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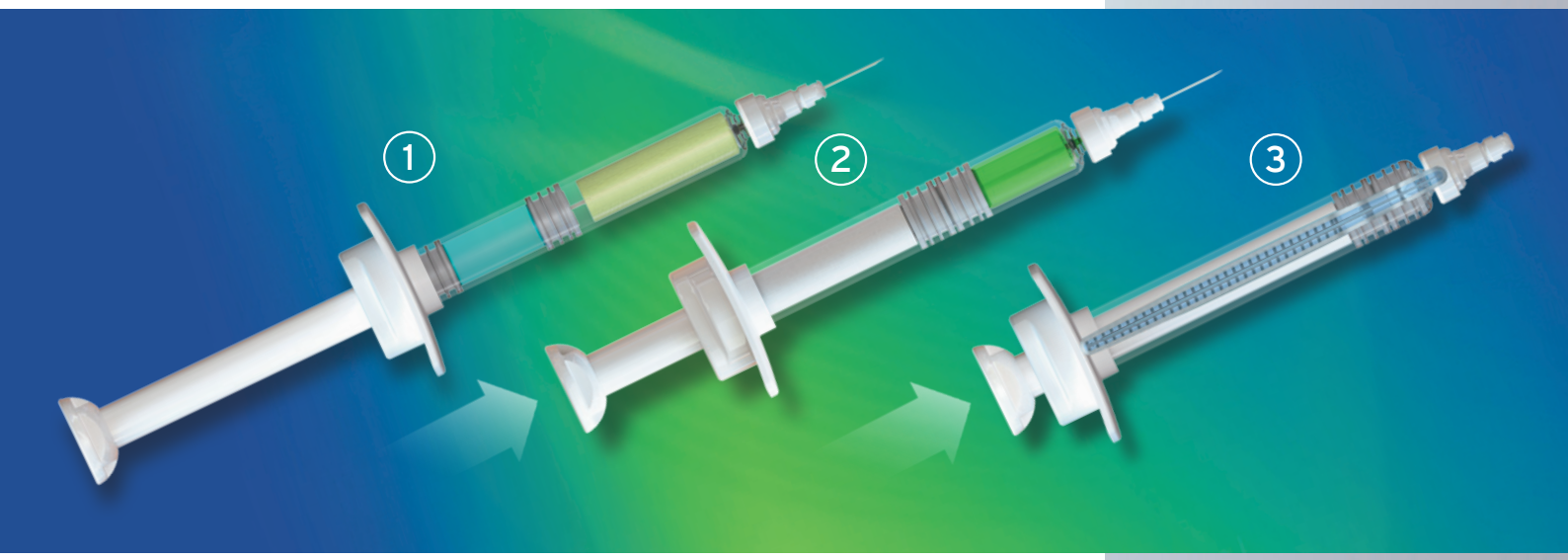

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DELIVERING INJECTABLES: DEVICES & FORMULATIONS

ONdrugDelivery Issue N° 186, May 18th, 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.

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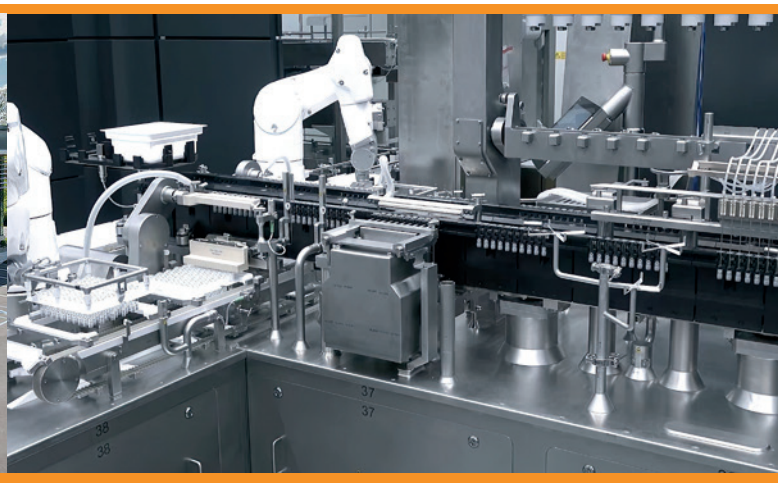

A Diverse and Dynamic Sector:

New Technologies in Injectable Drug Delivery

In this issue of ONdrugDelivery, we once more explore the world of injectable drug delivery. Injection is a diverse and dynamic sector within drug delivery, with major trends such as glucagon-like peptide-1s (GLP-1s), sustainability and increasing volumes and viscosities driving continuous innovation. This issue features a wide range of articles and, with contributors both familiar and new discussing the latest developments in this ever-evolving sector.

The issue begins with **SHL Medical**, our Outstanding Sponsor, looking back at the history of its Molly® autoinjector platform (Page 10), considering what drove Molly's remarkable success and how SHL Medical aims to drive innovation into the future. Accompanying this, **Quvara Medical** digs into how the massive demand for GLP-1s is creating challenges around the industry's available manufacturing capacity (Page 16) and **Gerresheimer** investigates the technology underlying its Gx InPuls™ and GxInPuls™ Flex infusion pumps (Page 22).

Continuing this theme, many of our regular contributors are here to provide insight into their innovative devices. **BD** focuses in on the design of its BD Neopak™ Glass prefillable syringe platform (Page 30), while **Kindeva** showcases its novel autoinjector technology for enabling easy delivery of microparticle formulations (Page 76). Moving to pen injectors, **Stevanato Group** presents Deora™ – a multi-use fixed-dose injection pen (Page 85) and **Nemera** considers its pen injector portfolio in the context of the GLP-1 boom (Page 90). Lastly, **MGS** discusses how its A.i.r. Platform™ has been designed with unmet patient needs in mind (Page 111).

On the topic of innovative technology, this issue also features three exciting Early Insights from across the industry. First, **Oncofuse** walks us through the world of radioligand therapy and presents its answer to the conundrum of how to enable prefilled technology for these medications (Page 56). Next, **Pacto Medical** shows us how its Slimshot™ and Slimshot™ Doser technologies answer clear unmet needs in the high-pressure frontier of emergency response and resource-constrained delivery, as well as their wider applications (Page 70). Lastly, **AEMS** pivots us to the formulation side of injectables, providing insights into its machine-learning technology for enabling formulators to analyse and explore three-, four- and five-component excipients (Page 116).

Of course, CDMOs represent a key voice in this discussion, including a Company Showcase from **Lifecore Injectables** CDMO (Page 38). **Phillips Medisize** follows on from its previous articles in 2020–2021 to provide a detailed update on the current state of large-volume injectables (Page 45), **PCI** considers the challenges and approaches to optimising the commercialisation process for combination products (Page 50), and **Adragos Pharma** presents an overview of the trends in sterile manufacturing (Page 82).

Expanding the range of discussion, **GELITA** shines the spotlight on the potential of collagen as an injectable and the innovation occurring in this space (Page 40) and **Enable Injections** considers the potential of subcutaneous delivery and wearable injectors in oncology (Page 63). Taking a peek into the transdermal world, **LTS** provides an assessment of microneedle technology (Page 94) and **WuXi AppTec** takes a broad view of how transdermal players are pushing the space forwards (Page 102). Rounding out the issue, **UPM** digs into how standard-grade labelling materials and adhesives open pharmaceutical manufacturers up to unnecessary risk that can be avoided by using suitable pharma-grade materials (Page 104).

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Interview: Celebrating 10 Years of Molly Enabling Patients' Independence

In this interview, **Nicholas Heaton** of **SHL Medical** looks back on the decade since Molly – the company's signature two-step autoinjector platform – received its first approval, reviewing what made the device platform a success, where Molly is positioned in the market today and how it will continue to evolve to meet the demands of the future.

Q What was the original vision behind the Molly autoinjector?

A Molly, as we know it today, is the culmination of more than 35 years of extensive, hands-on device engineering expertise that SHL Medical has built as a pioneer in the autoinjector space. It draws directly on the insights and learnings from its predecessor, the button-activated Disposable Autoinjector, which is widely regarded as a trailblazer for modern autoinjectors, helping to transition self-injection technology from its origins in military applications to patient-centric, at-home care – achieving this at a scale never seen before.

Figure 1: SHL Medical's Molly autoinjector platform.

"OVER THE YEARS, THESE CUSTOMER NEEDS HAVE TAKEN MANY FORMS, FROM BRANDING AND INDICATION-SPECIFIC USABILITY AFFORDANCES TO MANUFACTURABILITY AND OPERATIONS-DRIVEN OPTIMISATIONS; MOLLY HAS CONSISTENTLY PROVED CAPABLE OF MEETING THEM."

At Molly's inception, SHL Medical's two decades of understanding on how autoinjectors perform in real-world settings provided the groundwork to develop a reliable platform engineered to support emerging drug modalities and deliver consistent, high quality performance at scale. At the same time, Molly's creation was driven by a clear ambition: to bring an autoinjector to market that effectively balanced reliability with user-centric design.

To achieve this ambition, proven technologies were combined with new IP, yielding a result greater than the sum of its parts. The introduction of a novel two-step injection mechanism was the outcome of that vision, delivering simplicity for patients while ensuring robustness for pharmaceutical applications. Together, this blend of legacy expertise and an eye for innovation have defined Molly's versatility and have underpinned the platform's success to date (Figure 1).

Q How did early customer needs shape the development of Molly, and how did those needs manifest in the evolution of the technology across different device formats?

A Customer requirements have played a central role in shaping Molly's evolution. Early on, we collaborated with our pharma partners on highly specific use cases for the technology, ranging from metabolic emergency use applications to distinctive industrial design presentations. Over the years, these customer needs have taken many forms, from branding and indication-specific usability affordances to manufacturability and operations-driven optimisations; Molly has consistently proved capable of meeting them.

Those demands pushed us beyond conventional boundaries, both in terms of device engineering and industrialisation. Rather than viewing those requirements as challenges, we used them as opportunities to expand what an end-to-end device offering could deliver, ultimately strengthening Molly's versatility.

Once it was established, interest in leveraging the Molly autoinjector technology grew rapidly, and it quickly became clear that it was a compelling choice for pharmaceutical companies developing combination products. A strong example of this came when one of our longstanding partners presented us with a higher-dose biologic formulation requiring a 2 mL fill volume, creating a clear case for the Molly 2.25 mL format.

The resulting combination product was launched in 2020 for atopic disorders and marked the first autoinjector with a ≥ 2 mL label volume, enabling patients to access a higher-dose biologic in a convenient,

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Nicholas Heaton is the Global Head of Sales at SHL Medical, based at the company's headquarters in Zug. He leads the company's commercial teams, overseeing account management, business development and customer success teams across the United States, Europe and Asia. With more than three decades of experience in the life sciences industry, Mr Heaton brings deep commercial and strategic expertise to the organisation. He holds an MA (Hons) in Chemistry from the University of Oxford (UK).

"10 YEARS LATER, MOLLY IS A WELL-ESTABLISHED GLOBAL PLATFORM THAT HAS ENABLED THE REGULATORY APPROVAL OF MORE THAN 20 COMBINATION PRODUCTS, COVERING NEARLY 30 THERAPEUTIC INDICATIONS AND STILL GROWING."

at-home format. This paved the way for the next generation of high-dose self-administered injectables. It was a critical progression for the technology, and we look back on it as an important demonstration of how Molly has played a part in advancing the state of the art in drug delivery.

Q Can you expand on SHL Medical's operational approach to scaling Molly?

A As demand grew, it became clear that Molly needed to scale beyond individual project needs. This shift prompted deliberate investment in transforming it into a true platform from a design and development perspective, as well as across our operations. From an industrial design and IP viewpoint, the underlying technology was always consistent, effectively making it a platform from the outset. Therefore, the focus was on driving efficiency, ensuring consistent reliability and making it easier for both new and existing customers to adopt Molly.

A key part of this was the development of SHL Medical's own toolsets and equipment, which helped reduce the overall cost of ownership for customers while improving standardisation and scalability. SHL Medical's legacy of vertically integrated toolmaking, equipment development and manufacturing infrastructure was a big part of pulling that off (Figure 2). That platform mindset has since been a major enabler of Molly's success.

Q As Molly marks its 10th anniversary, what does this celebration actually represent in terms of Molly's presence and impact in the market today?

A Unsurprisingly, the benefits that Molly offered on the reliability and usability fronts would only find success if deployed in a way that also prioritised development simplicity and speed-to-market. Its market introduction, originally as a "preconfigured" solution, resonated well with what our customers were looking for – bear in mind that they would have spent the previous decade developing their precious, novel drug, only to arrive at this long-awaited final stage of combination product development. In 2016, we celebrated Molly's first approval in collaboration with one of our trusted pharmaceutical partners.

Today, 10 years later, Molly is a well-established global platform that has enabled the regulatory approval of more

Figure 2: SHL Medical's vertically integrated approach to development helps to reduce total cost of ownership for customers and improve both scalability and reliability.

than 20 combination products, covering nearly 30 therapeutic indications and still growing. It supports some of the industry's most prominent self-injection therapies, including blockbusters in the dermatologic, autoimmune and cardiometabolic spaces. In terms of scale, 90 million Molly devices reached patients in 2025, which places it as a leader in the marketplace.

Q Scale doesn't come without its challenges – how does SHL Medical ensure quality and reliability at such volumes?

A Reliability is a priority for SHL Medical and one of Molly's defining strengths. Over the years, we've developed a world-class quality organisation that tirelessly focuses on the quality of both our processes and outgoing products. With Molly's market-leading low complaint rate, performance is also consistently validated in real-world use, as devices leave our facilities and end up in the hands of patients. This reflects the robustness of Molly's design, the rigour of our process development and the maturity of our manufacturing operations. For pharmaceutical companies, that level of performance translates directly into reduced risk and greater confidence throughout the product lifecycle.

Q How do you collaborate with customers who may have unique needs outside of the design envelope?

A That's an important question, as customer needs vary significantly based on a wide variety of factors. We've developed a flexible platform approach that combines a high degree of standardisation with the ability to introduce targeted customisation within the Molly platform on pre-defined axes (Figure 3).

When a customer is interested in more bespoke developments, the core Molly technology can be leveraged to ensure that even a necessarily unique autoinjector solution benefits from what Molly brings to the table. This allows customers to profit from the efficiencies, speed and reliability of a proven platform, while still achieving meaningful differentiation where it matters most. Ultimately, it's about providing the right level of adaptability without compromising performance, regulatory robustness or development timelines.

"WHEN A CUSTOMER IS INTERESTED IN MORE BESPOKE DEVELOPMENTS, THE CORE MOLLY TECHNOLOGY CAN BE LEVERAGED TO ENSURE THAT EVEN A NECESSARILY UNIQUE AUTOINJECTOR SOLUTION BENEFITS FROM WHAT MOLLY BRINGS TO THE TABLE."

Q SHL Medical has historically prided itself on its vertical integration – where does that play a role in Molly, and do you find yourselves collaborating with other industry leaders?

A A significant differentiator with SHL Medical is our ownership of key toolsets and manufacturing equipment. By controlling these critical elements, we're able to reduce the total cost of ownership for our customers while enabling scalability. In a highly competitive and resource-intensive environment, our investment in unifying toolsets and equipment secures the market launch and lifecycle needs of our customers' combination products.

But to your point, we can't do it alone. We've built a strong alliance network with leading partners across the value chain. These include de-risked primary container providers and pre-validated final assembly services, to name a few. Together, we've worked to create a plug-and-play ecosystem that simplifies development and accelerates time to market.

Q Sustainability in drug delivery is becoming increasingly important – how is Molly evolving in this area?

A Like many of our customers, sustainability has been a key focus for us in recent years and will continue to be going forwards. We now offer a bio-based version of Molly that can reduce associated carbon emissions by up to 49%. This is a significant step in supporting our customers' environmental goals while maintaining the same performance in our products and robustness in our supply chain. This approach positions Molly as a leading choice for companies that are prioritising sustainability in their drug-device development strategies, while also looking for the benefits that a market-proven device has to offer.

Figure 3: Molly is highly customisable to suit customer requirements.

Q As it looks to support future growth, where is SHL Medical making investments today?

A We're continuing to invest in both subassembly and final assembly capabilities, which represent two distinct and strategically important areas of our offering and footprint. Regarding subassembly manufacturing, by the end of this year, we will be the only autoinjector platform manufacturer with operational sites across three continents. Our presence in North America, Europe and Asia enables a unique level of not only scale, but resilience and proximity to key markets as global demand grows. In parallel, we are strengthening our final assembly offering through the continued investment in SHL Medical Assembly & Services, bringing together our end-to-end service offerings, which are a significant lever when looking to reduce our customers' time to clinic as well as to market.

Q After 10 years, what do you think defines Molly's success, and what comes next?

A Molly's success is grounded in its modular design and a strong focus on incremental, effective innovation. Combined with SHL Medical's entrepreneurial spirit and commitment to going above and beyond customer and patient needs, we have created a solid foundation for the platform's continued advancement.

We are perpetually pushing the boundaries of the platform through improvements in functionality, reliability and development efficiency. Drawing on a decade of real-world insights across a wide range of therapies, use cases and customer programmes, we are uniquely positioned to advance Molly in ways that are currently unparalleled in the industry. We strive to continue the legacy of Molly, enabling our customers to bring therapies to market quickly and efficiently without compromising on quality.

Molly's success comes down to a combination of innovation, adaptability and execution. We've developed a platform that meets today's needs alongside both the vision and infrastructure to evolve with the future of self-administered drug delivery. Looking ahead, our focus is on scaling sustainably, expanding globally and continuing to push the boundaries of what an autoinjector platform can achieve.

"DRAWING ON A DECADE OF REAL-WORLD INSIGHTS ACROSS A WIDE RANGE OF THERAPIES, USE CASES AND CUSTOMER PROGRAMMES, WE ARE UNIQUELY POSITIONED TO ADVANCE MOLLY IN WAYS THAT ARE CURRENTLY UNPARALLELED IN THE INDUSTRY."

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Interview: GLP-1 Demand and the New Reality of Device Manufacturing Capacity

In this interview, **Andy Wertheim** of **Quvara Medical** discusses the growing shortage of available manufacturing capacity driven by the boom in GLP-1 therapies, why this means mid-volume development programmes across a range of sectors are struggling to move from development to industrialisation, and how Quvara is ideally positioned to provide the capacity that these programmes lack.

Q There is increasing discussion around glucagon-like peptide-1 (GLP-1) therapies dominating manufacturing capacity – what are you seeing in the market?

A First and foremost, we're seeing a structural shift in device manufacturing demand that is primarily being driven by the extraordinary growth in the number of GLP-1 therapies. These products require highly reliable delivery platforms, particularly autoinjectors and pen injectors, manufactured at high volumes – the scale-up requirements are unprecedented in modern drug delivery.

Market forecasts and analyst estimates suggest that global sales of GLP-1 therapies for diabetes and obesity could exceed US$100 billion (£74 billion) annually within the next decade. Behind that number sits an enormous requirement for delivery devices. Analysts estimate that demand for GLP-1 injection devices could reach well over one billion units per year, with production concentrated across a relatively small number of high-volume programmes.

Each of those programmes requires robust supply chains, validated cleanroom manufacturing, precision moulding, automated assembly and long-term capacity commitments. As a result, a significant proportion of the industry's available device manufacturing infrastructure is being absorbed by a handful of very large programmes.

This concentration of demand is creating a ripple effect across the industry. Programmes outside the GLP-1 space – whether in biologics, specialty pharmaceuticals, emergency medicine or rare diseases – are finding it increasingly difficult to secure manufacturing capacity. We're consistently hearing that timelines are slipping not because of device design challenges or regulatory hurdles but because suitable manufacturing partners simply don't have the available capacity. In many cases, the constraint is no longer innovation – it's industrialisation.

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Andy Wertheim is Chief Commercial Officer at Quvara Medical, a CMO specialising in autoinjectors, pen injectors and precision medical device components. He leads global commercial strategy, business development and marketing, focusing on expanding capacity partnerships for pharmaceutical and medtech customers. Prior to joining Quvara Medical in 2025, Mr Wertheim held senior commercial and portfolio leadership roles at Owen Mumford, where he led strategic growth initiatives for drug delivery devices and combination products. His experience spans device industrialisation, partner selection and scaling regulated manufacturing platforms that support complex injectable therapies.

"TIMELINES ARE SLIPPING NOT BECAUSE OF DEVICE DESIGN CHALLENGES OR REGULATORY HURDLES BUT BECAUSE SUITABLE MANUFACTURING PARTNERS SIMPLY DON'T HAVE THE AVAILABLE CAPACITY. IN MANY CASES, THE CONSTRAINT IS NO LONGER INNOVATION – IT'S INDUSTRIALISATION."

"THE IMPLICATION IS CLEAR: MANUFACTURING CAPACITY IS BECOMING A STRATEGIC ASSET RATHER THAN AN OPERATIONAL AFTERTHOUGHT."

Q Why is the demand for GLP-1 therapies having such a disproportionate impact?

A It comes down to scale, speed and certainty of demand. GLP-1 therapies are being produced at extremely high volumes, often requiring multiple dedicated production lines and multi-year commitments. A single successful programme can require hundreds of millions of devices annually, which may translate into several fully automated assembly lines running continuously.

The manufacturers supporting these programmes must allocate significant cleanroom space, automation infrastructure, engineering resources, quality oversight and supply chain bandwidth to them. These are not easily scalable overnight. The automation equipment alone can have lead times of 12–18 months, and highly automated assembly lines for drug delivery devices require extensive validation before commercial release.

Unlike traditional combination product programmes, where demand ramps gradually, GLP-1 products require immediate, sustained and high-volume output. Those requirements effectively lock down manufacturing capacity for extended periods. Once lines are committed, they are not easily redeployed without significant disruption.

This creates a structural imbalance. A relatively small number of large programmes are consuming a disproportionate share of the available production capacity, leaving smaller but clinically important programmes competing for limited resources.

Q Which types of programmes are most affected by this capacity constraint?

A We're seeing the greatest impact on the "missing middle" – the mid-volume combination products and emerging biologics that still require robust, regulated device manufacturing. These programmes may require 5–20 million units annually, which, historically, would have represented meaningful demand. In the current environment, however, those volumes can struggle to compete against programmes requiring 50–200 million units per year.

This includes therapies in the autoimmune disease, oncology, emergency medicine and specialty injectables sectors. Many of these programmes have completed device development and are ready to be transferred into manufacturing but are encountering delays purely due to lack of available cleanroom capacity.

