a smaller device presents fewer catch-points during daily activities and can reduce complications related to large adhesive patches (Figure 3).

One simple advantage comes from limiting the area of the skin occupied by the device, leaving more scarce body area for rotating sites. This is a simple but profound advantage for younger persons with Type 1 diabetes due to their smaller bodies. For insulin users, these factors contribute to simplified therapy management.

As already noted, NanoFlow will support delivery rate modulation in real time via data from a continuous glucose monitor and fully closed-loop control algorithms. This capability is a basic requirement for any future insulin delivery device seeking broad acceptance.

SAFETY MONITORING: REAL-TIME OCCLUSION DETECTION

Occlusion – the blockage of the delivery pathway – represents a common cause of therapy interruption present in all SC delivery systems, particularly with insulin delivery. Current mechanical pumps can detect occlusion through pressure sensing or by observing delivery failures. Detection latency varies by system, with some systems requiring hours at low delivery rates to identify an occlusion event.

Occlusion represents roughly 64,000 events reported to the US FDA each year for the latest versions of insulin delivery pumps – those that are "Alternate Controller Enabled (ACE) Infusion Pumps" with closed-loop controls. Occlusion may lead to elevated blood glucose, which may further advance to diabetic ketoacidosis if not alleviated.

NanoFlow will incorporate real-time occlusion detection by directly sensing resistance to flow in the nanocompressor. This technology enables algorithmic decision-making to minimise both false alarms and actual lack of delivery. For many therapeutic agents, acute phenomena in response to delayed dosing are not as likely as they are for insulin. However, other factors, such as excessive total time on body or lack of effect, may increase the value of this capability.

Additional Sensing Capabilities

Along with real-time occlusion sensing, NanoFlow also has the potential for real-time leak and air bubble detection. However, Torramics needs to fully understand the utility/capability balance for these attributes before committing to them in its existing design. Actual in-line flow-rate sensing and temperature sensing are also in consideration for additional potential benefits.

APPLICATIONS AND MARKET OPPORTUNITIES

Insulin: Established Market With Continued Growth

The global insulin pump market is valued at approximately US$8.2 billion (£6 billion), with projections to reach $22.5 billion by 2034, representing a compound annual growth rate of 13.4%. This growth is driven by the increasing prevalence of Type 1 diabetes, patient preference for automated delivery over multiple daily injections, expanding reimbursement coverage and increased use with Type 2 diabetes. Within this growing market, NanoFlow represents an alternative platform based on semiconductors that offers significant advantages over traditional mechanical delivery.

GLP-1 Agonists: Expanding Delivery Options

GLP-1 agonist therapy has expanded greatly, with new indications being found beyond Type 2 diabetes, including obesity management and cardiovascular risk reduction. Current delivery approaches include weekly SC injections (semaglutide, tirzepatide) and, more recently, daily administration of oral formulations.

Dosing via a weekly injection concentrates drug delivery into discrete events, which can produce adverse dose-related gastrointestinal events that limit dose escalation in some patients,

Figure 3: Torramics's NanoFlow system.

and contribute to a loss of adherence and persistence. Extended-release oral formulations present bioavailability, daily adherence and some retained gastrointestinal challenges.

A wearable patch capable of continuous, programmable delivery over extended periods, such as a once-weekly application delivering over seven days, would distribute drug exposure over time and potentially reduce dose-associated side effects. This delivery profile would be enabled by NanoFlow's precise rate-control, enabling the platform to manage blood levels, with a non-traumatic, once-weekly application. The device being on-body for the week could give patients the ability to adjust dosing to their individual tolerance rather than be subjected to doses designed for the mass population.

mAbs: High-Volume SC Delivery

mAb therapeutics represent one of the fastest-growing categories in drug development. Current delivery has been dominated by IV infusion or SC depot injection, with the latter limited by patient tolerance for large-injection volumes. IV administration of these agents is a costly regimen that involves visits to an IV centre every few weeks for a 30–60 min infusion over months or even years. As such, drug developers have been pursuing SC delivery for some time as a substantial improvement to the patient experience.

Makers of mechanical pump systems have rallied to develop devices that can enable this switch. However, mechanical systems face a volumetric constraint: the device itself is typically three to 10 times the volume of the drug payload – a device-to-drug ratio of 3:1 to 10:1. This ratio limits wearability for high-volume therapeutics and leads to changes in drug formulation to minimise the time that they need to be on-body out of regard for the burden of the system's size.

The much smaller semiconductor architecture of NanoFlow can achieve more efficient volumetric ratios, targeting 1:4 or better – where the device volume is much smaller than the therapeutic dose. This efficiency enables developers to pursue alternate dosing strategies, including wearable delivery of larger drug volumes, possibly multiple times per week, with reduced burden, thereby expanding SC delivery options and improving the success rate for mAb administrations. The strategic vision for this application is "person maximum/kit minimum", prioritising the patient's needs.