There is also a broader innovation risk. Smaller biotech companies, particularly those developing differentiated therapies, often lack the leverage to secure large-scale manufacturing commitments early. As a result, innovation timelines can be indirectly constrained by manufacturing access, rather than scientific progress. This is an important shift – historically, manufacturing followed innovation, whereas now innovation is increasingly being shaped by manufacturing availability.

Q Is this a temporary issue or a longer-term structural change?

A In my view, this is a structural shift rather than a short-term spike. Demand for GLP-1 therapies continues to grow, and additional entrants into the obesity and metabolic disease space are increasing the pressure even further. And, while new manufacturing capacity is planned, the timelines to bring regulated facilities online are significant.

Designing, building, equipping and validating a new cleanroom manufacturing facility can take 24–36 months. That includes equipment procurement, process development, installation qualification, operational qualification and performance qualification, all under regulated quality systems. Capital investment for highly automated device assembly can easily reach the tens of millions of pounds or dollars.

This means that, even with significant investment, expansion will lag behind growing demand. For the foreseeable future, manufacturing availability will remain constrained. The implication is clear: manufacturing capacity is becoming a strategic asset rather than an operational afterthought.

Q What risks does this create for pharmaceutical and medtech companies?

A The primary risk is timeline delay. If manufacturing capacity is not secured early, programmes can stall even after successfully meeting clinical and device development milestones. This can affect regulatory submissions, launch timings and, ultimately, patient access. Ultimately, this is not just an operational issue – delays in securing manufacturing capacity can directly erode programme value by pushing out launch timelines and impacting revenue realisation.

There is also a risk borne from supply chain concentration. When manufacturing is dominated by a small number of large programmes, reliance on a single supplier increases vulnerability. Companies are increasingly exploring dual-sourcing strategies or secondary manufacturing partnerships to mitigate this risk.

A similar emerging risk is geographic concentration. As companies reassess supply chain resilience, regional manufacturing capability is becoming more important. Programmes that rely on single-region manufacturing may face additional scrutiny. Overall, manufacturing is moving onto the critical path of programme strategy – it is no longer simply an execution step at the end of development.

Q How should companies respond to this environment?

A The first step is awareness. Organisations need to recognise that manufacturing capacity must be secured earlier in the development lifecycle. Increasingly, we are seeing companies engage manufacturing partners 12–24 months earlier than they used to.

Secondly, companies should diversify their manufacturing partnerships. Engaging with partners that have available capacity and the ability to scale reduces risk. This

may include working with specialised CMOs that can onboard programmes quickly.

There is also a growing trend towards designing supply strategies with dual manufacturing partners from the outset. This approach provides flexibility, reduces risk and improves resilience. Ultimately, manufacturing strategy needs to be integrated into product strategy much earlier than in the past.

Q Where does Quvara Medical fit into this landscape?

A Quvara Medical was established with precisely this market dynamic in mind. We combine more than three decades of regulated medical device manufacturing heritage with available cleanroom capacity, which is increasingly rare in the current environment. Our facilities include ISO Class 7 and 8 environments, precision injection moulding, automated and semi-automated assembly and quality systems aligned to combination product requirements.

However, capability alone is no longer enough. What differentiates organisations today is the ability to deploy that capability without delay and to onboard programmes quickly. Because we have availability now, we can engage immediately, but equally important is our ability to move efficiently from technical transfer through to validated production within compressed timelines. In a constrained market, availability and speed of execution become as valuable as capability itself.

We also focus on agility. Many large manufacturing networks are optimised for high-volume, long-term programmes. That can make onboarding of mid-volume or emerging programmes more challenging. Quvara's model is designed to support those programmes efficiently while maintaining regulated manufacturing standards. This allows us to help companies maintain momentum when manufacturing access becomes the bottleneck.

"SPEED MATTERS – THE ABILITY TO MOVE FROM TECHNICAL TRANSFER TO VALIDATED PRODUCTION WITHIN 12–18 MONTHS IS INCREASINGLY IMPORTANT."

Q Are companies actively looking for alternative manufacturing partners?

A Yes, increasingly so. We are seeing more and more organisations exploring secondary manufacturing partnerships, not necessarily to replace existing suppliers, but to expand capacity and reduce risk. This dual-sourcing approach is becoming more common, particularly for programmes where continuity of supply is critical. In some cases, companies are proactively establishing secondary manufacturing partners even before commercial launch.

There is also growing interest in partners that can support technology transfers. Programmes that were initially developed within large manufacturing networks may need additional capacity elsewhere. The ability to transfer processes efficiently and validate production quickly is becoming more highly valued.

Q What differentiates a CMO partner capable of supporting programmes in this environment?

A Three elements are essential: credibility, capability and capacity. Credibility comes from proven experience in regulated manufacturing. Capability includes technical expertise, automation and quality infrastructure. However, in the current environment, capacity is the true differentiator.

The key factors many companies are seeking in a CMO are available, validated cleanroom space and the ability to onboard programmes quickly. Speed matters – the ability to move from technical transfer to validated production within 12–18 months is increasingly important. Agility is also a key factor. Partners must be able to scale appropriately for mid-volume programmes without requiring the scale of the largest blockbuster therapies.

Q What is your outlook for the next 12–24 months?

A I expect demand for device manufacturing capacity to remain high. GLP-1 therapies will continue to absorb significant resources, and additional combination products will enter development. This will reinforce the importance of flexible manufacturing partnerships.

We may also see further investment in manufacturing infrastructure, but those investments will take time to translate into validated production lines. In the meantime, companies that proactively secure capacity and work with manufacturing partners able to scale will be best positioned to succeed. Ultimately, the goal is ensuring that innovative therapies reach patients without unnecessary delay. That requires a responsive and resilient manufacturing ecosystem.

Q Do you have any closing thoughts?

A The rapid growth of GLP-1 therapies is reshaping the device manufacturing landscape. While this creates challenges, it also highlights the importance of flexible, available manufacturing partners. The companies that succeed over the next few years will not be those with the best science alone, but those that secure manufacturing access early enough to realise it. At Quvara Medical, our focus is on providing the regulated device manufacturing capability, credibility and available capacity needed to support programmes when it matters most.

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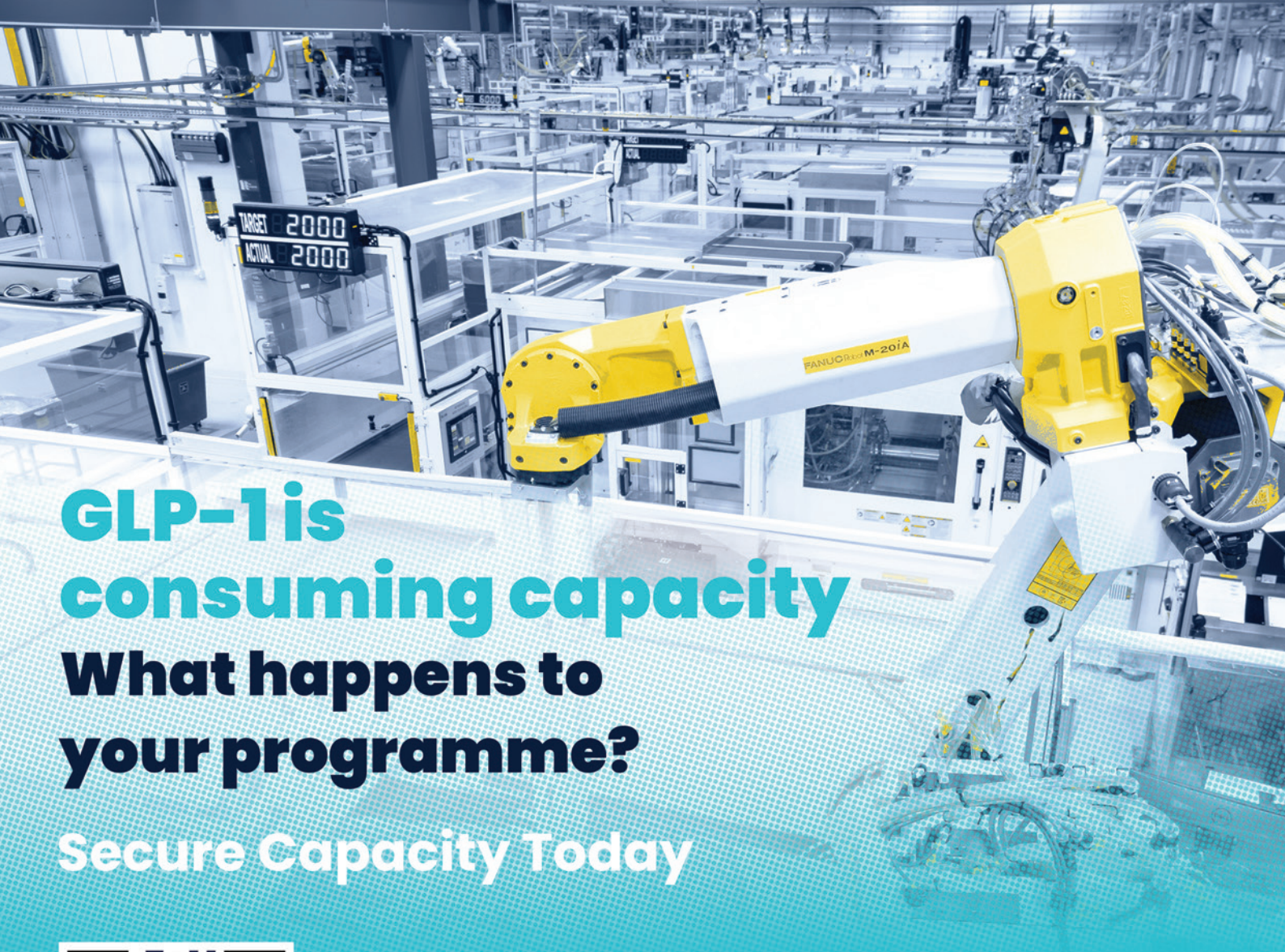

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FROM SMALL TO LARGE MOLECULES: ADVANCING PRECISION PUMP TECHNOLOGY FOR BIOLOGIC DRUG DELIVERY

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Dr Ines Rüstenberg, **Roger Müller** and **Dr Yannick Schmid**, all of **Gerresheimer**, discuss solutions for large-molecule drug delivery, highlighting the applicability of two infusors, Gx InPuls and Gx InPuls Flex, which employ micropump technology to overcome challenges with large-molecule delivery.

The biologics sector continues to grow, with an increasing number of drugs entering pharmaceutical pipelines and achieving market approval. Additionally, biologics are showing a clear tendency towards subcutaneous (SC) routes of administration. In 2025, the US FDA approved 46 new drugs with biologics, comprising 26% of total approvals. Nine of the biologics were monoclonal antibodies (mAbs), two were antibody-drug conjugates and one was a fusion protein,[1] with half of them formulated for SC delivery.

SC administration of large-molecule biologic drugs poses specific challenges due to their complex protein structures, sensitivity and high concentrations leading to higher viscosities. For dose volumes or delivery profiles that are unsuitable for autoinjectors, on-body or wearable infusion pumps are required. Such devices must provide the necessary infusion accuracy and flow rates for viscous large-molecule drug delivery. Concurrently, they must safeguard the structural integrity of sensitive proteins from physical factors such as shear stress or adsorption, which could cause aggregation, potentially affecting therapeutic efficacy. While infusion rates can be modelled reliably with fluid dynamic models, the risk of protein damage is not easily modelled and requires empirical experimentation.

MICROPUMP TECHNOLOGY FOR SC DRUG DELIVERY

Pumps for SC drug delivery on the market today employ various actuation technologies.

"THE SENSCORE MICROPUMP TECHNOLOGY IS INCORPORATED INTO THE GX INPULS CARTRIDGE-BASED, ON-BODY INFUSOR PLATFORM AND THE GX INPULS FLEX BELT-WORN, VIAL-BASED INFUSOR PLATFORM."

Piston-actuated pumps, for example, expel drugs by pushing on a cartridge stopper, forcing the drug out of the primary packaging and through the cannula.

Conversely, wetted pump systems, such as the SensCore from Gerresheimer, draw the liquid drug through a pump mechanism before expelling it through the fluid path. They are generally smaller than piston-pump systems, facilitating a more compact pump design and enabling a high level of infusion control over extended periods while also providing backflow resistance and infusion pause features.

Benefits of the SensCore Micropump

The design of the novel SensCore wetted micropump from Gerresheimer employs a rotary piston action. This provides a high level of infusion control across a broad range of infusion rates, including basal infusions over multiple days and rapid bolus injections at high flow rates.

The SensCore micropump technology is incorporated into the Gx InPuls™ cartridge-based, on-body infusor platform and the Gx InPuls Flex™ belt-worn, vial-based infusor platform designed to support the high accuracy requirements of small-molecule infusions (Figure 1). In these devices, the SensCore micropumps are implemented downstream of a primary drug container. The simple, two-component design comprises a pump housing and a pump shaft, with each pump having a stroke volume representing the smallest dosing increment that can be delivered per rotation. Currently, two configurations are developed with stroke volumes of 2 and 10 µL.

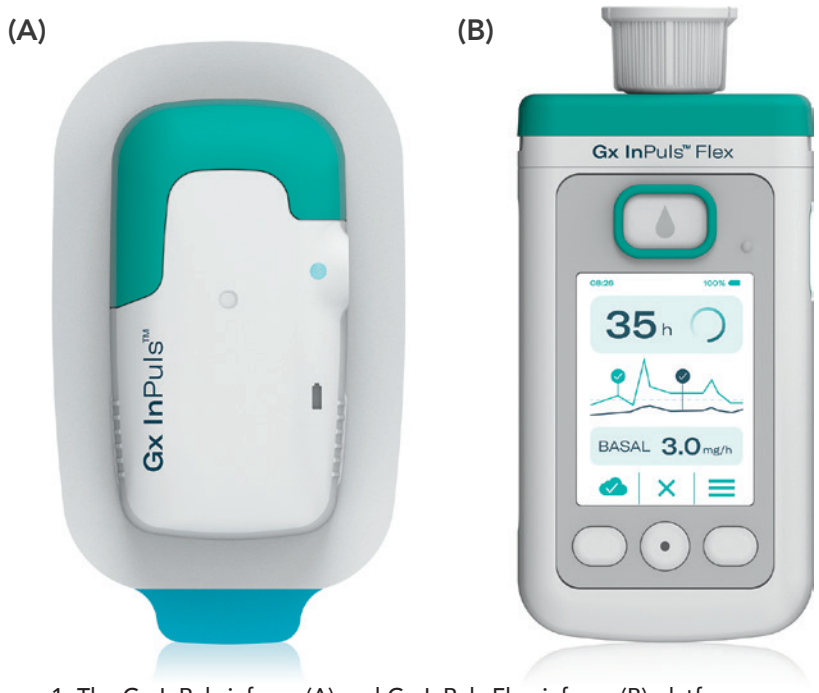

Figure 1: The Gx InPuls infusor (A) and Gx InPuls Flex infusor (B) platforms.

The valve structure in the pump mechanism provides double protection against free flow and backflow, as there is only ever one pathway open – when the pump is inactive, both valves are closed simultaneously (Figure 2). This has benefits for infusions with pulsatile infusion characteristics, paused infusions and low infusion rates where low pressure differentials alone would not prevent backflow.

Free flow and backflow in on-body or belt-worn infusion medical devices may represent clinical risks, as they can disrupt the intended controlled delivery of medication. Free flow refers to uncontrolled infusion of drug fluid into the patient when the device is no longer regulating the flow, which can result in unintended rapid dosing or multiple boluses. Backflow may cause inaccurate or reduced drug delivery and may also promote clogging in an infusion set, particularly at low flow rates. Both issues could compromise therapy accuracy and thus increase patient risk through treatment failure or contamination.[2]

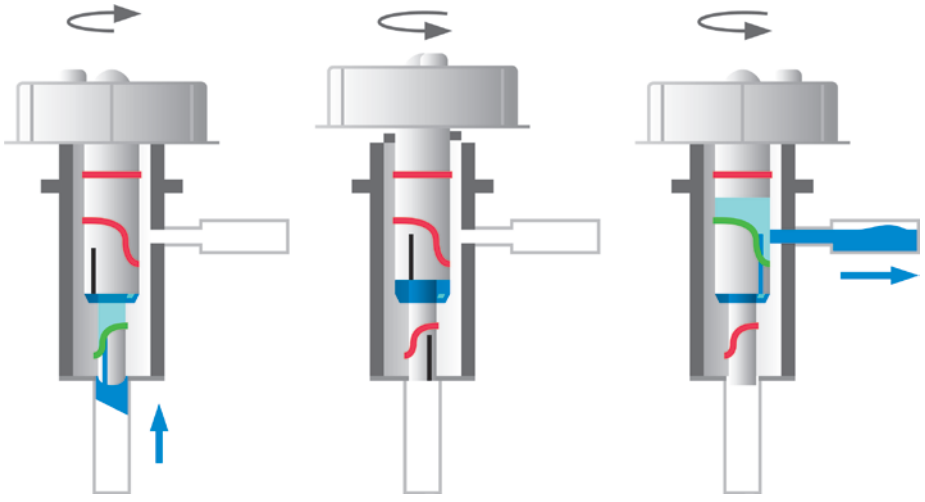

Figure 2: SensCore micropump shaft and housing show drug flow. Green: valve open. Red: valve closed.

CHALLENGES OF EXTENDING MICROPUMP TECHNOLOGY TO LARGE MOLECULES

Combination products based on the Gx InPuls and Gx InPuls Flex with the SensCore micropump are currently approved and marketed in the US and Europe for delivery of small-molecule drugs. However, large molecules, such as immunoglobulin G (IgG) and mAbs, are more challenging to deliver due to their high protein concentrations (up to approximately 150 mg/mL) and their vulnerability to aggregation, which may lead to loss of biologic functionality.

To evaluate the suitability of the micropump for delivery of large molecules, it was necessary to investigate both the potential for aggregation and the capability to deliver higher viscosities at required flow rates.

> "COMBINATION PRODUCTS BASED ON THE GX INPULS AND GX INPULS FLEX WITH THE SENSCORE MICROPUMP ARE CURRENTLY APPROVED AND MARKETED IN THE US AND EUROPE FOR DELIVERY OF SMALL-MOLECULE DRUGS."

Potential Impact of Shear Rates on Aggregation

Mechanical stresses encountered during the manufacturing and delivery of protein therapeutics – such as stirring, pumping, filtration and temperature cycles – may destabilise proteins. This could lead to partial unfolding and exposure of aggregation-prone regions, ultimately triggering proteins to aggregate. Such aggregates can reduce therapeutic efficacy and may trigger immune responses, highlighting the need to carefully control physical stresses during formulation, storage and administration of biologics.

Analysis of the SensCore micropump using fluid dynamic models found that the shear rate between the pump shaft and the pump housing during pump rotation was 200 s^{-1} compared with shear rates of up to 6,000 s^{-1} experienced by a drug moving through a commonly used, 27G thin wall needle (Figure 3). The negligible effect of shear rate was confirmed by expelling an IgG and a mAb through the micropump at a constant flow rate of 30 mL/h, then probing the molecular integrity of the pumped molecules using size exclusion chromatography and capillary electrophoresis.

Potential Impact of Surface Interactions

With a wetted pump design, as employed in the SensCore micropump, multiple surfaces come into contact and potentially interact with a protein in a biologic drug. Initial testing with a large-molecule formulation revealed that subvisible particles were present after the drug was expelled via the micropump. A hypothesis was established that proteins might interact with the pump shaft surface and then aggregate during pumping, resulting in particles appearing in the expelled liquid drug.

Assuming the hypothesis was correct, two options were identified that could potentially mitigate this effect: hydrophilic surface modification of the pump shaft or replacement of the shaft material to reduce protein adsorption.[3]

COMBATTING SURFACE INTERACTIONS

To confirm or disprove the hypothesis of surface interaction, 18 new shaft materials and coatings with various hydrophilic properties were selected and implemented into a prototype micropump system. Initial testing revealed that three of these produced significantly lower subvisible particles: one new pump shaft material and two coating options. Subsequent testing was performed on the three selected options, using light obscuration according to US Pharmacopeia (USP) <787> and focusing on the number of subvisible particles in the range of ≥ 10 µm and ≥ 25 µm, as defined by the standard. A significant reduction of subvisible particles was observed for each of the options in comparison to the original micropump.

The results showed that the shaft material option was highly compatible with the tested mAbs but less compatible with the IgG, whereas the coating options were compatible to a greater or lesser degree with both the mAbs and the IgG. To understand these results, the formulations of the tested drugs were evaluated.

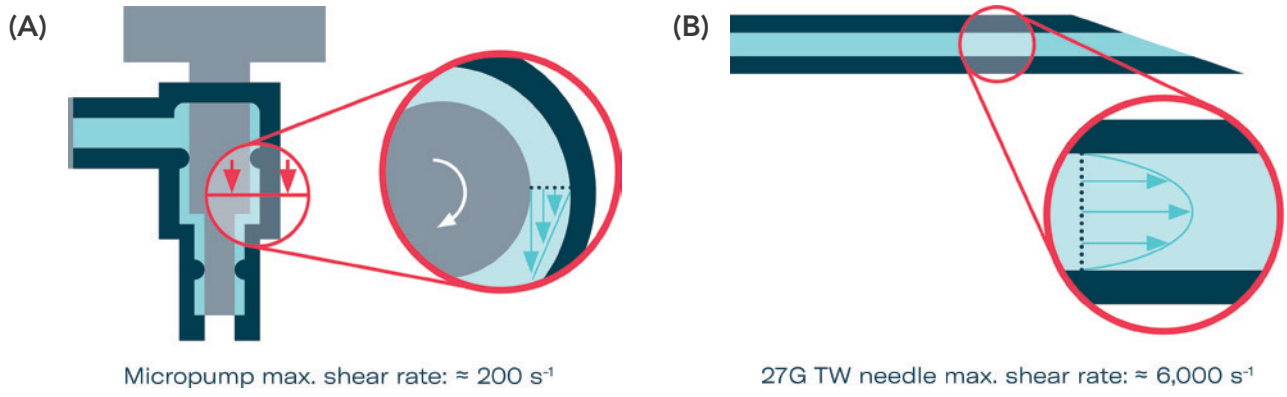

Figure 3: (A) Illustration of flow through a 10 µL SensCore Micropump compared with (B) a 27G thin wall needle.

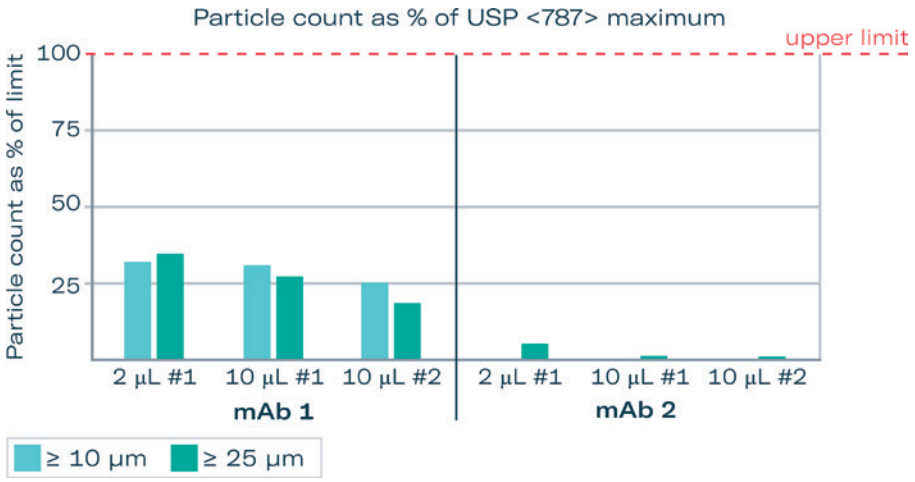

Figure 4: Subvisible particle count measured with light obscuration and assessed in comparison with particle limits specified in USP <787>.

Significantly, the IgG formulation used in the experiments did not contain a surfactant, while the mAbs were formulated with polysorbate. An assumption was made that the combination of hydrophilic modifications and surfactants used in the mAbs contributed to the lower surface interactions. To confirm this, 100 mg/L of polysorbate 80 was added to the IgG and then retested with the new shaft material. The turbidity was reduced to a comparable level with that measured on a reference sample, confirming the assumption.

As more than 90% of SC mAbs approved by the FDA between 2002 and 2020 contained surfactants at concentrations between 100 and 2000 mg/L,[4] the new shaft material was selected as the optimal solution for delivering the majority of large-molecule biologic drug products.

EFFICACY OF OPTIMISED SENSCORE MICROPUMP FOR LARGE MOLECULES

Optimised Material Exceeds Requirements for Particle Count

Following the success with the prototype micropump, the new shaft material was implemented into the existing 2 and 10 µL micropumps used in Gx InPuls and Gx InPuls Flex for confirmation of the previously observed results. Two approved mAbs (mAb 1 and mAb 2) were selected for testing. mAb 1 had an API concentration of 120 mg/mL and surfactant concentration of 100 mg/L. mAb 2 had an API concentration of 140 mg/mL and surfactant concentration of 600 mg/L. These mAbs were considered representative of typical formulations as referenced above.

Both mAbs were pumped through a 2 and 10 µL micropump and subvisible particle counts were measured using light obscuration (Figure 4). All micropump and mAb combinations were considerably lower than the USP <787> limits for ≥ 10 µm and ≥ 25 µm particle sizes.

High Flow Rate for High-Viscosity Infusions

SensCore micropumps were designed to be highly precise at low flow rates. To confirm suitable delivery of high flow rates for high-viscosity infusion too, the Gerresheimer development team conducted a series of tests. Glycerol and distilled water were mixed in varying viscosities according to an established calculation script. Both micropump sizes were tested with a variety of commonly used needle sizes.

Results showed that the two micropumps can cover infusion rates between 10 and 60 mL/h and viscosities of up to approximately 50 cP with an accuracy error of ≤5% (Figure 5).

"THE TWO MICROPUMPS CAN COVER INFUSION RATES BETWEEN 10 AND 60 mL/H AND VISCOSITIES OF UP TO APPROXIMATELY 50 cP."

This demonstrates the scope of the pumps to handle a significant proportion of the viscosities of marketed mAbs.[5] Testing by the expert laboratory team at a Gerresheimer site or the customer site enables confirmation of delivery parameters for a specific formulation.

Versatility for Varied Therapy Regimens

The micropumps with new shaft material can be incorporated into the Gx InPuls on-body infusor and the Gx InPuls Flex belt-worn infusor platforms from Gerresheimer, expanding their capabilities to handle a wide variety of viscosities, flow rates and delivery profiles.

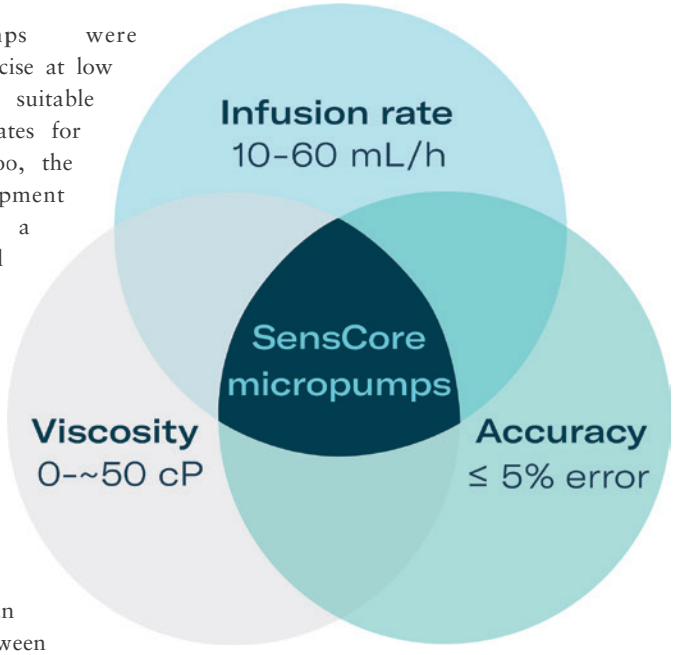

Figure 5: The tested capabilities of the SensCore 2 and 10 µL micropumps to handle various flow rates and viscosities.

The Gx InPuls on-body infusor platform incorporates a 2 µL SensCore micropump and 3 mL prefilled cartridge for precise, controlled drug delivery. A combination product based on the platform is already approved by the FDA for treatment of oedema in congestive heart failure, which minimises future development risk. The cartridge-based infusor is particularly suited for slow basal infusions, with different pre-defined flow rates and boluses. It is now proven to effectively deliver high-flow rate infusions of high-viscosity drugs, for example 15 cP, 30 mL/h with a 29G regular needle. For delivery of larger volumes, a concept is in development that employs the tested 10 µL micropump and a 10 mL prefilled cartridge.

The Gx InPuls Flex is a belt-worn infusor for 24/7 therapy delivery up to 20 mL. The Flex platform design allows for fast adaptation to a specific drug formulation and can deliver slow basal infusions with different pre-defined flow rates and boluses, as well as high-flow rate injections of high-viscosity drugs, for instance, 50 cP, 40 mL/h with a 27G thin wall needle. A combination device based on the Gx InPuls Flex is approved in Europe for treatment of Parkinson's disease, highlighting its suitability for treatment of chronic diseases, as delivery profiles can be adjusted to individual patients' needs.

CONCLUSION

Biologic therapeutics, particularly mAbs and other proteins, are expected to substantially influence the future development of SC drug formulations. Advances in formulation science, including high-concentration protein formulations and stabilisation strategies, together with the development of device-enabled delivery systems (e.g. on-body or belt-worn delivery devices), are facilitating the SC administration of larger volumes and doses.

These developments support a shift towards more patient-centred delivery of therapies in a home-care setting. This supports patient independence and reduces treatment burden, thereby complementing or replacing intravenous in-clinic infusions in select cases. Consistent with this trend, recent scientific reviews and regulatory approvals highlight SC formulations of established biologics as well as novel SC biologic products.

The optimisation of SensCore micropump technology in the Gx InPuls and Gx InPuls Flex infusor platforms responds to the market trend by transforming them into robust, versatile solutions for the effective and precise delivery of both small- and large-molecule drugs. Through shear stress analysis and surface interaction experiments, Gerresheimer has successfully addressed potential causes of aggregation and

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"THROUGH SHEAR STRESS ANALYSIS AND SURFACE INTERACTION EXPERIMENTS, GERRESHEIMER HAS SUCCESSFULLY ADDRESSED POTENTIAL CAUSES OF AGGREGATION AND DEMONSTRATED THE CAPABILITY OF THE DEVICES TO HANDLE HIGH-FLOW, HIGH-VISCOSITY INFUSIONS WHILE MAINTAINING THE INTEGRITY OF LARGE-MOLECULE BIOLOGIC DRUG FORMULATIONS."

demonstrated the capability of the devices to handle high-flow, high-viscosity infusions while maintaining the integrity of large-molecule biologic drug formulations.

The versatility of Gx InPuls and Gx InPuls Flex platforms allows Gerresheimer to cater to a variety of therapeutic needs, offering reliable, adaptable infusion control and precise dosing for SC administration. As the devices are already on the market as part of approved combination products, pharma companies can rely on the experience of the Gerresheimer team to efficiently and effectively support the full development process, from early-phase formulation testing through regulatory submission and manufacturing at scale.

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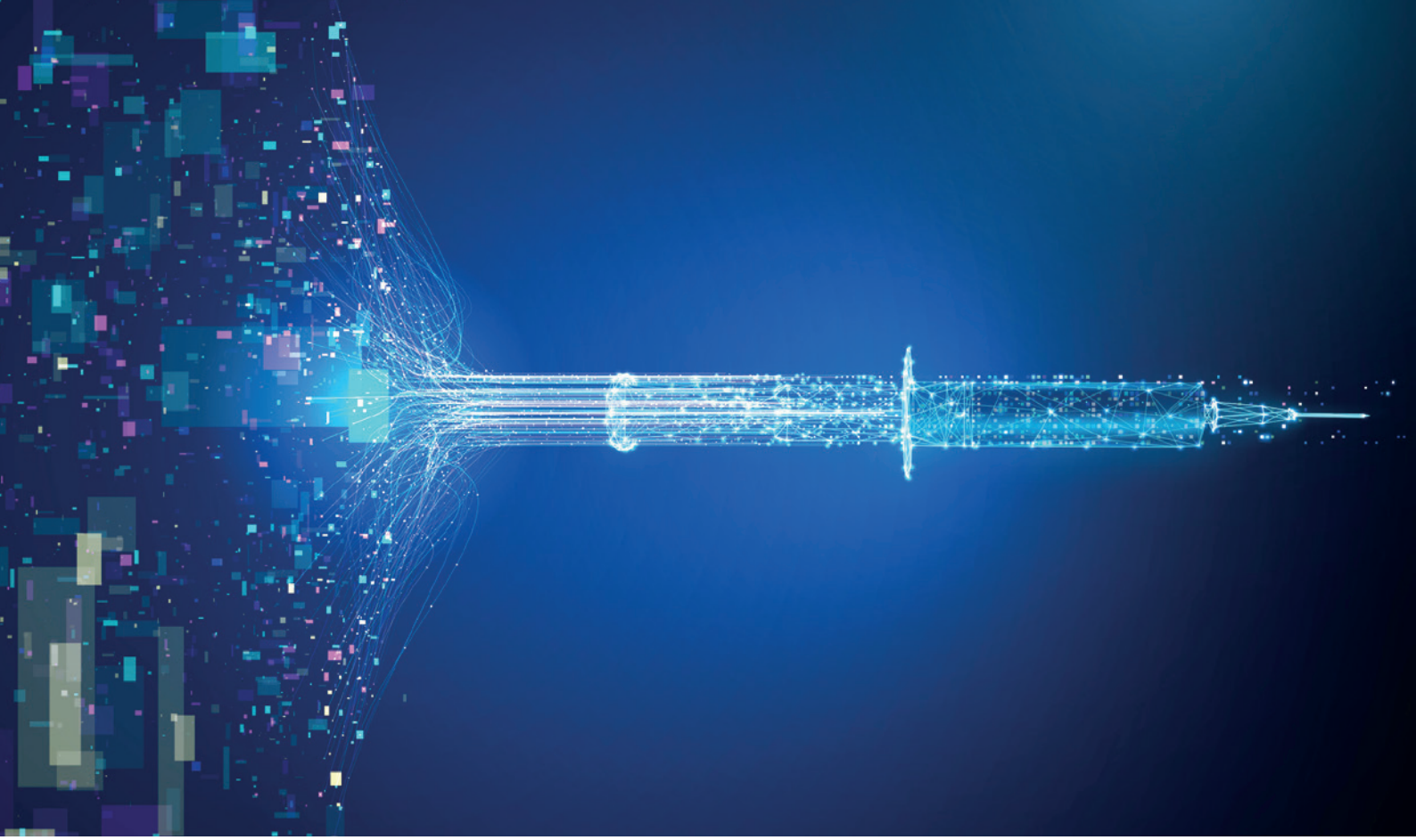

EXPANDING SUBCUTANEOUS DESIGN BRICK BY BRICK: THE BD NEOPAK™ GLASS PREFILLABLE SYRINGE PLATFORM

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Hervé Soukiassian and **Sophie Lelias** of **BD** discuss the established injection platforms built to achieve reliable and efficient subcutaneous delivery, going further to examine new injectable devices in development that are designed for an optimised patient experience as well as higher-volume, higher-viscosity delivery.

Over the past decade, the landscape of subcutaneous (SC) drug delivery of biologics has shifted significantly. The rapidly growing pipeline for these drugs is now characterised by increasingly complex and sensitive formulations, rising viscosities, larger fill volumes and expanding therapeutic applications. These trends have steadily pushed the limits of traditional primary containers and delivery devices.

As pharmaceutical companies continue to advance the development of SC biologics, they must balance a wide set of complementary and competing requirements. These include drug-container compatibility, operational efficiency, usability, patient preference, time-to-market, rising regulatory expectations and more (Figure 1). This growing complexity has underscored the importance of primary containers and delivery systems that can evolve with the biologics they are designed to deliver.

"AS PHARMACEUTICAL COMPANIES CONTINUE TO ADVANCE THE DEVELOPMENT OF SC BIOLOGICS, THEY MUST BALANCE A WIDE SET OF COMPLEMENTARY AND COMPETING REQUIREMENTS."

Figure 1: Key goals of drug development.

Since the launch of the BD Hypak™ Glass Prefillable Syringe in 1954 – the first mass-produced sterile glass disposable syringe – BD has played a central role in shaping the evolution of primary container technologies for injectable therapies (Figure 2). A pivotal milestone occurred in 2009 with the introduction of the BD Hypak™ for Biotech Glass Prefillable Syringe, specifically engineered to address emerging biologic-drug compatibility challenges. This is now considered an industry standard, with more than 7 billion units sold in the past decade. BD's decades of experience, combined with extensive collaboration with pharmaceutical partners, revealed the need for a next-generation platform capable of supporting the continuously expanding and ever-evolving design space of biologics.

Introduced in 2013, the BD Neopak™ Glass Prefillable Syringe platform was purpose-built as a future-ready platform for SC biologics. Unlike legacy syringe formats, the BD Neopak™ Glass Prefillable Syringe is engineered as a modular platform architecture composed of "technology bricks" that serve distinct functional purposes and can be combined to serve emerging needs within the SC drug delivery design space. These technology bricks address some of the most pressing challenges facing biologic developers today, including drug-container compatibility, high-mass drug formulations and operational flexibility at commercial scale.

As the requirements for patients, molecules and combination product delivery ecosystems have continued to evolve the BD Neopak™ Glass Prefillable Syringe platform has expanded accordingly. Technologies such as the BD Neopak™ XSi™ and BD Neopak™ XtraFlow™ have built upon the platform's foundation to further reduce drug-device development risks and enable expanded design space flexibility that go beyond historical constraints.

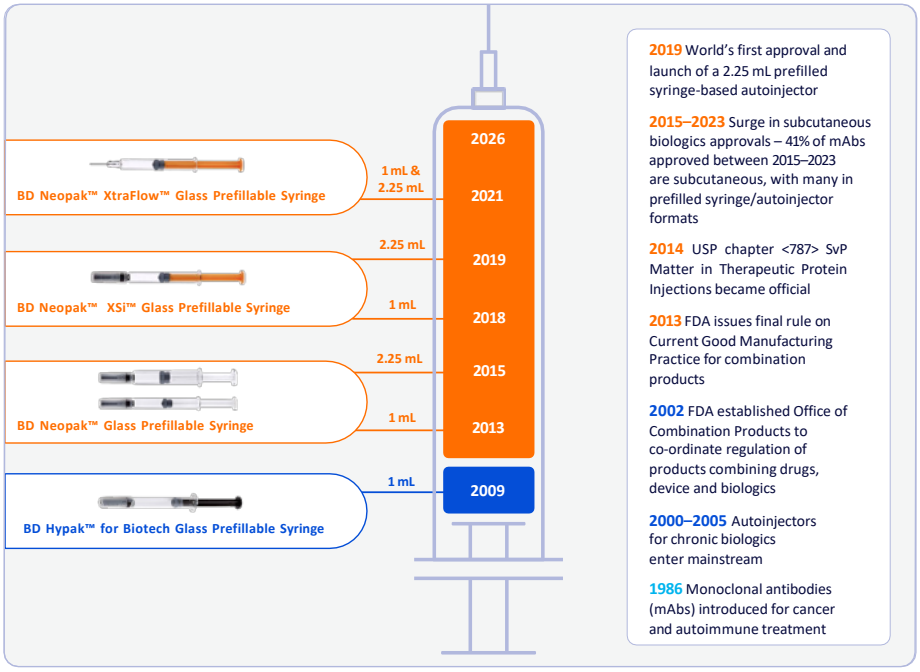

Figure 2: Timeline of BD syringe developments and industry milestones for biologic device combination products.

THE BD NEOPAK™ GLASS PREFILLABLE SYRINGE PLATFORM: A FUTURE-READY FOUNDATION

Although a syringe may appear to be a simple solution, its performance depends on the precise interaction of many interdependent scientific and engineering domains. Understanding drug-container interactions requires deep expertise in materials science and chemistry. Consistent injection performance relies on controlled mechanics and a comprehensive knowledge of fluid dynamics. Manufacturability and process stability depend on robust industrial design and metrology. These disciplines do not traditionally operate in the same space, yet they must converge seamlessly to produce a primary container that performs reliably across a wide range of biologic formulations and delivery conditions.

The BD Neopak™ Glass Prefillable Syringe platform was designed to bridge these domains, translating theoretical principles into practical, reproducible outcomes. The BD Neopak™ Glass Prefillable Syringe (Figure 3) was developed by following a quality-by-design approach to achieve excellent product performance attributes, aiming at Six Sigma level quality. This foundation reflects a deliberate effort

"THIS FOUNDATION REFLECTS A DELIBERATE EFFORT TO ENGINEER A SYRINGE PLATFORM CAPABLE OF DELIVERING HIGHLY REPEATABLE AND PREDICTABLE PERFORMANCE, AT SCALE."

to engineer a syringe platform capable of delivering highly repeatable and predictable performance, at scale. The BD Neopak™ Glass Prefillable Syringe manufacturing process incorporates tightened specifications,* automated visual inspection, strengthened dimensional controls* and fully indexed manufacturing lines, ensuring no glass-to-glass contact. These process controls were built to help reduce rejection rates and de-risk the transition from clinical development to manufacturing at scale.

Managing drug-container interactions is another central pillar of the BD Neopak™ Glass Prefillable Syringe platform. Compared with small-molecule drugs, biologics may face additional challenges due to their inherent susceptibility to physical and chemical degradation.[1]

Developers must also address various regulatory expectations related to extractables and leachables, particulate control and material compatibility. To support these needs, the BD Neopak™ Glass Prefillable Syringe portfolio includes low and ultra-low tungsten options, low-silicone variants and robust controls designed to reduce extractables and leachables, all intended to safeguard sensitive biologic formulations and maintain a stable drug-container interface.

Equally important is the platform's ability to ensure reliable secondary device integration. Prefillable Syringe-based autoinjectors have become foundational to the self-administration of biologics, and the BD Neopak™ Glass Prefillable Syringe platform is designed to support reliable compatibility with autoinjectors, with robust specifications for length-under-flange and length-under-shoulder to enable predictable autoinjector fit and functionality.

Figure 3: BD Neopak™ Glass Prefillable Syringe 1 and 2.25 mL.

Together, these elements establish the BD Neopak™ Glass Prefillable Syringe platform as a robust foundation for SC biologic delivery. With more than 45 drugs approved across global markets, its adoption demonstrates performance across diverse molecules, delivery systems and therapeutic areas. As SC biologic therapies continue to move towards higher viscosities, larger fill volumes and increasingly complex and sensitive formulations, its technology bricks play an essential role in expanding the design space for next-generation combination products.

ENABLING HIGH-MASS DOSE DESIGN

The evolution of the SC biologics development pipeline has been marked by an increase in the required mass of doses, driven by larger fill volumes, higher drug concentrations, increasing viscosities or an exponentially linked combination of these factors.[2] These expanding requirements have placed new demands on primary container systems, which must enable efficient drug delivery while preserving patient usability and maintaining reliable device performance.

Originally established as a 1 mL platform, the BD Neopak™ Glass Prefillable Syringe platform was subsequently expanded in 2015 to include a 2.25 mL format, enabling higher-volume SC delivery. This expanded design space supports emerging therapies while maintaining the precision, manufacturability and drug-container and secondary device compatibility that define the BD Neopak™ Glass Prefillable Syringe platform foundation.

However, as biologic formulations have become increasingly concentrated and viscous, volume expansion alone is no longer sufficient. Higher concentrations and viscosities have introduced challenges related to injection forces and injection times, potentially impacting patients' acceptance and experience. In response, BD introduced the BD Neopak™ XtraFlow™ Glass Prefillable Syringe as a technology brick designed to expand the high-mass-dose design space beyond what standard syringe and cannula offerings could support.

The BD Neopak™ XtraFlow™ Glass Prefillable Syringe combines an 8 mm needle length and thinner-wall cannula technologies, introducing ultra- and extra-thin wall offerings. This combination offers a solution to balance injection force, time, volume and viscosity requirements without requiring patient experience trade-offs.[3] For a 30 cP viscosity, the BD Neopak™ XtraFlow™ may allow for an up to 46%

"FOR A 30 cP VISCOSITY, THE BD NEOPAK™ XTRAFLOW™ MAY ALLOW FOR AN UP TO 46% REDUCTION IN INJECTION FORCE AND UP TO 57% REDUCTION IN INJECTION TIME."