> "THE DEVICE BEING ON-BODY FOR THE WEEK COULD GIVE PATIENTS THE ABILITY TO ADJUST DOSING TO THEIR INDIVIDUAL TOLERANCE RATHER THAN BE SUBJECTED TO DOSES DESIGNED FOR THE MASS POPULATION."

Additional Therapeutic Applications

Beyond the therapeutic areas already discussed, NanoFlow's precise rate control and compact form factor support application to other SC therapies, potentially including pain management, hormone replacement, ADHD medication and emerging biologic agents. In particular, NanoFlow has the potential to shine in applications where controlled delivery, extended delivery and delivery-on-demand can offer clinical options that are not currently available.

CONCLUSION

SC drug delivery has evolved substantially through advances in mechanical engineering. The transition to monolithic semiconductor technology represents a platform shift, replacing moving mechanical assemblies with nanoscale thermal actuation. This change represents the potential to reduce device sizes, energy consumption and delivery variability – advantages that could open new possibilities for insulin, GLP-1 agonists, mAbs and other therapies where precise, extended, wearable delivery can improve patient outcomes.

A technology shift of this nature follows previous technology swaps from vacuum tubes to transistors, from individual transistors to millions of transistors on a single semiconductor device, from chemical photographic films to complementary metal-oxide-semiconductor image capture. Torramics is working with its partners and investors to bring this new approach to drug delivery and enhance not only delivery efficiency and the patient experience, but also give patients the freedom to live the active lifestyles they deserve.

David Johnston

David Johnston, Co-Founder and Chief Product Officer at Torramics, is a leader in injectable drug and drug delivery product development, having worked with Abbott, Baxter, Medtronic and others. In his various roles in the industry, Mr Johnston's teams have taken various injectable antibiotics, diagnostic, epidural, intrathecal and subcutaneous delivery devices to market, along with specialised systems for inactivating pathogens in blood products. As a consultant, he has contributed to product development in delivering insulin, mAbs, intraocular lenses and others, along with regulatory process optimisation and design transfer strategies. Mr Johnston is a graduate of the University of Michigan (Ann Arbor, MI, US) in Biochemical Engineering.

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2026/27 Editorial Calendar

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

SEP/OCT Dual Chamber Delivery Systems DEADLINE PASSED	**OCT** Prefilled Syringes & Injection Devices DEADLINE PASSED	**OCT/NOV** Sustainability in Drug Delivery DEADLINE: **Sep 17, 2026**
NOV Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 1, 2026**	**DEC** Delivering Gene & Cell Therapeutics DEADLINE: **Nov 5, 2026**	**JAN 2027** Prefilled Syringes & Injection Devices DEADLINE: **Dec 10, 2026**
FEB Oral Drug Delivery DEADLINE: **Jan 7, 2027**	**MAR** Ophthalmic Drug Delivery DEADLINE: **Feb 4, 2027**	**APR** Pulmonary & Nasal Drug Delivery DEADLINE: **Mar 4, 2027**
APR/MAY Sustainability in Drug Delivery DEADLINE: **Mar 18, 2027**	**MAY** Delivering Injectables: Devices & Formulations DEADLINE: **Apr 1, 2027**	**MAY/JUN** Dermal, Transdermal & Microneedles DEADLINE: **Apr 15, 2027**
JUN Industrialising Drug Delivery DEADLINE: **May 6, 2027**	**JUL** Oral Drug Delivery DEADLINE: **May 20, 2027**	**SEP** Wearable Injectors DEADLINE: **Aug 5, 2027**

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Enable Injections develops and manufactures the enFuse drug delivery system, the first-ever purely mechanical hands-free wearable technology designed to deliver large volumes of therapeutics subcutaneously. The small and discreet enFuse on-body injector features a hidden, retractable needle and no additional wiring or tubing, allowing for patient mobility during administration.

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Gerresheimer is an innovative system and solution provider and global partner for the pharma, biotech and cosmetics industries. The company offers a comprehensive portfolio of pharmaceutical packaging, drug delivery systems, medical devices and digital solutions. With around 13,400 employees and more than 40 production sites in 16 countries, Gerresheimer has a global presence and produces locally for regional markets.

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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.

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As a specialist in ultrasonic welding of plastic components, **Herrmann** has been developing safe and efficient welding systems for over 65 years. With the services of Herrmann Engineering, more than 650 employees excite customers all over the world. The guiding principle "Bonding – More Than Materials" stands for a respectful and reliable collaboration. In this way, Herrmann ensures a sustainable and economical welding process in the long term as a trusted advisor.

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Quvara Medical is a UK-based CMO specialising in precision medical devices for injectable drug delivery. With more than 30 years of heritage, Quvara combines validated cleanroom capacity, regulatory expertise and scalable manufacturing to support pharma and biotech partners from development through to commercial supply, delivering quality, compliance and speed to market.

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