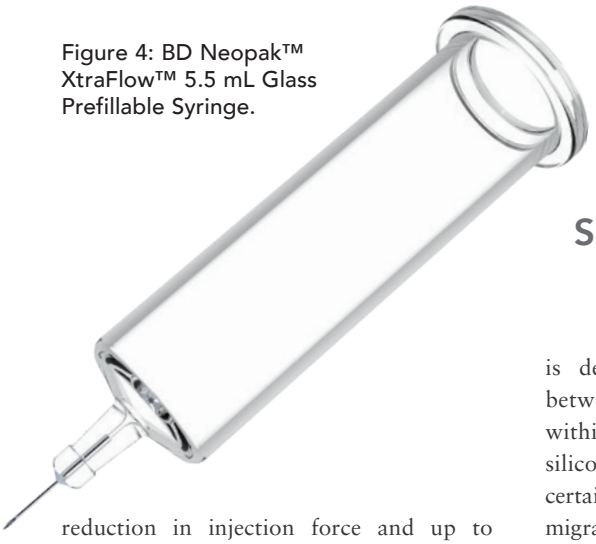

Figure 4: BD Neopak™ XtraFlow™ 5.5 mL Glass Prefillable Syringe.

reduction in injection force and up to 57% reduction in injection time.† In a human factors study, the BD Neopak™ XtraFlow™ Glass Prefillable Syringe was found to reduce needle-related anxiety in patients and demonstrated a positive impact on the patient experience for self-injecting patients with chronic diseases.[3]

To expand this design space even further, BD has recently introduced the BD Neopak™ XtraFlow™ 5.5 mL Glass Prefillable Syringe (Figure 4), designed for large-volume (> 2.25 mL) SC injections. Building on the same BD Neopak™ XtraFlow™ Glass Prefillable Syringe platform architecture, this 5.5 mL format is intended to support higher-volume, higher-viscosity biologics and further enhance large-volume autoinjector systems by maximising flow efficiency and reducing injection time** – critical factors within the emerging large-volume SC delivery design space.

DRUG-CONTAINER COMPATIBILITY

Biologic formulations are inherently sensitive to their container environment, and even small interactions between the drug and its primary container can affect stability, particle formation and patient safety.[1] Sources of incompatibility in prefillable syringes are well documented, and they can present risks for protein aggregation or elevated subvisible particle levels. As biologics become increasingly complex, maintaining control over these interactions has been an essential design requirement for primary container systems.

The BD Neopak™ XSi™ Glass Prefillable Syringe technology brick is designed to address the interaction between the drug and silicone oil within the syringe barrel. Traditional silicone-oil-based lubricants can, under certain conditions, lead to silicone droplet migration or destabilisation of sensitive proteins.[4,5] The BD Neopak™ XSi™ Glass Prefillable Syringe technology introduces a cross-linked silicone coating to the platform syringe to act as a barrier to silicone emulsification, thereby reducing silicone oil migration from the barrel. This technology has demonstrated significantly fewer subvisible particles while maintaining the functional performance needed for reliable injections.[6]

Beyond subvisible particle control, the improved coating stability also supports drug-container compatibility during long-term storage. In controlled studies, the BD Neopak™ XSi™ Glass Prefillable Syringe maintained lubricant layer thickness and distribution more effectively than conventional silicone syringes over 12–24 months of refrigerated storage, yielding lower silicone migration and no adverse effects on monoclonal antibody stability profiles.[6] This technology brick supports a more controlled and reliable interface between biologic formulations and their container systems, helping to reduce risk, enable and widen the formulation design space, and support the long-term stability required for sensitive biologic therapies.

"THE BD NEOPAK™ XSi™ GLASS PREFILLABLE SYRINGE TECHNOLOGY INTRODUCES A CROSS-LINKED SILICONE COATING TO THE PLATFORM SYRINGE TO ACT AS A BARRIER TO SILICONE EMULSIFICATION, THEREBY REDUCING SILICONE OIL MIGRATION FROM THE BARREL."

WHAT NEXT?

To address the complexities and diversity across the global biologics pipeline, the BD Neopak™ Glass Prefillable Syringe platform was intentionally designed as a platform system composed of several technology bricks, shifting the primary container from a passive component to an active enabler of combination-product success. The development of these technology bricks, including BD Neopak™ XSi™ and BD Neopak™ XtraFlow™, has relied on extensive data generation, analysis and application across materials science, process engineering, performance characterisation and more.

Looking ahead, the next major transformation shaping the pharmaceutical industry is artificial intelligence (AI). As the ecosystem advances into the era of Pharma 4.0™,[7] success will depend on the ability to use data not only to meet rising regulatory expectations, but to drive continuous improvement, operational excellence and deeper process understanding. The challenge is not data availability. Fill-finish operations already generate vast volumes of information across manufacturing, inspection, assembly and packaging. The challenge lies with data fragmentation as – too often – data remain confined within isolated systems, limiting their potential value.

Figure 5: BD iDFill™ Individual Syringe Identification with the BD Neopak™ 1 mL Glass Prefillable Syringe.

To address this gap, BD has developed the BD iDFill™ Individual Syringe Identification technology (Figure 5), which extends the role of a prefillable syringe beyond its physical function as a drug container into a digital enabler. BD iDFill™ enables end-to-end connectivity across fill-finish operations, from syringe manufacturing, through filling, visual inspection and ultimately all the way to the patient. By linking these separate data streams, the BD iDFill™ Individual Syringe Identification establishes a trusted, connected data backbone that supports unit-level traceability while remaining fully aligned with global regulatory expectations.

This integrated approach may unlock new opportunities to reduce manual work, improve root-cause analysis and accelerate data-driven decision making, which may translate to enhanced overall equipment effectiveness and reduced exposures to manufacturing risks. Over time, such connectivity lays the groundwork for advanced analytics and AI-enabled insights to be applied at scale, supporting predictable quality and more resilient supply chains.

In this context, the BD Neopak™ Glass Prefillable Syringe platform continues to evolve beyond physical design innovation alone. The combination of a robust, modular syringe foundation with data-driven enablement tools reflects a broader shift towards smarter, more connected primary container platforms that are designed to meet today's biologic delivery challenges and anticipate those of tomorrow.

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†With BD Neopak™ XtraFlow™ 27G 8 mm ultra-thin wall syringe when compared with a 12.7 mm 27G special thin-wall syringe. Ejection force and injection time values were simulated through a mathematical model based on the Hagen-Poiseuille equation. For injection time reduction, a constant force was defined. For injection force reduction, a fixed time was defined.
**As compared with BD Hypak™ for Biotech Glass Prefillable Syringe.*
***When compared with 12.7 mm special thin wall needle.*

BD Neopak™ XtraFlow™ 5.5 mL Glass Prefillable Syringe and BD iDFill™ Individual PFS Identification are products in development. Some statements are forward-looking and are subject to a variety of risks and uncertainties.

Hervé Soukiassian

Hervé Soukiassian is Associate Director, R&D Programme Leader at BD Pharmaceutical Systems, with over 19 years of experience in new product development and driving the digital transformation of containers and process understanding. His work focuses on applying digital twins, advanced modelling and the batch of one concept to strengthen collaboration with pharmaceutical partners and enhance drug delivery system performance. Mr Soukiassian led the successful development and commercialisation of the BD Neopak™ Glass Prefillable Syringe platform, including innovations such as BD XtraFlow™ and BD XSi™ technology, supporting the industry's transition to sensitive biologics and high viscosity formulations. He actively contributes to global industry standards and technical guidance generation. Prior to BD, Mr Soukiassian held several roles at Hewlett-Packard and served on the Board of Directors of ActiCM, a start up specialised in optical measurement technology. He holds a Bachelor's in Mechanical and Industrial Engineering and a Master's in Materials Science from INSA Lyon, France.

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Sophie Lelias is an Associate Director of Business Development at BD Pharmaceutical Systems. In her role, she drives end-to-end business development across the Prefillable Solutions portfolio, from early concept through commercialisation. Prior to this, Ms Lelias led global strategic portfolio marketing for the Biologics Prefillable Syringe portfolio, including the BD Hypak™ for Biotech and BD Neopak™ Glass Prefillable Syringe platforms. She collaborates closely with cross-functional teams globally to deliver value-driven solutions to pharmaceutical partners. Ms Lelias has held roles across the BD Interventional – Surgery, BD Medical – Infusion Preparation and Delivery and BD Medical Pharmaceutical Systems businesses, with a strong focus on strategic innovation marketing. She holds a Bachelor's degree in Public Health from Brown University (Providence, RI, US).

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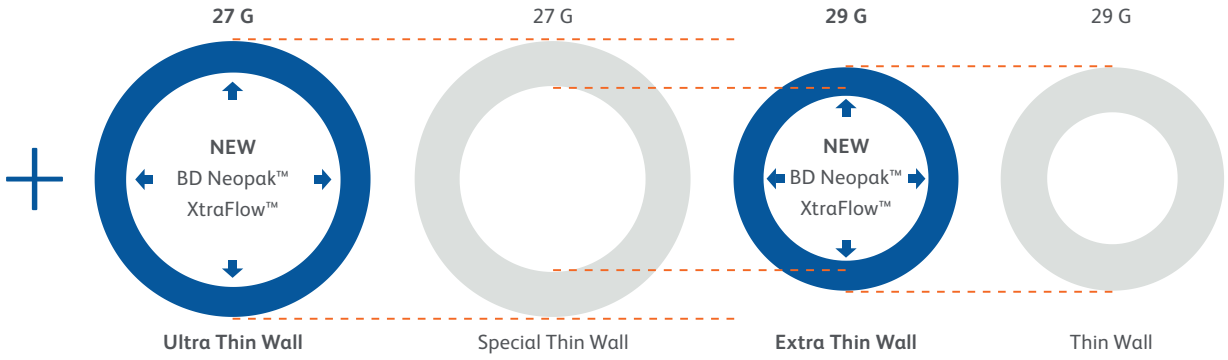
Optimize delivery of viscous drug formulations and improve patient experience

The **BD Neopak™ XtraFlow™ Glass Prefillable Syringe** combines an 8mm needle length with thinner wall technology, enabling you to optimize injection performance for high-viscosity and/or high-volume therapies, positively impacting patients' self-injection experience.[1,2]

Choose from Two Needle Technologies



Compared to conventional needle technologies, BD Neopak™ XtraFlow™ offers:

Up to 46%
reduction in injection force‡[1]

Up to 57%
less injection time‡[1]

2.5x to 8x
lower risk of IM injectionsμ[2,4]

Reduce
needle-related anxiety in patientsμ[2]

Positively impact preference
for self-injecting patients with chronic diseases μ[2]

A Trusted Solution for Biopharmaceuticals

With 50+ years of expertise, BD is a global leader in prefillable parenteral drug delivery systems. 30+ drugs have been approved in BD Neopak™ Glass Prefillable Syringe[3], supporting biologics development with a proven platform.

Contact BD today to explore how BD Neopak™ XtraFlow™ can enhance your drug delivery system.

μ With BD Neopak™ XtraFlow™ 27G 8mm ultra-thin wall syringe when compared to a 12.7mm 27G special thin-wall syringe. ‡ For a 30cP solution. With BD Neopak™ XtraFlow™ 27G 8mm ultra-thin wall syringe when compared to a 12.7mm 27G special thin-wall syringe. Ejection force and injection time values were simulated through a mathematical model based on the Hagen-Poiseuille equation. For injection time reduction, a constant force was defined. For injection force reduction, a fixed time was defined.

1. Injection time and ejection force calculation [internal study], Le Pont-de-Claix, France; Becton, Dickinson and Company; 2021. **2.** Pager A, Combedazou A, Guerrero K, et al. User experience for manual injection of 2 mL viscous solutions is enhanced by a new prefillable syringe with a staked 8 mm ultra-thin wall needle. Expert Opin Drug Deliv. 2020;17(10):1485-1498. doi:10.1080/17425247.2020.1796630 **3.** Registration status of drugs in BD Neopak™ Glass Prefillable Syringe, May 31st, 2024 [Internal regulatory report]. Pont-de-Claix, FR: Becton Dickinson and Company; 2024. **4.** Gibney MA, Arce CH, Byron KJ, Hirsch LJ. Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations. Curr Med Res Opin. 2010;26(6):1519-1530. doi:10.1185/03007995.2010.481203

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Lifecore®
INJECTABLES CDMO

Company Showcase

CONQUERING COMPLEXITY WITH LIFECORE INJECTABLES

Figure 1: Lifecore is a go-to partner for complex injectables programmes.

"WHEN UNEXPECTED ISSUES ARISE, SUCCESS DEPENDS ON A HIGHLY TECHNICAL TEAM THAT IS ACCUSTOMED TO ADAPTING QUICKLY, KEEPING PROGRAMMES ON TRACK DESPITE EVOLVING COMPLEXITIES."

Injectable drug products can vary significantly in complexity, and even seemingly straightforward formulations can present hidden challenges. For example, some formulations can be relatively easy to fill but require special handling due to oxygen or light sensitivity; other programmes demand extremely precise process control, where conjugation or other chemical reaction steps need to be controlled within seconds or risk the product's physical form changing, leading to the product not meeting release specifications.

These challenges are not always apparent at the outset of a development programme – injectables are inherently complex. When unexpected issues arise, success depends on a highly technical team that is accustomed to adapting quickly, keeping programmes on track despite evolving complexities.

A CAN-DO CULTURE BUILT ON DIFFICULT FORMULATIONS

As a US-based injectables CDMO, Lifecore Injectables has built a reputation for embracing complex process development and manufacturing challenges that others avoid (Figure 1). This mindset is rooted in the company's legacy as a manufacturer of sodium hyaluronate, a highly viscous material known for being difficult to filter and fill. Developing expertise in such demanding formulations early on laid the foundation for Lifecore's distinct technical capabilities.

Since initiating aseptic filling operations in 1989, Lifecore has accumulated decades of experience working with highly viscous and sensitive compounds. This history has fostered a culture defined by technical confidence and a willingness to tackle complexity head-on.

UNIQUE CAPABILITIES BACKED BY PROVEN QUALITY

No matter the challenge, Lifecore's work is supported by a robust quality management system (QMS). The effectiveness of this system has been demonstrated through

"SINCE INITIATING ASEPTIC FILLING OPERATIONS IN 1989, LIFECORE HAS ACCUMULATED DECADES OF EXPERIENCE WORKING WITH HIGHLY VISCOUS AND SENSITIVE COMPOUNDS."

Figure 2: Lifecore has a global quality and compliance track record of over 40 years.

successful drug product, medical device and combination product submissions across all stages of development.

With hundreds of millions of commercial units distributed worldwide and more than 40 years of quality and compliance experience, Lifecore has established a strong regulatory track record (Figure 2). The company's QMS continues to evolve through close engagement with global regulatory bodies and extensive oversight, including more than 60 audit days per year conducted by regulators and customers.

SOLVING THE PROBLEMS OTHERS CANNOT

Lifecore is frequently engaged by customers encountering manufacturing hurdles that cannot be resolved elsewhere. In one example, a customer approached Lifecore to fill and finish a polymer-based formulation so viscous that it was nearly solid at room temperature. The original equipment manufacturer deemed the product impossible to fill.

"LIFECORE IS FREQUENTLY ENGAGED BY CUSTOMERS ENCOUNTERING MANUFACTURING HURDLES THAT CANNOT BE RESOLVED ELSEWHERE."

Lifecore's team developed a solution by designing custom equipment to heat the product, enabling it to flow consistently throughout the manufacturing process. Filling machines were retrofitted with heating capabilities to ensure reliable flow through the narrow internal diameters of the filling needles.

Among Lifecore's sterile filtration solutions, a proven high-pressure sterile filtration skid enables aseptic filtration of high-viscosity formulations (up to 100,000 cP). This capability addresses a critical need for products that cannot be terminally sterilised and has been validated for use in a variety of applications.

Viscosity-related challenges can also impact device performance. Increased injection pressure in high-viscosity formulations may cause syringe needles to detach at the Luer. To mitigate this risk, Lifecore has collaborated with customers to implement custom assembly and packaging solutions that incorporate needle retention devices. While seemingly straightforward, successfully scaling these solutions required the design of custom automated machinery capable of meeting commercial production demands.

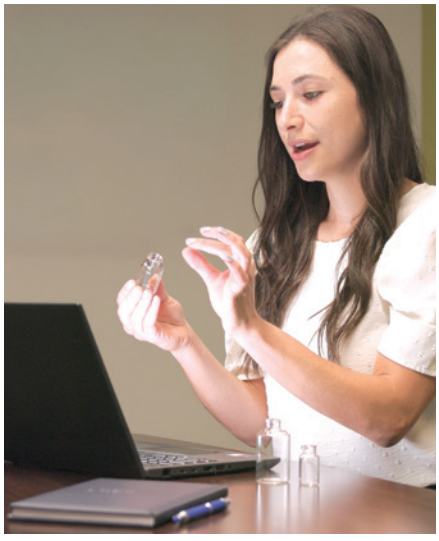

Figure 3: Lifecore can support a range of vial, syringe and cartridge options.

READY WHEN IT MATTERS MOST

Has Lifecore encountered every challenge imaginable? No. But with confidence grounded in decades of experience, a proven record of technical problem-solving and a culture that embraces complexity and has a quality system to back it up, Lifecore is prepared for the future challenges that will inevitably arise (Figure 3). At Lifecore, conquering complexity is not an exception – it is at the core of the company's ethos and how it supports its customers when it matters most.

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INJECTABLE COLLAGEN – PRESENT AND FUTURE POTENTIAL

GELITA

Martin Junginger of **GELITA** discusses the advantages and challenges of delivering collagen via injection, considering the role that collagen plays in the current healthcare landscape, including the company's own VACCIPRO® and MEDELLAPRO® collagen grades, and sharing insights on how that role may grow and adapt going forwards.

In modern medicine, next to oral intake, injection remains the administration method of choice for the delivery of a wide range of therapeutics, from glucagon-like peptide-1 (GLP-1) agonists and biologic medications to vaccines. As a result, the sector has seen rapid growth over recent years, and continues to grow in multiple therapy areas, driven by a variety of factors, such as increased interest in subcutaneous and intra-articular delivery and a greater focus being placed on patient-centricity across healthcare.

One such example of growth is the expansion of collagen-based injectables. Collagen has a long history of use in the medical field, first appearing in haemostatic sponges, sutures, membranes and wound dressings. Since its introduction, collagen has become established in multiple key therapeutic roles, including:

- Vaccine stabilisers, particularly for combination vaccines and lyophilised APIs
- Carriers for biologic, peptide and small molecule injectables
- Hydrogel components in regenerative and aesthetic medicine
- Adjunct excipients in diagnostic imaging agents and embolisation systems
- An API in plasma expanders.

Parenteral administration is a key part of collagen's success in therapeutic applications. If administered orally, collagen-based systems, especially bioactive collagen peptides, while effective, must

"ALTHOUGH IT HAS MULTIPLE ESTABLISHED USE CASES, AND EVEN MORE POTENTIAL ONES, COLLAGEN IS MOST WIDELY KNOWN IN MEDICINE FOR AESTHETIC AND REGENERATIVE THERAPIES."

be taken regularly for long periods, whereas topical administration is only useful for surface-level applications, failing to penetrate to internal sites of action. Therefore, depending on the intended use, for collagen to reach its full potential as a therapeutic ingredient, it is important to consider that injection may be the ideal route of administration, especially if fast action is a priority.

USING COLLAGEN FOR INJECTABLE APPLICATIONS

Advantages of Therapeutic Collagen

Although it has multiple established use cases, and even more potential ones, collagen is most widely known in medicine for aesthetic and regenerative therapies. Collagen is ideally suited to these applications due to its combination of biocompatibility, biodegradability, bioactivity and architectural versatility. As a therapeutic, exogenous collagen is enzymatically degraded, thereby avoiding long-term accumulation, and its inherent binding motifs support cell adhesion, migration and differentiation – key processes in tissue repair. For formulators, collagen is enormously versatile, able to be formulated into solutions, gels, sponges, membranes, microcapsules or *in situ*-forming hydrogels. Additionally, chemical modifications, such as methacrylation or peptide functionalisation, allow formulators to fine-tune its mechanical strength, degradation kinetics and biological performance.

These properties, coupled with current trends in the medical sector, are driving ever-increasing interest in injectable collagen. In particular, collagen aligns with the move towards more patient-centric healthcare, allowing healthcare professionals to opt for less-invasive treatment options for tissue regeneration. Additionally, as the human body's naturally most common structural protein, collagen readily replicates and interacts with the extracellular matrix (ECM).

Overcoming the Challenges of Collagen Production

So, with all its myriad advantages, what has held collagen back? Until relatively recently, collagen was necessarily derived from animals, most commonly being of porcine, bovine, equine or marine origin, meaning that it carries a risk of immunogenicity or pathogen transmission, as well as the religious and ethical concerns associated with using animal-derived materials. Today, by making the effort to ensure traceability of all animal-derived materials and implement modern extraction and purification technologies, particularly the removal of telopeptides to produce atelocollagen, collagen producers can significantly reduce the antigenicity and improve the clinical tolerability of the final product.[1]

Additionally, recent advances in biotechnology have seen the emergence of recombinant collagen as a potential alternative or complementary production method. Recombinant collagens, produced in engineered cells, yeast or plants, offer high molecular precision, batch-to-batch consistency and freedom from zoonotic contaminants, making it an exciting frontier in collagen production – especially in markets where non-animal products are prioritised.

However, all forms of collagen are notably susceptible to contamination by endotoxins. This represents a considerable risk to patients if not properly controlled for, with endotoxins able to elicit strong inflammatory responses even at very low concentrations – controlling endotoxin levels in healthcare settings is essential to prevent endotoxemia, septic shock and other life-threatening complications. As such, regulators enforce strict standards on parenteral collagens to ensure patient safety across all collagen applications.

"COLLAGEN IS ENORMOUSLY VERSATILE, ABLE TO BE FORMULATED INTO SOLUTIONS, GELS, SPONGES, MEMBRANES, MICROCAPSULES OR *IN SITU*-FORMING HYDROGELS."

Controlling endotoxin levels when manufacturing collagens requires a robust, multilayered approach, integrating material qualification, process design, monitoring and analytical verification. This starts with considered sourcing of the raw materials and exercising careful control over the supply chain, including full traceability for all materials and supplier validation. Continuing the process, manufacturing must also be subject to stringent environmental monitoring, particularly regarding water purity.

As well as validating and controlling input materials and the manufacturing environment, collagen producers can also reduce endotoxin contamination by using established processing techniques, such as high-temperature depyrogenation, adsorption or filtration-based removal, minimised hold times and optimised aqueous processing conditions.[2,3] Additionally, it is critical to conduct a thorough analysis of outputs to validate endotoxin levels in the finished product. Collectively, these measures establish a comprehensive framework that ensures collagen-based injectables maintain the stringent safety standards required for injectable applications and emphasise the importance of sourcing collagen from an expert supplier.

Collagen Versus Alternatives

Within the field of soft-tissue and regenerative biomaterials, parenteral collagen offers a unique combination of biocompatibility, biodegradability and bioactivity, setting it apart from both its well-established peers and newer entrants into the sector. Collagen's most obvious competitor in this field is hyaluronic acid, which is the most widely used injectable biomaterial in aesthetic and orthopaedic practice due to its viscoelasticity, strong hydrating capacity and excellent safety profile. However, unlike collagen, hyaluronic acid does not offer inherent bioactivity and can be rapidly degraded by hyaluronidases, which means it is generally a more short-term solution than collagen.

Material	Key Properties	Advantages	Limitations	Typical Applications
Collagen	Bioactive, cell-adhesive, resorbable, ECM-mimetic	Supports regeneration, natural tissue integration, tuneable structure	Historically short persistence, source-related immunogenicity (mitigated in newer systems)	Dermal fillers, soft-tissue repair, regenerative matrices
Hyaluronic Acid	Hydrating, viscoelastic, enzymatically degradable	Immediate volume, reversible, safe	Lacks bioactivity, short-medium persistence	Aesthetic fillers, viscosupplementation
Chondroitin Sulfate	Cartilage glycosaminoglycan, anti-inflammatory	Symptomatic osteoarthritis relief, synergistic with HA	Weak mechanical strength, rarely used alone	Joint injections, cartilage therapies (in blends)
Elastin Matrices	Elastic, flexible	Mimics tissue elasticity	Limited clinical use, requires combination materials	Soft-tissue engineering (research stage)
Synthetic Polymers (PEG, PCL, PLLA)	Tuneable mechanics, slow degradation	Long-lasting, controlled architecture	Non-bioactive, may induce inflammatory responses	Long-term fillers, scaffolds, drug delivery
Composite Systems (HA + Collagen)	Hybrid of hydration + structure	Enhanced stability, biocompatibility, ECM mimicry	More complex manufacturing and regulation	Advanced fillers, regenerative hydrogels

Table 1: Comparison of biomaterials.

Other notable alternatives in the sector include chondroitin sulfate, elastin-derived matrices, composite systems (such as a combination of hyaluronic acid and collagen) and synthetic polymers. The advantages and disadvantages of these alternatives are summarised in Table 1. Compared with the competition as a whole, collagen offers distinct advantages in terms of its inherent versatility and bioactivity – especially when it comes to its genuine regenerative potential. Further to that, composite systems that incorporate collagen with another material, such as hyaluronic acid or chondroitin sulfate, have demonstrated significant potential, and are at the forefront of rapid advances in the sector, making collagen a key driver of next-generation injectable systems in this space.

ESTABLISHED COLLAGEN HYDROLYSATES

As an innovation leader for gelatine and collagen, GELITA is ideally positioned to supply the medical sector with these key materials and provide its expert insights into collagen product development. GELITA is committed to delivering safe and sustainable collagen peptides to pharmaceutical partners, with dedicated teams and processes ensuring that the company's concepts and solutions are aligned with the industry's current and future needs. Key to this commitment is the GELITA Pharma Institute, which serves as a knowledge and innovation hub for GELITA's pharmaceutical collagens.

"GELITA IS COMMITTED TO DELIVERING SAFE AND SUSTAINABLE COLLAGEN PEPTIDES TO PHARMACEUTICAL PARTNERS, WITH DEDICATED TEAMS AND PROCESSES ENSURING THAT THE COMPANY'S CONCEPTS AND SOLUTIONS ARE ALIGNED WITH THE INDUSTRY'S CURRENT AND FUTURE NEEDS."

A standout example of GELITA's pharmaceutical portfolio is its VACCIPRO® collagen hydrolysates. VACCIPRO® collagen grades have been designed to enable precise formulation strategies, with chain-length profiles, endotoxin control and tissue affinity ideal for pharmaceutical and biomedical applications, from vaccine stabilisation to advanced hydrogel systems. As standard for GELITA's portfolio, VACCIPRO® offers a narrowly defined molecular weight distribution of approximately 2.5 kDa, while VACCIPRO® HMW is designed with much longer chain lengths, averaging molecular weights of approximately 12 kDa. VACCIPRO® and VACCIPRO® HMW demonstrate GELITA's ability to engineer its collagen grades to support formulators to achieve precise, predictable performance.

VACCIPRO® collagen peptides are well-established within the industry, with a long history of use as vaccine stabilisers, in large part due to their molecular architecture and stronger interactions (e.g. hydrogen bonding), enabling them to protect delicate antigens during lyophilisation and storage. They are recognised for their high purity, low allergenic potential and excellent cell-tissue affinity. VACCIPRO® HMW in particular has proven especially valuable for lyophilised vaccines, protecting the

integrity and potency of the sensitive actives throughout the freeze-drying process, as well as helping to control rehydration behaviour during reconstitution.

However, collagen hydrolysates such as VACCIPRO® have multiple applications beyond vaccine stabilisation. They have demonstrated their value in other injectable drug delivery systems as carriers and stabilisers for various micro- and nanoparticle formulations, with their natural amino-acid composition enabling collagen matrices to encapsulate and support therapeutic APIs while also being biodegradable and physiologically compatible – which is of key importance for sustained-release applications.

Further to this, collagen hydrolysates can be combined with injectable hydrogels and scaffolds to improve hydration, impart biological signalling and improve the dispersion of bioactive compounds. And, as a final example application, collagen can contribute similar benefits as an auxiliary excipient when used in injectable therapeutics intended to support plasma expansion, coagulation management or microvascular interventions. These examples demonstrate the vast breadth of applications where collagen has enhanced injectable therapies, and their potential is even greater.

FUTURE POTENTIAL – RECOMBINANT COLLAGEN

Recombinant collagen technology represents a potentially transformative paradigm shift in the biomaterials sector, offering a path towards safer, more consistent and ethically aligned injectable collagens. Compared with traditional animal-based sources, recombinant collagens enable experts such as GELITA to provide much more precise molecular definition and completely eliminate the risks associated with using animal tissues, while also aligning with increasingly prevalent societal preferences for animal-free products.

A key limitation of animal-based collagen that can be eliminated by recombinant collagen is batch-to-batch consistency. Because traditional collagen sources are derived from animals, its production is at the mercy of the inherent variability in the source material – differences in age, species, extraction and purification can create significant deviations in the material properties. Recombinant collagen, on the other hand, enables manufacturers to tightly control the bioengineering process (Figure 1), leading to a highly reproducible end product, which is a major advantage in the strictly regulated pharmaceutical sector.[4]

Recombinant collagen does not only resolve challenges faced by traditional methods, however – it opens up new possibilities. By taking advantage of recent advances in genetic engineering, protein expression and post-translational processing, it can enable unprecedented control over molecular architecture, offering new design opportunities beyond what is feasible with native tissues. Compared with traditionally manufactured collagen, recombinant collagens demonstrate lower immunogenicity,[5] superior molecular uniformity and greater adaptability. These characteristics make recombinant collagen not only an alternative to animal-sourced collagen but a platform for next-generation biomedical innovation.

Taking an example from GELITA's counterpart portfolio of endotoxin-controlled excipients, MEDELLAPRO® BD45 is a recombinant collagen fragment with a molecular weight of up to approximately 45 kDa, produced with controlled hydroxylation and low endotoxin levels, making it suitable for biomedical use. Crosslinking MEDELLAPRO® BD45 further increases its effective molecular weight, enhances network connectivity

"RECOMBINANT COLLAGEN ENABLES MANUFACTURERS TO TIGHTLY CONTROL THE BIOENGINEERING PROCESS, LEADING TO A HIGHLY REPRODUCIBLE END PRODUCT, WHICH IS A MAJOR ADVANTAGE IN THE STRICTLY REGULATED PHARMACEUTICAL SECTOR."

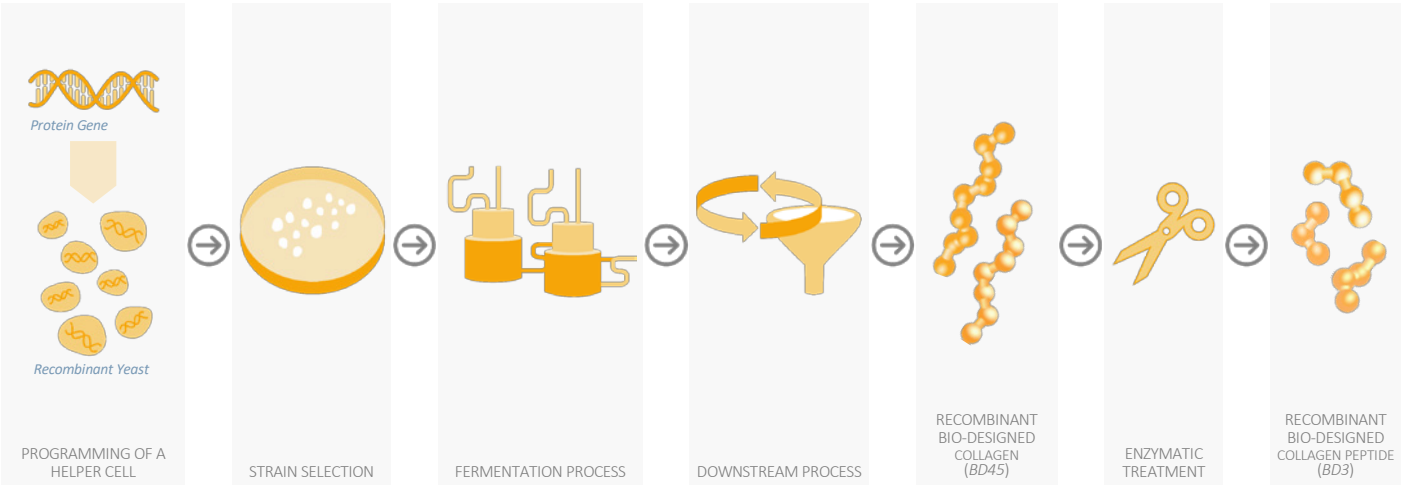

Figure 1: GELITA's bioengineering process for producing recombinant collagen.

and modulates its viscoelastic regime – this structural adjustability is foundational for tailoring product performance across applications requiring soft, flexible matrices or firmer, more robust scaffolds. From a bioengineering perspective, MEDELLAPRO® BD45 offers a tuneable platform; by adjusting concentration, crosslinking or chemical modifications, formulations can be optimised for:

- Cold-flow injectability (lower viscosity, faster needle extrusion)
- *In situ* gelation with rapid structural stabilisation after injection
- Self-healing behaviour for dynamic tissues
- Load-bearing performance where elastic recovery is needed.

The rheological and gelation characteristics of MEDELLAPRO® BD45 demonstrate the potential represented by recombinant collagens. Experts in the field will be able to translate this potential into collagens that can serve versatile application pathways spanning injectable hydrogels, controlled-release systems and regenerative scaffolding, opening up new therapeutic possibilities.

CONCLUSION

With innovation in the injectables space continuing to rapidly advance, it is imperative that the biomaterials available to formulators keep pace. With both a well-established history and as-yet untapped potential, collagen is set to remain a key material for injectable formulations. As an expert and global provider of collagen, with a deep wealth of experience and knowledge, GELITA is perfectly positioned to support the pharmaceutical industry in realising its full potential across a range of applications, and in spearheading innovation in recombinant collagens to provide the biomaterials of the future.

Martin Junginger

Martin Junginger is the Global Category Manager for Pharma & Bioscience at GELITA. He joined the company in 2017 and has extensive experience in the field of medical devices. He is the expert responsible for the strategic management and development of the pharmaceutical-grade gelatine portfolio. His particular focus is on soft capsule applications and advanced excipient solutions. He is the driving force behind the Endotoxin Controlled Excipient portfolio, which supports emerging bioscience applications, such as regenerative medicine, vaccine stabilisation and tissue engineering. He also oversees GELITA's global innovation process and plays a key role in GELITA's Pharma Institute. Mr Junginger has more than 20 years of experience in the medical device field. He has a strong background in regulated product and process development. This enables him to translate complex technical and regulatory requirements into market-ready pharmaceutical and bioscience solutions.

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LVSC DELIVERY: HOW VOLUME AND CONCENTRATION REQUIREMENTS ARE RESHAPING DEVICE SELECTION

Phillips Medisize
a molex company

Tony Bedford of **Phillips Medisize** considers how the rise in biologic formulations together with a strong shift towards subcutaneous administration is shaping the drug delivery industry, particularly in relation to large-volume subcutaneous delivery.

In previous *ONdrugDelivery* articles (2020–2021), Phillips Medisize has explored the wearable drug delivery market and how on-body injector (OBI) devices were struggling to break through in the <5 mL market. These articles explored the "identity crisis" of such devices, with multiple descriptors and acronyms, the rise in biologic formulations and the potential for wearables delivering greater than 5 mL – with oncology and the trend towards switching from intravenous (IV) to subcutaneous (SC) delivery as possible drivers.

Fast forward to 2026, and it is now increasingly evident that the growth in biologics, combined with a strong drive towards SC administration, is pushing the industry towards a much wider range of delivery volumes and, consequently, the potential for a broader set of device options.

THE RISE OF SC FORMULATIONS

It is now 20 years since Abbott's (now AbbVie)[1] Humira®[2] (adalimumab) and Amgen/Immunex's Enbrel®[3] (etanercept) were first approved in autoinjectors, both of which achieved substantial market success with these devices.

Compared with IV infusion administered in hospital or clinic settings, the advantages of an SC route of administration (RoA) are well established. For patients, this includes greater tolerability and increased convenience, with reduced treatment times (minimal preparation, drug administration in seconds) and no need for time-consuming in-patient visits. Increasingly, the drug can be self-administered at a time and place that suit the patient.

From a healthcare industry perspective, this reduces burden, with fewer patients requiring healthcare professional (HCP) administration or infusion chair occupancy. For pharmaceutical companies, SC delivery can provide a means of patent life extension and differentiation, with benefits extending to HCPs and patients by providing greater convenience. This is reflected in the fact that, of the top 10 best-selling proprietary drug products by sales revenue, eight are approved and available in SC form, with the remaining two approved in oral RoA, as shown in Table 1.

To further illustrate the rise of SC delivery, as of 2024, approximately half of all approved and clinical proprietary injectables were formulated this way.[4]

WHAT THIS MEANS FOR LVSC DELIVERY

Many SC drug agents can readily be self-administered using established formats such as autoinjectors, prefilled syringes (PFSs) or pen injectors, largely because their delivery volumes are in the sub-2 mL range, and the advantages of these devices are well documented.

Since 2012, many large-volume subcutaneous (LVSC) drugs, defined here as those administered subcutaneously with volumes > 2 mL, have been approved. This includes a small number of anti-cancer agents that originated or switched from IV to SC administration.

In terms of delivery, these products generally fit into one of four categories:

- **Multiple Bolus Injections**: Depending on the volume required, the full dose may be delivered via two or more injections using autoinjectors or PFSs. Typically, this means each injection is limited to no more than ~2 mL. Studies have explored the suitability of using autoinjectors for large-volume injection.[5]

- **Bolus "Push" Injection Enabled by Hyaluronidase**[6]: This approach refers to larger-volume injections, typically delivered from a syringe and administered by an HCP in a clinical setting. An example is Johnson & Johnson's DARZALEX FASPRO

Drug Name	Owner(s)	Therapeutic Area	2025 Sales*	Approved With SC Form?
KEYTRUDA®	Merck	Cancer	$31.7B	Yes
MOUNJARO®	Lilly	Diabetes	$22.9B	Yes
OZEMPIC®	Novo Nordisk	Diabetes	$19.9B	Yes
DUPIXENT®	Sanofi/ Regeneron	Autoimmune	$17.8B	Yes
SKYRIZI®	AbbVie	Autoimmune	$17.5B	Yes
ELIQUIS®	Bristol Myers Squibb/Pfizer	Cardiovascular	$14.4B	No
DARZALEX®	Johnson & Johnson	Cancer	$14.3B	Yes
BIKTARVY®	Gilead	HIV	$14.3B	No
ZEPBOUND®	Lilly	Obesity	$13.5B	Yes
WEGOVY®	Novo Nordisk	Obesity	$12.4B	Yes

** All figures from respective owners' full year reported financial results.*

Table 1: Top ten drug products by 2025 sales revenue.

Drug Name	Typical SC Volume
VELCADE® (bortezomib)	Circa 2 mL (more than one injection can be administered)
HERCEPTIN HYLECTA™ (trastuzumab and hyaluronidase-oysk)	5 mL
RITUXAN HYCELA® (rituximab/hyaluronidase human)	11.7 mL/13.4 mL
PHESGO® (pertuzumab/trastuzumab/hyaluronidase-zzxf)	10 mL/15 mL
DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj)	15 mL
TECVAYLI® (teclistamab-cqyv)	< 2 mL per injection (more than one injection can be administered)
TALVEY® (talquetamab-tgvs)	< 2 mL per injection (more than one injection can be administered)
OPDIVO® QVANTIG (nivolumab and hyaluronidase-nvhy)	5 mL/7.5 mL/10 mL
RYBREVANT® (amivantamab-vmjw)	< 29 mL
KEYTRUDA QLEX™ (pembrolizumab and berahyaluronidase alfa-pmph)	2.4 mL/4.8 mL

Table 2: LVSC cancer agents.

(daratumumab and hyaluronidase-fihj), delivered as a 15 mL bolus over three to five minutes. Several drugs of this type contain the permeation enhancer hyaluronidase, facilitating faster and more convenient SC delivery of larger volumes. Table 2 shows approved cancer agents in SC form, demonstrating the prevalence of hyaluronidase.

- **OBI**: A patch-pump device with an integrated needle, worn directly attached to the body. Devices may be electromechanical or mechanically powered. Currently approved devices require some level of user loading or filling but are suited for self-administration.

- **Near-Body Injector (NBI)**: An ambulatory pump with a tethered cannula or infusion set. These devices may be electromechanical or mechanically powered and can deliver injections or infusions at controlled rates appropriate to the application.

Research by Green *et al* shows that a considerable percentage of injectables are in SC form, with a number anticipated to be developed as LVSCs, in many cases with increasing drug concentrations.[4] This trend is expected to continue in the coming years.

CHALLENGES FOR THE DEVICE INDUSTRY

This LVSC pipeline trend presents several challenges for the device industry, particularly the need to deliver injections across a wide range of volume tiers, as illustrated in Figure 1. The largest "segment" falls within the 2–5 mL volume range.

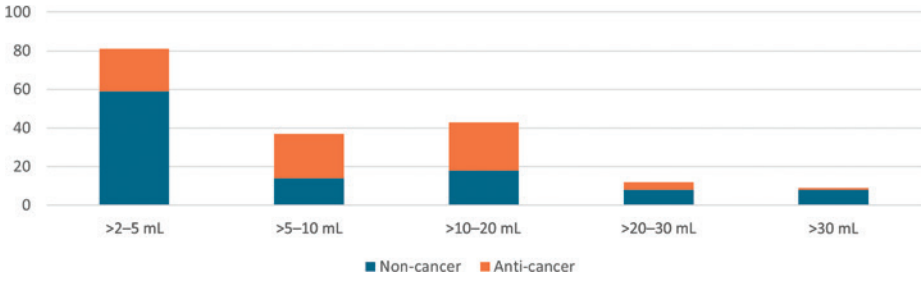

Figure 1: Volume requirements of potential LVSCs.[4]

"FROM A TECHNOLOGY PERSPECTIVE, THE FOCUS OF DEVELOPMENT IS ON BALANCING INJECTION SPEED, FORMULATION COMPLEXITY AND USABILITY, BUT THE MATHS STILL NEEDS TO ADD UP."

Besides injection volume, evolving delivery technology must also address additional needs, including:

- Drugs for chronic self-injection
- HCP administration in a range of settings
- Delivery of biologics, which may involve challenging characteristics such as greater viscosity or cold-chain considerations
- A shift towards less frequent dosing.

Anecdotally, prefilled solutions using proven primary containers are preferred, although user-filled or user-loaded devices offer an acceptable alternative.

DEVICE OPTIONS ARE DIVERSE

An examination of approved and emerging LVSC devices shows a wide range of configurations, with no single solution clearly dominating, as shown in Table 3.

LVSC devices in development are largely focused on devices capable of delivery volumes between 5 and 50 mL, although the lower end of this range may remain within reach of large-volume autoinjectors (or PFSs), particularly where the economics of multiple autoinjectors/PFSs (or even a single syringe and manual push) are competitive. In these instances, the drug is transferred from vial to syringe for manual bolus push, although a small number of cancer centres have adopted near-body syringe pumps.[7] Roche's PHESGO (pertuzumab trastuzumab/hyaluronidase-zzxf) 10 mL injection (maintenance dose) is approved in the EU for administration outside of clinical settings.[8] From a technology perspective, the focus of development is on balancing injection speed, formulation complexity and usability, but the maths still needs to add up.

	Prefilled & pre-loaded	Prefilled, user-loaded	User-filled	Integrated needle	Tethered cannula	Mechanical	Electro-mechanical
Handheld; Vial and Syringe			✓	✓	✓		
Autoinjector/PFS	✓			✓		✓	✓
OBI	✓	✓	✓	✓		✓	✓
NBI		✓	✓		✓	✓	✓

Launched and marketed combination devices | Theoretically possible or in development | Not in development/impractical

Table 3: Potential device configurations for LVSC.

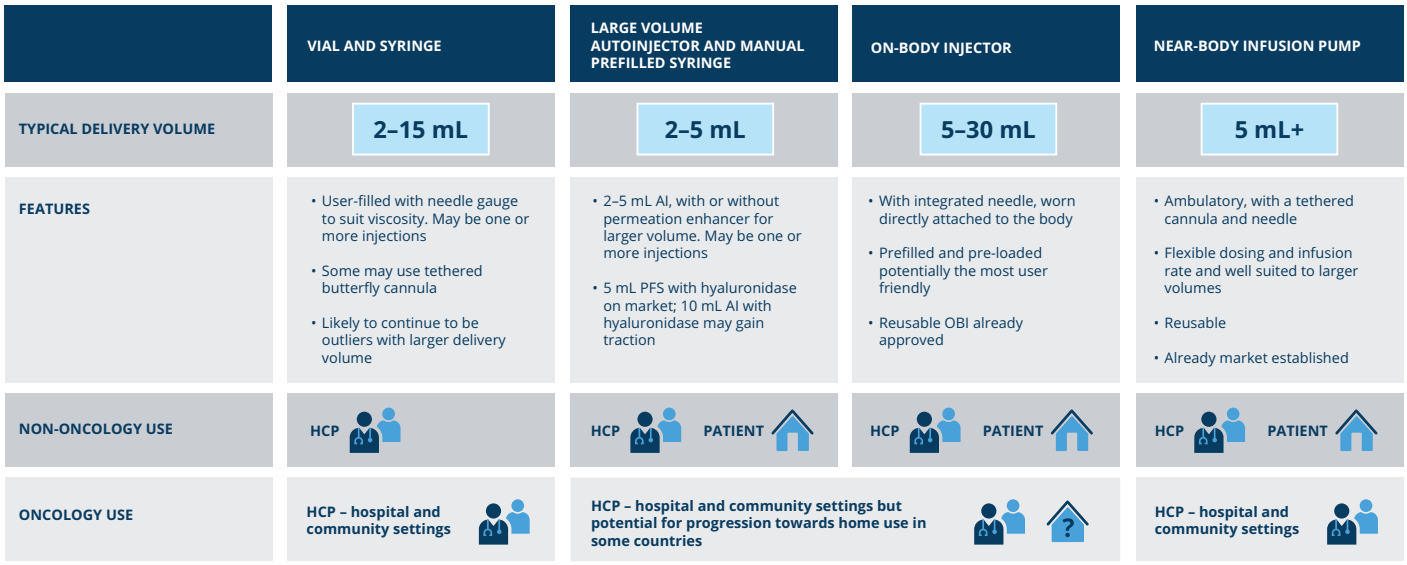

Figure 2: Predictions for LVSC delivery technology.

A PREDICTION FOR DEVICES

The diversity of needs and technologies suggests that a range of device solutions will be necessary to support the growing LVSC market.

Based on current trends, it is reasonable to expect that over the next few years the LVSC pipeline will continue to grow, with some high-dose drugs being developed exclusively for SC administration, bypassing the IV route altogether. LVSC biosimilars may also emerge, further expanding the market. Additional permeation enhancers beyond hyaluronidase are anticipated to become available, complementing the market success of Halozyme's (San Diego, CA, US) ENHANZE® and increasing the ease with which larger volumes can be delivered subcutaneously, with Alteogen's (Daejeon, South Korea) berahyaluronidase being approved in Merck's (Darmstadt, Germany) KEYTRUDA QLEX® (pembrolizumab).

What might this mean for LVSC delivery technology? Continued emphasis on self-administration is likely, focusing on convenience for the patient and HCP, away from hospital settings. A recent approval of note is Johnson & Johnson's DARZALEX becoming the first oncological injectable approved for administration by patients or caregivers in Europe and delivered directly from a PFS.[10]

"INCREASINGLY, IT APPEARS THAT THE INDUSTRY IS AT THE BEGINNING OF AN IMPORTANT AND DYNAMIC PERIOD FOR LVSC DRUG DELIVERY."

Near-body injection devices have recently been rolling out globally, with examples including the continuous infusion of Parkinson's drugs (for example, AbbVie's Vyalev™ (foscarbidopa and foslevodopa) pump and for frequent injection of myasthenia gravis and SC immunoglobulin drugs (for example, KORU's (Chester, NY, US) FreedomEDGE™).[11]

Such devices offer performance characteristics resembling traditional syringe pumps but in a more compact, ambulatory form, and could be considered for the replacement of manual push currently employed in cancer care. At the same time, mechanically powered OBIs could represent a significant breakthrough for LVSC devices and cancer care alike. Indeed, the Sanofi (Paris, France) Sarclisa® (isatuximab-irfc) cancer drug has been recommended for EU approval by the Committee for Medicinal Products for Human Use using Enable's (Evendale, OH, US) EnFuse® OBI.[12]

Market acceptance of larger-volume handheld devices remains uncertain. Autoinjectors in the 5 mL range are well advanced in development (for example, Ypsomed's (Burgdorf, Switzerland) YpsoMate® 5.5 and SHL Medical's (Zug, Switzerland) Maggie® 5.0), while manual self-administered PFSs are already approved and marketed (Argenx (Amsterdam, Netherlands) VYVGART Hytrulo® (efgartigimod alfa and hyaluronidase-qvfc)).[13]

If uptake of large-volume autoinjectors is limited, the market may open further for OBIs in the >5 mL space, perhaps with lower volumes continuing to be addressed by multiple bolus injections (for example, with more than one autoinjector). Two OBIs with injection volumes of ≥10 mL have already been approved with others in development, including the BD Libertas™, which is currently undergoing clinical trials.[14] Conversely, large-volume autoinjectors such as Halozyme's HVAI™, an autoinjector developed for up to 10 mL formulations containing ENHANZE, could disrupt this trajectory.

In the near term, whether or not we see more of these devices reach the market, wider adoption of syringes and manual push may continue, although this is unlikely to represent an optimal outcome for the patient or end users. Figure 2 summarises these predictions across delivery modalities and volume ranges.

Increasingly, it appears that the industry is at the beginning of an important and dynamic period for LVSC drug delivery. For pharmaceutical teams, this reinforces the importance of making device and delivery decisions early, in parallel with formulation strategy, balanced against the uncertainties that high-concentration formulation can bring during earlier stages of development.

ACKNOWLEDGEMENTS

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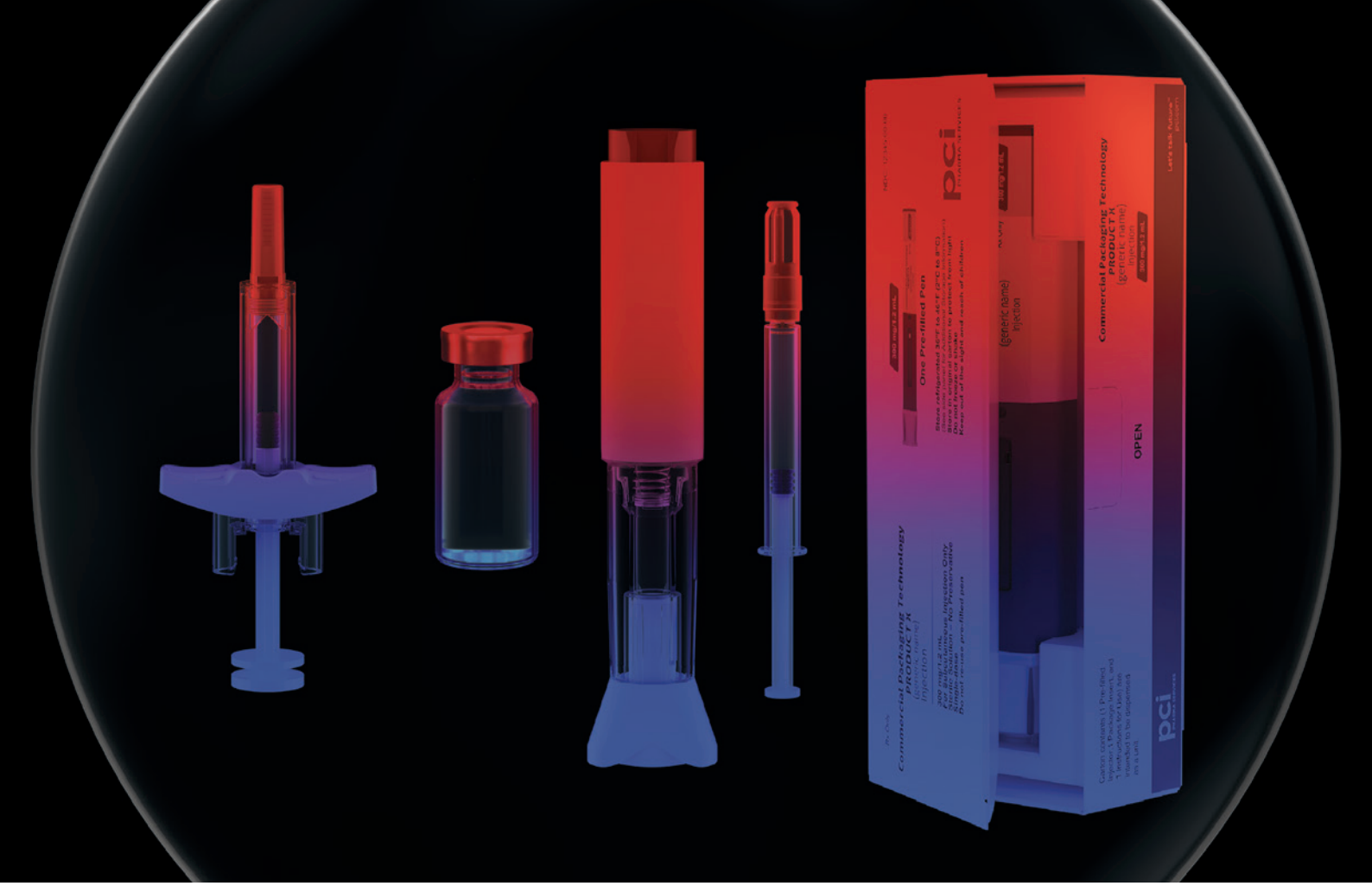

EARLY DECISIONS, FASTER LAUNCH: OPTIMISING COMBINATION PRODUCT COMMERCIALISATION

pci PHARMA SERVICES

Bill Welch of **PCI Pharma Services** explores how early development selections, structured timelines and adoption of a "path of least resistance" can reduce technical, regulatory and commercial risk, thereby optimising product commercialisation.

Bringing a drug-device combination (DDC) product to market is one of the most operationally complex undertakings in pharmaceutical development. Unlike traditional small-molecule programmes, combination products require synchronised formulation science, primary packaging, device engineering, human factors validation, regulatory strategy and commercial-scale manufacturing. Misalignment between any of these factors can delay approval or defer launch, even if the clinical data package is strong.

The differentiator between smooth commercialisation and late-stage disruption is rarely speed alone. Rather, it is the timing of key decisions, the degree of value chain integration and the willingness to reduce optionality early in favour of risk mitigation.

DEFINING THE DDC PRODUCT STRATEGY DURING EARLY CLINICAL DEVELOPMENT

The foundation of a streamlined commercialisation pathway is established before the first pivotal trial begins. During preclinical development and Phase I

> "THE FOUNDATION OF A STREAMLINED COMMERCIALISATION PATHWAY IS ESTABLISHED BEFORE THE FIRST PIVOTAL TRIAL BEGINS."

planning, sponsors must define the intended clinical and commercial positioning of the product. This includes the route of administration, intended use environment, patient population characteristics, anticipated dose volume and viscosity, and whether the programme represents a new molecular entity, a lifecycle extension or a biosimilar strategy.

These elements shape the target product profile, which, for DDC products, must explicitly integrate drug container and device attributes alongside drug performance characteristics. A therapy intended for chronic, at-home subcutaneous administration in an elderly population carries fundamentally different device requirements than a hospital-administered injectable. If such factors are not resolved early, development teams will often face reformulation efforts, container incompatibility findings or usability redesign late in Phase III.

The optimal window to align on – and begin actioning – a DDC product strategy is between pre-IND activities and early Phase II. Waiting beyond Phase IIb to define device intent significantly increases the likelihood of stability restarts, extractables and leachables reassessments, and repeated human factors work, adding additional cost and time.

DEVICE PLATFORM SELECTION: THE PHASE II DECISION THAT SHAPES LAUNCH TIMING

One of the most consequential inflection points in a DDC programme occurs during Phase II – the selection of the commercial-intent device platform. Many organisations delay this choice to preserve flexibility while dose-ranging or exploring market positioning. However, maintaining optionality too long often compresses the time available for verification, validation and regulatory documentation into an unsustainable window prior to submission.

Ideally by the end of Phase II, the specific primary container configuration and delivery platform – such as a 1 mL long prefilled syringe or a 2.25 mL autoinjector platform – should be selected, and design verification planning should be initiated. By this stage, stability studies should be underway in the final container-closure system, and extractables and leachables assessments should be progressing against materials that reflect commercial reality.

When device selection is deferred until Phase III, cascading consequences can follow. Stability studies may need to restart in the final configuration. Human factors validation can become constrained by compressed timelines. Assembly, testing and packaging equipment procurement will often overlap with registration batch production.

The discipline required to make a platform decision in early-to-mid Phase II often represents the single most effective measure in DDC development to protect timelines. Table 1 shows key milestones at each stage of product development. Sponsors who select a platform during Phase II often reduce commercialisation timelines by 6–12 months.

Development Stage	Key Combination Milestone
Phase I	Feasibility device studies
Early Phase II	Select commercial platform presentation
Late Phase II	Initiate design verification
Phase III start	Freeze design inputs

Table 1: Key development milestones in product design.

INTEGRATING DRUG AND DEVICE TIMELINES

Historically, drug substance, drug product and device engineering teams have operated on separate parallel tracks. While technically logical, this separation frequently produces misaligned reviews and incompatible milestone sequencing.

A streamlined programme deliberately integrates drug and device timelines at critical milestones:

1. **Formulation Lock:** Drives primary container compatibility
2. **Device Design Freeze:** Enables validation protocol execution
3. **Process Performance Qualification (PPQ):** Must align with stability data availability
4. **Human Factors Validation:** Requires production-equivalent units.

Failure to align these streams often leads to either the drug being ready but the device validation package being incomplete at submission, or the device being ready but commercial sterile fill-finish capacity not being validated in time to support launch volumes.

Best practice is to build a unified development plan that overlays clinical milestones with device verification, human factors activities, stability intervals, PPQ and regulatory module preparation. Programmes that treat the device as a co-equal development workstream rather than secondary packaging consistently reduce approval and launch risk (Figure 1).

Figure 1: Key product considerations in device design.

THE QUANTIFIABLE BENEFITS OF STARTING EARLY

Beginning device and packaging development activities during Phase II generates measurable downstream benefits. First, it reduces the need for bridging studies, whereas any late change in container-closure system or device configuration may trigger comparability assessments or additional analytical justification. In certain circumstances, clinical bridging may even be required. Locking configuration early minimises regulatory uncertainty and limits supplemental data requests.

Second, early investment in human factors engineering substantially improves validation outcomes. Human factors validation failures remain one of the most common late-stage setbacks for DDC products. Conducting iterative formative studies beginning in Phase II enables teams to refine instructions for use, labelling and ergonomic design before summative validation. Attempting to correct usability issues after formal validation often results in timeline resets.

Third, early engagement with component and device suppliers strengthens supply chain resilience. Tooling lead times for springs, plungers or moulded housings can extend beyond 12 months. In high-demand segments, such as prefilled syringes and autoinjector platforms, late procurement can delay launch by quarters rather than weeks. Sponsors who defer procurement until Phase III frequently encounter bottlenecks that delay commercial readiness independent of regulatory review timelines.

> "IN MANY CASES, THE FASTEST AND LOWEST-RISK PATH TO COMMERCIALISATION LIES IN USING ESTABLISHED DEVICE PLATFORMS RATHER THAN PURSUING FULLY BESPOKE SOLUTIONS."

Similar principles apply when partnering with a CDMO. Partnering with a CDMO that can provide integrated pharmaceutical development, sterile fill-finish, drug-device assembly, testing and packaging solutions across the product lifecycle, from concept to commercialisation, will streamline supply chains, ensuring seamless continuity and expedited pathways.

CHOOSING THE PATH OF LEAST RESISTANCE: PLATFORM VERSUS BESPOKE DEVICES

When speed to market is critical, platform selection is often the single most important lever. In many cases, the fastest and lowest-risk path to commercialisation lies in using established device platforms rather than pursuing fully bespoke solutions. Commercially available platforms often come with mature design history files, established manufacturing processes and extensive performance characterisation.

Regulatory agencies, such as the US FDA and the EMA, expect robust evidence that the device part of the DDC product performs safely and effectively in the intended use population. Established platforms frequently benefit from regulatory precedent and well-documented testing, which can simplify dossier preparation and reduce review cycles. Additionally, the common device platforms are also built around standard container-closure systems, allowing for additional use of existing precedents and documentation.

Bespoke devices, however, may offer differentiation and branding advantages that can be particularly beneficial, especially in competitive therapeutic categories. However, they introduce greater technical risk, higher non-recurring engineering costs and longer development timelines. For lifecycle management programmes, such as transitioning from vial-and-syringe to an autoinjector, platform solutions typically represent the most pragmatic route.

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

Table 2: Bespoke versus platform design.

The "path of least resistance" does not imply minimal rigour; rather, it reflects the use of proven engineering and manufacturing infrastructure wherever possible to reduce variables under regulatory scrutiny. Table 2 shows the pros and cons of using a device platform versus bespoke solutions.

MITIGATING COMMERCIALISATION RISK

Risk mitigation in DDC products should be structured across five domains:

1. Technical risks often stem from incomplete verification, insufficient extractables and leachables data, or failures in container closure integrity. These can be mitigated by initiating protocol development early and aligning analytical methods with anticipated commercial specifications.
2. Human factors risks are best addressed through iterative formative testing using representative patient populations under real-world conditions. Early identification of use errors can prevent the need for costly redesigns after validation.
3. Regulatory risk frequently arises from unclear primary mode of action determinations or fragmented documentation across drug and device modules. Early scientific advice meetings and proactive agency engagement can clarify expectations before submission.
4. Manufacturing risk focuses on equipment lead times, tooling qualification and scale-up reproducibility. Parallel process development during Phase II, combined with early equipment procurement, or early CDMO partnership prevents compression of PPQ activities.
5. Supply chain risk has become increasingly visible in recent years. Dual sourcing of critical components, geographic diversification and strategic outsourcing partnerships can reduce vulnerability to disruption during the launch window.

"STREAMLINING THE PATH TO COMMERCIALISATION FOR DDC PRODUCTS IS LESS ABOUT ACCELERATING INDIVIDUAL TASKS AND MORE ABOUT DISCIPLINED EARLY DECISION-MAKING."

CONCLUSION

Streamlining the path to commercialisation for DDC products is less about accelerating individual tasks and more about disciplined early decision-making. Selecting a commercial-intent device platform during Phase II, integrating drug and device timelines, initiating stability and compatibility studies in final configuration early, and using established platforms, tooling libraries and partnering with CDMOs with flexible, scalable solutions where appropriate, can collectively reduce regulatory and operational friction.

Organisations that approach DDC product development as a unified, risk-based programme rather than a sequential transfer between drug and device teams consistently protect launch timelines and reduce uncertainty. In an increasingly competitive self-administration landscape, early integration, proactive risk mitigation and thoughtful platform selection are not merely best practices; they are strategic imperatives for timely and successful commercialisation.

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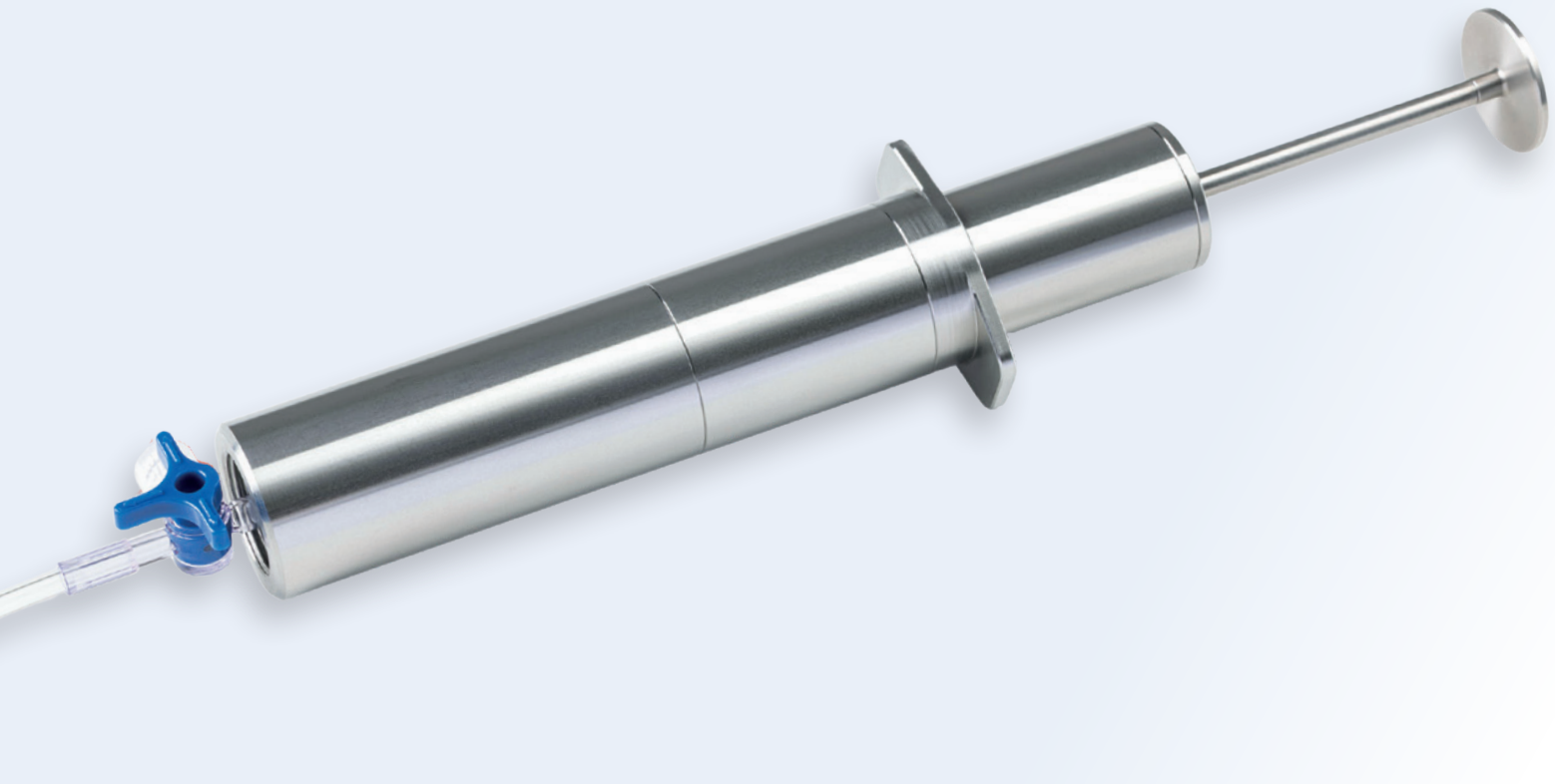

Early Insight

SCALING RADIOLIGAND THERAPY: WHY PACKAGING AND DELIVERY SYSTEMS MUST EVOLVE

ONCOFUSE MED

Dr Eva Littringer and **Dr Roland Starlinger** of **Oncofuse** discuss the exciting new frontier of radioligand therapy and the imminent bottleneck presented by current delivery methods running into strict limits on handling radioactive materials. They go on to introduce the Oncofuse prefilled-syringe-based system as a novel approach to containment and handling of these therapies, enabling radioligand therapy to expand beyond niche specialist clinics and hospitals.

Radioligand therapy (RLT) is progressing rapidly from specialised nuclear medicine departments into broader oncology practice. The clinical success of lutetium-based therapies, regulatory momentum and a rapidly expanding development pipeline have transformed RLT from a niche modality into a major area of pharmaceutical investment and development. As RLT programmes advance, the question shifts from "Can we treat?" to "Can we deliver reliably, safely and at scale?"

This shift reveals a central challenge: the delivery infrastructure for RLT is not scaling at the pace of its clinical and commercial expansion. This is partly because RLT products are inherently radioactive, introducing handling and workflow demands that traditional pharmaceutical operations are not accustomed to managing, such as decay-driven time pressure, limited shelf life and stringent shielding requirements that complicate preparation,

> "THESE RADIOACTIVITY-DRIVEN CONSTRAINTS AMPLIFY THE NEED FOR DELIVERY SYSTEMS THAT REDUCE EXPOSURE, MINIMISE MANIPULATIONS AND SUPPORT HIGHLY CO-ORDINATED WORKFLOWS."

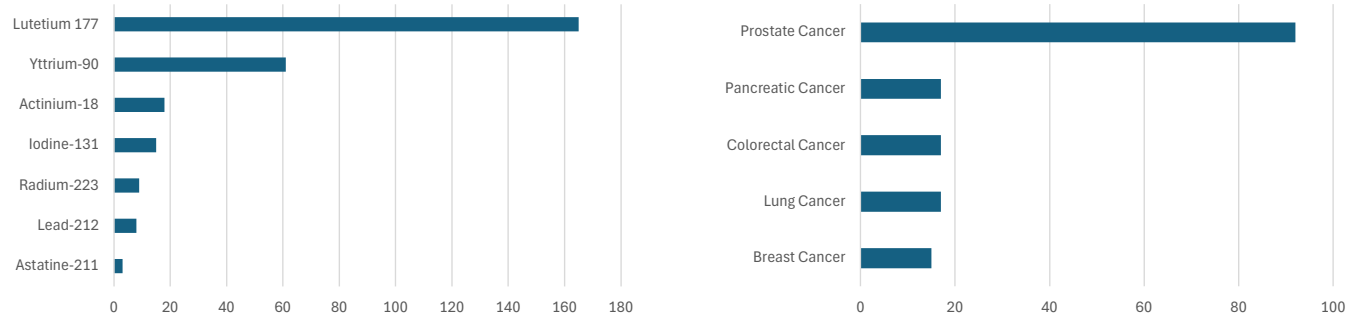

Figure 1: RLT is experiencing rapid global expansion, with more than 200 active clinical treatment trials across diverse isotopes and cancer types, and participation from 38 companies ranging from major pharmaceutical organisations to emerging biotechs (only actively recruiting trials, only treatment trials; data from clinicaltrials.gov, accessed Apr 2026).

transport and administration. These radioactivity-driven constraints amplify the need for delivery systems that reduce exposure, minimise manipulations and support highly co-ordinated workflows.

Today, most therapeutic radiopharmaceuticals still arrive in shielded vials – a legacy of diagnostic practice that functions well in expert hands but becomes increasingly strained as the demand for treatments rises across broader oncology networks. By contrast, transitioning to prefilled syringes (PFSs), paired with integrated protective packaging, reduces handling steps, improves consistency and supports tighter end-to-end lifecycle control from transport through to waste. The move towards PFSs is already underway – official administration materials for PLUVICTO® (lutetium-177 vipivotide tetraxetan (177Lu-PSMA-617), Novartis) explicitly describe both vial- and PFS-based administration, signalling a shift towards formats that support scalable, standardised delivery.

Packaging and delivery systems – traditionally an afterthought in radiopharmaceutical development – have therefore become essential enablers for sustainable growth. Oncofuse was specifically designed to fill this gap as an integrated packaging and handling system that reduces manipulations, maintains continuous shielding and supports transport, preparation, administration and disposal in one consistent workflow.

RLT TODAY: A RAPIDLY EXPANDING FIELD

The growth trajectory of RLT is steep and accelerating. According to TheranosticTrials.org, there are more than 200 active trials underway globally across numerous isotopes and cancer types, with 38 companies participating, from pharmaceutical leaders to emerging biotechs (Figure 1). Approvals, such as for 177Lu-PSMA-617, have demonstrated significant improvements in overall and progression-free survival, helping to establish RLT as one of the most promising targeted therapeutic modalities of the past decade.[1]

Commercial data underscore this momentum – according to Medi-Tech Insights (Brussels, Belgium), current forecasts project the RLT market to exceed US$13 billion (£9.6 billion) by 2030, with a compound annual growth rate (CAGR) of more than 30% (Figure 2). In parallel, nuclear medicine societies highlight rapidly widening implementation gaps between eligible patients and those who are actually treated. The trajectory is clear: RLT demand is rising faster than health systems can operationally absorb it.

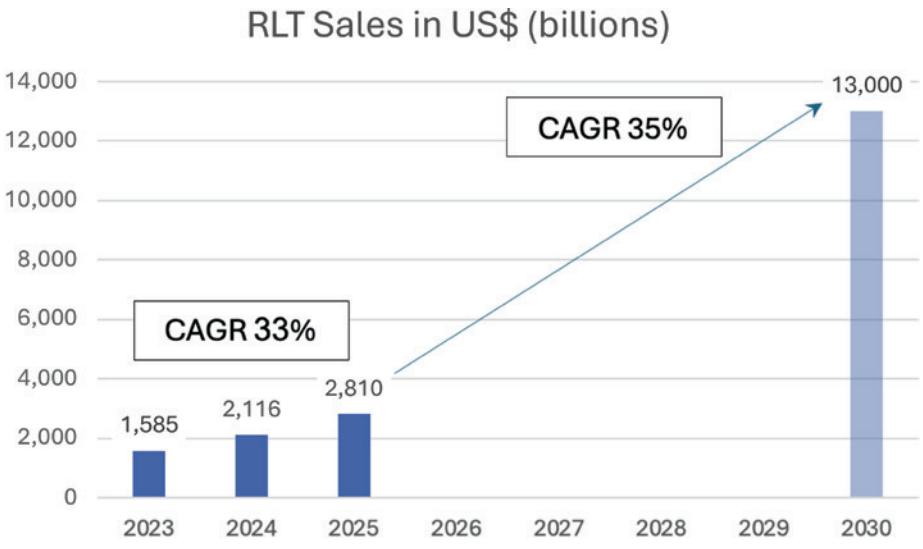

Figure 2: RLTs are demonstrating a strong upward market trajectory, reflected in current forecasts projecting global RLT sales to reach approximately $13 billion by 2030 (based on publicly reported data from Novartis and Medi-Tech Insights).

What Are RLTs?

RLTs pair a tumour-targeting ligand, such as small molecules, peptides or antibodies, with a radioactive isotope. After intravenous administration, the ligand selectively accumulates at tumour sites and delivers highly localised ionising radiation, most commonly β-particles (e.g. lutetium-177) or α-particles (e.g. actinium-225) to malignant cells and their surrounding microenvironment.

A closely related diagnostic form of the same or a closely related ligand can be labelled with a γ- or positron-emitting radionuclide, enabling high-sensitivity single-photon emission computed tomography (SPECT) or positron emission

tomography (PET) imaging prior to therapy. This allows clinicians to visualise target expression, assess whole-body tumour burden and confirm patient suitability before administering therapy. In certain theranostic applications, radionuclides such as lutetium-177 additionally permit SPECT imaging using the therapeutic radiopharmaceutical itself, owing to their concurrent β- and γ-emissions. In selected settings this also allows the assessment of tumour burden and its changes during the course of treatment. Together, these paired diagnostic and therapeutic agents form the basis of theranostics – a unified modality that integrates patient selection, molecular imaging and targeted radiotherapy within one molecular platform (Figure 3).

Lutetium-177-based radioligands are now established in the treatment of neuroendocrine tumours and prostate cancer, and developers are actively exploring new isotopes, targets and indications. With the number of clinical programmes increasing and more isotopes entering the pipeline, operational readiness – not scientific potential – is likely to determine how quickly patients will gain access to RLTs.

"WITH THE NUMBER OF CLINICAL PROGRAMMES INCREASING AND MORE ISOTOPES ENTERING THE PIPELINE, OPERATIONAL READINESS – NOT SCIENTIFIC POTENTIAL – IS LIKELY TO DETERMINE HOW QUICKLY PATIENTS WILL GAIN ACCESS TO RLT."

A NEW CHALLENGE FOR PHARMACEUTICAL DEVELOPMENT AND COMMERCIALISATION

Beyond the clinical promise, RLT introduces a practical novelty for many pharmaceutical organisations: routine interaction with radioactive material across development, manufacturing, distribution and post-use management. Historically, many pharma companies have built operating models around non-radioactive products, with radiation expertise concentrated in small pockets of specialists or external partners.

Therapeutic radioligands require pharma companies to integrate radiation considerations into mainstream development and supply activities: time-critical logistics driven by radionuclide half-life, specialised packaging and shielding, and handling constraints that influence everything from process design to site operations. This affects interfaces across functions that are not always accustomed to radioactivity, such as analytics, stability, quality assurance, external manufacturing and distribution planning. In this context, packaging and delivery systems become part of the "technology stack" required to make an RLT programme viable at scale, not an accessory added near launch.

Oncofuse helps to operationalise these cross-functional challenges by standardising physical interfaces and reducing the number of exposure-relevant manipulations, supporting more predictable processes from manufacturing to the clinic.

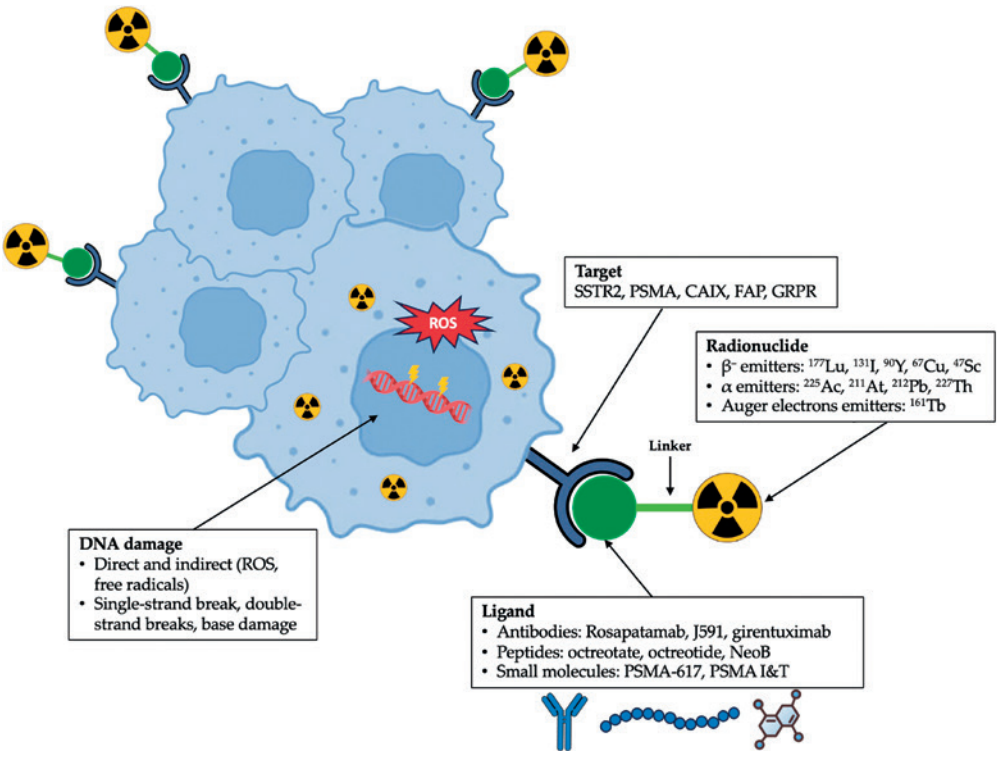

Figure 3: Schematic representation of radioligand therapy agents, illustrating their components and mechanism of action. Reproduced from Ninatti *et al* (2025).[2]

The Unique Handling Challenges of RLT

RLT shares many of the requirements of conventional sterile injectables, including sterility, container integrity and accurate dosing, but also adds a persistent risk dimension due to ionising radiation. Actions that are routine for traditional injectables become exposure-relevant for radiopharmaceuticals. Three factors dominate real-world workflows:

1. Occupational exposure limits
2. Time pressure from short shelf life
3. Mandatory radioactive waste management.

Each additional handling step increases exposure and constrains throughput. Oncofuse reduces these steps by providing a single, shielded containment system that remains consistent across receiving, preparation, administration and disposal.

RLT delivery also spans multiple professional domains – radiopharmacy, radiation protection, nuclear medicine and oncology – making standardised physical interfaces enormously valuable. By unifying these interfaces, Oncofuse reduces ambiguity, training burden and site-to-site variation.

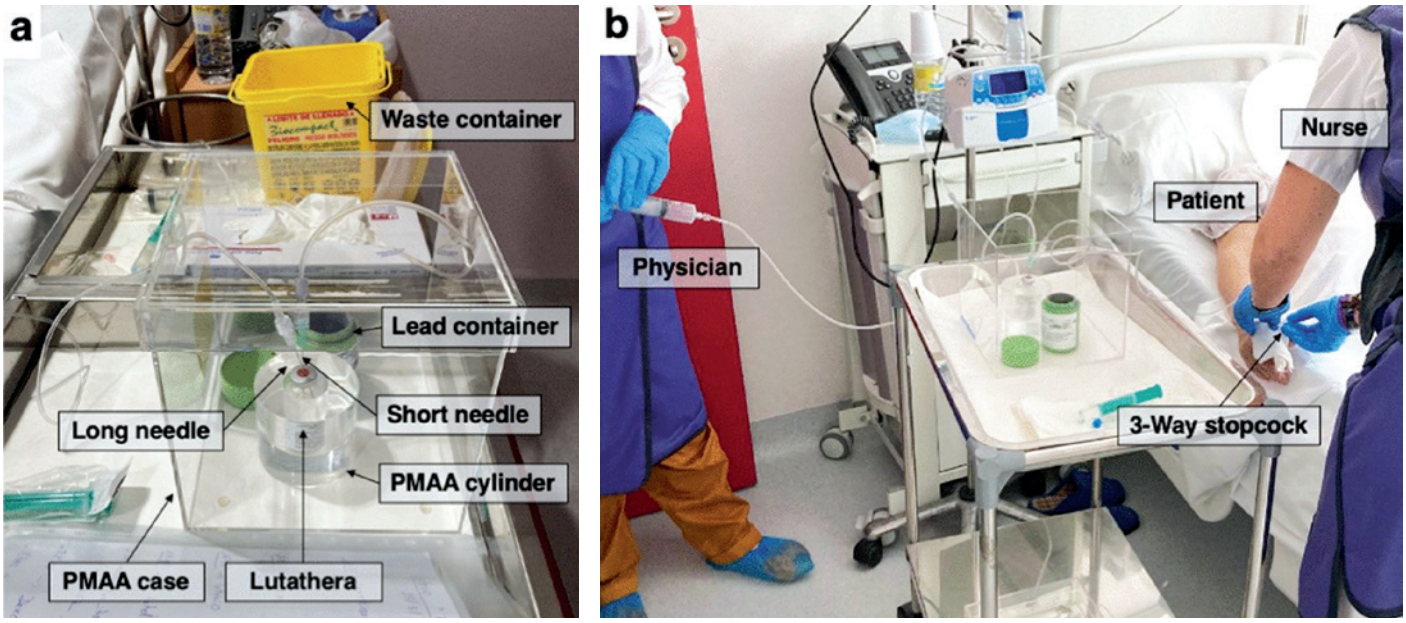

Figure 4: Set-up used during PRRT-Lu administration. (a) Lutathera vial positioned outside the lead pot and placed within a polymethyl methacrylate (PMMA) shielding cylinder, with infusion needles inserted for controlled transfer. (b) Workflow positions of clinical staff and the patient during final air infusion, highlighting the operational complexity and radiation-protection requirements of current delivery systems. Reproduced from Riveira-Martin *et al (2023)*.[3]

Scalability and the Emerging Exposure Capacity Gap

Despite the complex administration set-up (Figure 4), RLT works well because it is delivered to relatively few patients in highly specialised nuclear medicine departments, where staff are trained and equipped to handle radioactive materials safely. In this controlled environment, workflows are efficient and radiation exposure is managed effectively. Based on data published by the Lancet Oncology Commission, the number of prostate cancer patients currently treated with 177Lu-PSMA-617 is around 22,000 patients globally, whereas the number of eligible patients is around 158,000.[4]

However, as the number of eligible patients increases, these specialised centres are approaching a capacity limit. The bottleneck is not the efficacy of the treatment but the dose restrictions that staff must adhere to, as occupational radiation exposure is cumulative. This creates a finite ceiling on how many procedures can be performed, regardless of patient need. A recent evaluation of radiation exposure during lutetium-177 therapy demonstrated that, even with proper shielding and adherence to safety protocols, theoretical annual dose limits for the most exposed staff members correspond to only 15–49 patients per year, depending on the dose metric used.[3]

The unmet needs of radiopharmaceutical therapies were addressed at the ASTRO Radiopharmaceutical Symposium 2026, where the need for increased collaboration between nuclear medicine and radiation oncology (including sharing revenue and resources) was identified.[5] Ultimately, this means that it will be necessary to extend the administration of radioligand therapies out of the specialised nuclear medicine departments to other departments, such as radiation oncology.

The situation becomes even more challenging when the growing demand requires RLT to be delivered in less specialised hospitals. These settings may not routinely work with radioactive materials, meaning that staff will require additional training, oversight and infrastructure. This not only slows adoption but also increases the risk that cumulative exposure limits are reached sooner, further constraining throughput.

In short, while RLT is clinically effective, scaling it beyond expert centres will be limited by staff exposure constraints and the readiness of non-specialised sites, making exposure-reducing workflow and system innovations essential for sustainable growth. Oncofuse is designed to help reduce exposure-relevant steps and support more scalable workflows by reducing manipulation steps, maintaining shielding throughout the workflow and limiting staff proximity and time to unshielded radioactive components.

THE CASE FOR PFSs IN RLT

Prefilled syringes are a mature packaging format in many injectable markets because they can reduce preparation steps, support dose accuracy and improve workflow consistency. In RLT, those same advantages translate directly into exposure reduction and scalability. A PFS-based presentation can remove or

"BY SHIFTING COMPLEXITY UPSTREAM INTO CONTROLLED MANUFACTURING AND FILL-FINISH ENVIRONMENTS, PFSs CAN SUPPORT A SAFER AND MORE REPEATABLE POINT-OF-CARE WORKFLOW."

Figure 5: The Oncofuse system enables safer, simplified radioligand handling through a unified, shielded packaging and delivery approach.

minimise the manual dose-withdrawal step and reduce the number of manipulations performed close to the radioactive source. It can also reduce site-to-site variability by offering a more standardised delivery unit. By shifting complexity upstream into controlled manufacturing and fill-finish environments, PFSs can support a safer and more repeatable point-of-care workflow.

From a system perspective, PFSs also enable more consistent integration of safety features, such as compatible shielding and standardised interfaces, and can reduce reliance on site-specific workarounds. The transition from vials to PFSs is therefore not merely a convenience improvement – it is a structural change that helps decouple patient throughput from manual handling intensity and the cumulative exposure experienced by specialised staff.

Beyond the Syringe: Integrated Packaging for Transport, Administration and Disposal

For RLTs, the primary container is only one element of the system. The therapy must be transported, stored, administered and disposed of under radiation constraints. Consequently, scalable solutions must consider packaging as an integrated part of the product lifecycle. A robust concept should:

- Provide shielding during transport and storage
- Enable administration with minimal manipulation
- Transition seamlessly into waste handling after use.

Maintaining containment and shielding throughout the product lifecycle reduces exposure opportunities, simplifies procedures and supports more consistent implementation across sites.

Designing Waste Management into the System

Radioactive waste is a built-in feature of RLTs. Minimising the number of contaminated components and the need for post-administration handling can reduce exposure and operational burden. Single-dose formats with a low residual volume and packaging designed for direct, controlled disposal can simplify decay storage and reduce repeat handling. Importantly, waste handling is part of the total exposure picture. If packaging can reduce manipulations not only during administration but also post-use sorting, transfer and storage, the cumulative benefit can be meaningful, especially at higher patient throughputs.

Oncofuse: An Integrated PFS Packaging Concept

Oncofuse addresses these challenges by building on the established advantages of PFSs and integrating them into a single, shielded containment platform that remains intact from arrival to decay storage. By maintaining a continuous protective barrier, Oncofuse reduces the opportunities for exposure, ensures consistent handling across sites and eliminates unnecessary repackaging or component transfers. Its single-dose, low-residual-volume configuration further minimises contaminated waste and simplifies the transition into decay storage, reducing post-treatment sorting and limiting cumulative exposure as treatment volumes grow.

This concept is noteworthy because it treats packaging, shielding and end-of-life handling as one coherent system rather than separate add-ons. If shielding and containment remain with the product through transport, administration and disposal, the number of times staff must

directly handle radioactive components can be reduced, addressing a core scalability constraint (Figure 5).

OPPORTUNITIES FOR PHARMACEUTICAL DEVELOPMENT PROGRAMMES AND SUPPLY CHAINS

Integrated packaging can offer value well before commercial launch. In development, radioactive samples require repeated handling and storage. Shielded, system-level packaging concepts can support safer storage and enable routine tasks, such as removing stability pulls or preparing samples for testing, with fewer exposure-relevant steps.

This is more than a laboratory convenience. As RLT portfolios grow, development organisations may need to run multiple stability programmes in parallel and handle increasing numbers of samples and analytical timepoints. Reducing the exposure relevance of routine actions supports more sustainable ways of working and can make it easier to integrate RLT activities into broader development organisations, rather than confining them to a small number of specialists with limited time that people can work in the lab with radioactive materials.

Across clinical supply chains, system-level packaging may support more robust transport and receiving workflows and reduce the need for site-specific adaptations. Oncofuse frames its concept as an end-to-end packaging system for transport, administration and waste management intended to simplify workflows and support scalability. In addition, with new guidance from the US FDA on dose-finding studies, the Oncofuse system further provides freedom in dose adaption by enabling easy adjustment of volumes.

More generally, integrated concepts can strengthen time-critical supply reliability by reducing repackaging steps, standardising interfaces and helping clinical teams to focus on administration rather than packaging manipulation. This becomes increasingly relevant if RLTs expand beyond a small number of specialised hospitals and into broader networks where consistency and simplicity are essential.

"ONCOFUSE FRAMES ITS CONCEPT AS AN END-TO-END PACKAGING SYSTEM FOR TRANSPORT, ADMINISTRATION AND WASTE MANAGEMENT INTENDED TO SIMPLIFY WORKFLOWS AND SUPPORT SCALABILITY."

CONCLUSION AND OUTLOOK

RLTs are quickly moving from a specialist-use-only application into the

broader oncology landscape. In that transition, packaging and the associated delivery workflow become strategic enablers rather than downstream details. Many RLT products still follow a vial-based paradigm inherited from diagnostic radiopharmaceutical practice. That legacy approach can be workable in a niche setting, but it becomes increasingly misaligned as patient numbers rise, treatment moves beyond centres of excellence and organisations attempt to industrialise and standardise delivery across multiple sites.

A shift from vials towards PFS-based presentations, paired with integrated protective packaging, offers a pathway to reduce handling steps, improve workflow consistency, lower occupational exposure and strengthen end-to-end lifecycle management across transport, administration and radioactive waste handling. Oncofuse builds directly on this trajectory. By unifying transport shielding, administration support and waste-ready containment into one continuous system, it illustrates how next-generation packaging can remove exposure-relevant steps, simplify workflows and help bridge the scalability gap that RLT now faces.

ABOUT THE COMPANY

Oncofuse is an Austria-based developer of packaging and handling systems for radiopharmaceuticals, with a particular focus on the operational requirements of RLT. Its core technology, Oncofuse, is an integrated packaging concept that supports all key stages of radiopharmaceutical use – transport, preparation, administration and waste management – within a single containment system.

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Dr Eva Littringer

Eva Littringer, PhD, is Co-Founder and Chief Executive Officer of Oncofuse, where she leads the development of integrated, next-generation packaging solutions designed to improve the safety, efficiency, and scalability of RLT delivery. She holds a Master's in Pharmacy and a Master's and PhD in Pharmaceutical Engineering. With over 15 years of experience across the pharmaceutical value chain, including senior R&D roles at Sandoz and Novartis, expertise in pharmaceutical excipients, prior work as an expert at the Austrian Medicines Agency and as an expert member of the European Directorate for the Quality of Medicines & Healthcare, she brings deep scientific, technical and commercial expertise to advancing safer, scalable radiopharmaceutical workflows. She is the inventor on multiple filed patents, including a granted patent, and has received several innovation awards, including recognition at the European Forum Alpbach, the Best of Biotech Award and the Drug Delivery to the Lungs Pat Burnell Young Investigator Award.

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ANTIBODY-DRUG CONJUGATES: AN EMERGING FRONTIER IN IV TO SC CONVERSION

Dr Mehul Desai of Enable Injections, **Dr Michael Hageman** of the University of Kansas and **Dr Wei Chen** of WuXi Biologics examine the growing antibody-drug conjugate market, the unique formulation challenges these therapies present for subcutaneous delivery and how innovations in on-body injector technology may offer a practical path forwards.

THE ADC LANDSCAPE: A DRUG CLASS COMING OF AGE

Before exploring the formulation challenges that antibody drug conjugates (ADCs) present for subcutaneous (SC) delivery, it is important to understand their history, structure and mechanism of action. At their core, ADCs are engineered molecules that combine the specificity of a monoclonal antibody with the cell-killing potency of a cytotoxic small-molecule payload. As shown in Figure 1, ADCs have three components: the antibody, the linker and the payload (usually a cytotoxic agent). The antibody component targets a specific antigen expressed on the surface of tumour cells, while the payload, connected via a chemical linker, is released once the ADC is internalised, delivering the cytotoxic agent directly to the cancer cell.[1] A simplification of this process is depicted in Figure 2.

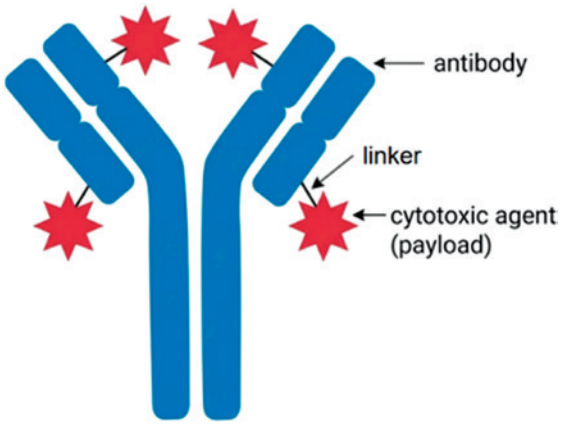

Figure 1: ADC components – the location of the payload can vary based on the molecule.

This targeted approach offers a clear therapeutic advantage: it concentrates the chemotherapy at the tumour site while minimising systemic

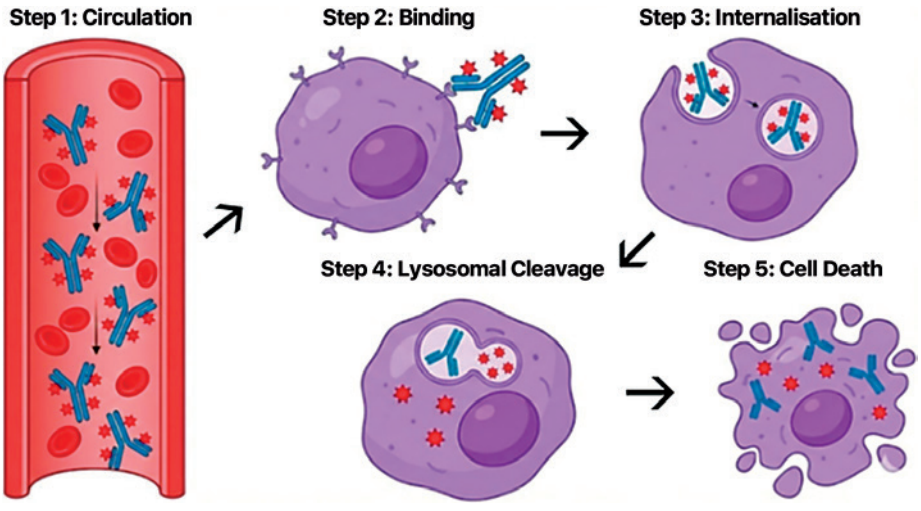

Figure 2: Simplified ADC process.

"THIS TARGETED APPROACH OFFERS A CLEAR THERAPEUTIC ADVANTAGE: IT CONCENTRATES THE CHEMOTHERAPY AT THE TUMOUR SITE WHILE MINIMISING SYSTEMIC EXPOSURE, WHICH CAN REDUCE THE SIDE EFFECTS TYPICALLY ASSOCIATED WITH CONVENTIONAL CHEMOTHERAPY APPROACHES."

exposure, which can reduce the side effects typically associated with conventional chemotherapy approaches. This concept has translated into meaningful clinical outcomes and the ADC market is rapidly growing as a result. Estimates suggest that the value of this drug class will grow from approximately US$15 billion (£11 billion) in 2025 to $20 billion in 2026. By 2031, it is projected to reach $71 billion, which reflects a compound annual growth rate of nearly 29% between 2026 and 2031.[2] More than 15 ADCs have received US FDA approval and over 400 are currently in clinical development globally to treat a wide range of autoimmune diseases and cancers.[3,4]

A critical parameter for understanding the delivery of ADCs is the drug-to-antibody ratio (DAR), which refers to the average number of cytotoxic payload molecules conjugated to each antibody. To help visualise what the DAR means with regards to the molecular structure, Figure 3 shows a simplified comparison of three different DAR levels. The DAR is one of the most important variables of an ADC, influencing its efficacy and formulation behaviour. Higher DAR values increase the amount of cytotoxic drug delivered per antibody molecule, which can enhance anti-tumour activity. However, a higher DAR also increases hydrophobicity, which can accelerate aggregation, reduce stability and complicate formulation development.[5]

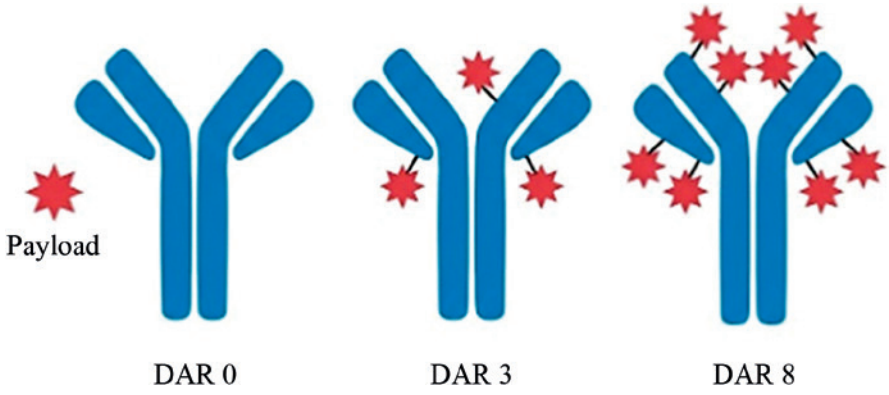

Figure 3: Visualisation of DAR levels.

The DAR also has specific implications for SC delivery. When an ADC is injected subcutaneously, it forms a depot in the tissue that is gradually absorbed into systemic circulation. During this dwell time, skin proteases, including cathepsin B, can cleave the linker and release the cytotoxic payload locally.[6] Essentially, this would be Step 4 in Figure 2 occurring prematurely within the SC layer. A DAR 8 ADC, such as trastuzumab deruxtecan or sacituzumab govitecan, carries four times more payload per molecule than a DAR 2 ADC, meaning the local exposure to free cytotoxic drug at the injection site is proportionally greater. This makes linker stability in the SC environment a key consideration for the ADC delivery strategy. Many approved ADC payloads are hydrophobic and prone to aggregation at higher concentrations, while newer payloads like DXd have been engineered for reduced hydrophobicity.

As shown in Table 1, a notable feature shared by all but one FDA-approved ADC is lyophilisation. This is not coincidental. ADC linkers, particularly

ADC	Target	DAR	Payload	Linker Type	Formulation	Route
Gemtuzumab ozogamicin	CD33	~2.5	Calicheamicin	Cleavable	Lyophilised	IV
Brentuximab vedotin	CD30	~4	MMAE	Cleavable	Lyophilised	IV
Ado-trastuzumab emtansine	HER2	~3.5	DM1	Non-cleavable	Lyophilised	IV
Inotuzumab ozogamicin	CD22	~6	Calicheamicin	Cleavable	Lyophilised	IV
Polatuzumab vedotin	CD79b	~3.5	MMAE	Cleavable	Lyophilised	IV
Enfortumab vedotin	Nectin-4	~3.8	MMAE	Cleavable	Lyophilised	IV
Trastuzumab deruxtecan	HER2	~7.8	DXd (topoisomerase I inhibitor)	Cleavable	Lyophilised	IV
Sacituzumab govitecan	Trop-2	~7.6	SN-38 (topoisomerase I inhibitor)	Cleavable	Lyophilised	IV
Loncastuximab tesirine	CD19	~2.3	SG3199 (PBD dimer)	Cleavable	Lyophilised	IV
Tisotumab vedotin	Tissue Factor	~4	MMAE	Cleavable	Lyophilised	IV
Mirvetuximab soravtansine	FRα	~3.5	DM4 (maytansinoid)	Cleavable	Liquid	IV
Datopotamab deruxtecan	Trop-2	~4	DXd (topoisomerase I inhibitor)	Cleavable	Lyophilised	IV
Telisotuzumab vedotin	c-Met	~3.1	MMAE	Cleavable	Lyophilised	IV

Table 1: Commercially available FDA-approved ADCs and key characteristics.[3,4,7,8] All FDA approved ADCs are administered intravenously and all but one are formulated as lyophilised powders for reconstitution.

peptide-based linkers, are highly sensitive to temperature and shear forces, making them susceptible to premature cleavage in liquid formulations. Lyophilisation removes water from the product, creating a more stable environment that minimises these degradation pathways.[9] While lyophilisation solves the stability problem, it introduces its own downstream challenges for drug delivery.

WHY ADCs ARE STRONG CANDIDATES FOR SC CONVERSION

The broader trend of converting intravenous (IV) biologics to SC formulations has been well established over the past decade. Monoclonal antibodies for oncology have successfully transitioned to SC delivery, driven by shorter administration times, reduced healthcare resource use and patient preference. ADCs, despite their additional complexity, share several characteristics that make them attractive candidates for SC conversion.

First, ADCs are increasingly being used in earlier lines of therapy. Trastuzumab deruxtecan has moved into frontline HER2-positive breast cancer, enfortumab vedotin is now approved in frontline urothelial carcinoma (in combination with pembrolizumab) and multiple ADCs are being studied in frontline settings across solid tumours. Earlier line use means longer treatment duration and a greater total number of infusions over the course of the therapy. Each IV infusion requires clinic chair time, nursing resources and patient and caregiver travel. The cumulative burden on both patients and healthcare systems is already substantial and continues to grow.

Second, the pharmacokinetic (PK) profile of SC delivery may offer advantages for ADCs. SC administration inherently produces a lower C_{max} and a more gradual absorption profile compared with IV delivery. Exposure-response analyses of trastuzumab deruxtecan across 639 patients demonstrated that different ADC toxicities are driven by different PK metrics – grade ≥3 interstitial lung disease was associated with peak intact ADC concentrations (C_{max}), while haematologic toxicities such as neutropenia and thrombocytopenia were driven by average free payload concentrations over time.[10] Whether the lower C_{max} profile associated with SC delivery could favourably influence specific ADC toxicities remains to be established clinically, but the pharmacological rationale warrants investigation.

Third, for a growing number of patients, the ADC may be the only IV therapy in their regimen. Several ADCs are used as monotherapies and combination partners are increasingly becoming available as SC formulations. With the recent approval of SC pembrolizumab, a combination such as enfortumab vedotin plus pembrolizumab could theoretically be delivered entirely without IV access if the ADC component were available as an SC formulation.[11] For these patients, converting the ADC to SC delivery could eliminate the need for infusion chair time altogether, potentially enabling administration outside of a traditional infusion suite.

> "EARLIER LINE USE MEANS LONGER TREATMENT DURATION AND A GREATER TOTAL NUMBER OF INFUSIONS OVER THE COURSE OF THE THERAPY."

CHALLENGES OF TRANSITIONING ADCs TO SC DELIVERY

Despite the compelling rationale, transitioning ADCs from IV to SC delivery presents formulation and delivery challenges that go beyond those encountered with conventional monoclonal antibodies. These challenges have contributed to a limited, and somewhat troubled, history of SC ADC development.

Linker stability in SC tissue

The SC space contains numerous protease enzymes, including cathepsin B, which is known to cleave the peptide-based linkers used in many ADCs.[12] When a linker is cleaved prematurely at the injection site, the cytotoxic payload is released locally rather than at the tumour. For certain ADCs, this has manifested as erythema and tissue necrosis at injection sites in preclinical models.[13,14] While newer linker technology may offer improved stability, comprehensive characterisation of linker behaviour in the SC compartment remains limited.

> "ALMOST ALL FDA-APPROVED ADCs ARE LYOPHILISED. THIS REQUIRES RECONSTITUTION WITH A DILUENT BEFORE ADMINISTRATION, ADDING PREPARATION STEPS, TIME AND THE POTENTIAL FOR HUMAN ERROR."

Lyophilised formulations

As noted earlier, almost all FDA-approved ADCs are lyophilised. This requires reconstitution with a diluent before administration, adding preparation steps, time and the potential for human error. Lyophilised products are difficult to deliver with traditional SC delivery devices, such as autoinjectors and prefilled syringes, due to the fact that these devices are primarily designed for ready-to-use liquid formulations. Reconstitution at the point of care is feasible in clinical settings but adds complexity for at-home infusion.

Volume requirements

ADC doses are often weight-based and, when reconstituted at current IV concentrations, can result in volumes ranging from approximately 5 mL to well over 20 mL depending on the specific ADC and patient weight. This far exceeds the capacity of conventional SC delivery devices such as autoinjectors and presents significant challenges for manual syringe delivery.[15,16] Concentrating ADC formulations to reduce volume is particularly difficult because the linked cytotoxic payloads are inherently hydrophobic, which drives aggregation and increased viscosity at higher concentrations far more readily than with normal antibodies. Developing a high-concentration liquid SC

formulation of a molecule that cannot be stored as a lower-concentration liquid for IV use represents a formidable, and in many cases impractical, development challenge.[17]

WHAT THE PRECLINICAL DATA SHOW AND DO NOT SHOW

In February 2026, preclinical data were presented demonstrating hyaluronidase co-formulation with two approved ADCs, both with DAR ~8, identified as ADC 1 and ADC 2. The data, generated in a Yucatan minipig model with three animals per SC group and a single IV control animal, showed reduced injection site ADC retention with hyaluronidase co-formulation versus SC alone (87% reduction for ADC 1, 51% for ADC 2 at 24 hours) and a lower serum C_{max} with SC versus IV administration (75% lower for ADC 1, 61% lower for ADC 2).[18]

Despite injection site tolerability being the central challenge for SC delivery of ADCs, no formal safety endpoints were included in the study design. No histopathology scoring, inflammation markers or macroscopic injection site observations were described. While these data represent an encouraging signal for the broader SC delivery opportunity of ADCs, several limitations warrant careful consideration.

The IV control group consisted of a single animal (N=1), limiting the reliability of any cross-route PK comparison, while the SC groups included only three animals each. The study was single-dose only and did not report bioavailability despite equivalent doses being administered across all groups. However, PK modelling projected that a higher SC dose would be needed to achieve equivalent systemic exposure to IV, implying that SC bioavailability was meaningfully lower. This higher dose was modelled but never tested, meaning the tolerability conclusion is based on a potentially sub-therapeutic dose level.

Most critically, the study did not measure linker stability within the SC tissue. For ADCs, linker integrity in the extracellular environment is a critical variable in determining suitability for SC delivery, as premature cleavage releases the cytotoxic payload into healthy tissue rather than within the target tumour cell. It was acknowledged that free payload measurements may have been overestimated due to linker instability during sample processing and analysis, further underscoring the limitations of the available data in addressing this fundamental question.

Importantly, the C_{max} reduction demonstrated in this study is a fundamental property of the SC route of administration itself, not unique to hyaluronidase co-formulation. The SC-alone groups (without hyaluronidase) also showed substantially lower C_{max} compared with IV, which is an expected and well-understood consequence of slower absorption from SC tissue. Any SC delivery method, whether administered via syringe, pump or on-body injector (OBI), would be expected to produce a similar reduction in C_{max} relative to IV. This inherent benefit of SC delivery should not be conflated with that of hyaluronidase.

What this data does demonstrate is that the hyaluronidase co-formulation has faster clearance of intact ADC from the injection site – supported by the tissue PK data – with meaningful reductions in local ADC retention at 24 hours compared with SC alone.

However, the metric of greatest clinical relevance for ADC safety is not how quickly the intact molecule clears but how much free cytotoxic payload is released locally. On this measure, the presented data show no meaningful differentiation between SC only and SC with hyaluronidase. Free payload concentrations in both the serum and skin tissue tracked closely between the two groups, with overlapping variability at all measured timepoints. If both SC delivery approaches produced comparable free payload profiles and if local tolerability was reported as acceptable in both groups, this raises a fundamental question: is hyaluronidase co-formulation necessary at all for SC delivery of ADCs?

This question has practical implications. OBIs, pumps and syringes can deliver the same large volumes subcutaneously without requiring reformulation of the drug product. For ADCs, which are universally formulated as lyophilised powders requiring reconstitution, avoiding the additional complexity of co-formulating with a permeation enhancer represents a meaningful reduction in time, cost and risk.

OBIs: A DEVICE-CENTRIC APPROACH

OBIs offer an alternative approach to large-volume SC delivery that does not require co-formulation with a permeation enhancer, although they are compatible with them. This preserves existing formulation integrity and avoids the complexity of adding a second biologic excipient. Crucially, the larger volume capacity of OBIs removes the pressure to formulate a high-concentration format, allowing the ADC to remain in a more stable, lower-viscosity solution.

Published data indicate that the tissue surface area exposed to an injected drug is primarily a function of injection volume rather than flow rate.[19] However, the lower, more consistent tissue pressures generated by elastomeric delivery, compared with tissue pressure characteristics associated with rapid bolus injection, may reduce local tissue disruption and the associated inflammatory response, which is relevant for ADCs given that inflammation can upregulate protease activity at the injection site.[20,21] While this hypothesis has not been directly tested with ADCs, the mechanistic rationale is consistent with the goal of preserving linker integrity during SC transit.

Clinical evidence supporting OBI technology for large-volume SC oncology delivery continues to build. In the Phase 3 IRAKLIA trial, which evaluated isatuximab delivered via an OBI versus IV in patients with relapsed/refractory multiple myeloma, infusion reactions occurred in only 1.5% of OBI injections, compared with a 25% infusion reaction incidence with IV administration – a near 17-fold reduction.[22] Notably, 99.9% of OBI injections were completed without interruption. Preference for the OBI over manual syringe push has been demonstrated for physicians, pharmacists, nurses and, most importantly, patients.[15,16,22–24]

ADDRESSING THE LYOPHILISATION CHALLENGE

As all approved ADCs are lyophilised, any SC delivery solution must address the reconstitution step. Published literature has identified the reconstitution step as the largest source of error among patients self-administering lyophilised drugs, with confusion around the number of steps

and supplies contributing to deviations and sterility breaches.[25] Integrating reconstitution into a device workflow would reduce this complexity.

Several approaches to automated or semi-automated reconstitution are emerging across the drug delivery landscape. Dual-chamber syringes and cartridges separate the lyophilised drug and diluent within a single container, allowing mixing at the point of use without manual transfer steps. However, these systems require the drug manufacturer to reformulate and repackage the product into a new primary container, which adds development time, regulatory complexity and cost.

An alternative approach uses a dual-vial design in which the original drug product vial and a separate diluent vial are both loaded into the delivery device simultaneously (Figure 4). The system reconstitutes and transfers the drug product, while preserving the original container closure system. For ADCs, where all approved products are manufactured and stored in vials, this approach avoids the need for new primary container development and maintains the validated stability profile of the existing formulation. This may be particularly relevant for enabling at-home administration of lyophilised, large-volume SC biologics, where simplifying the reconstitution process is essential for safe, reliable use outside of clinical settings.

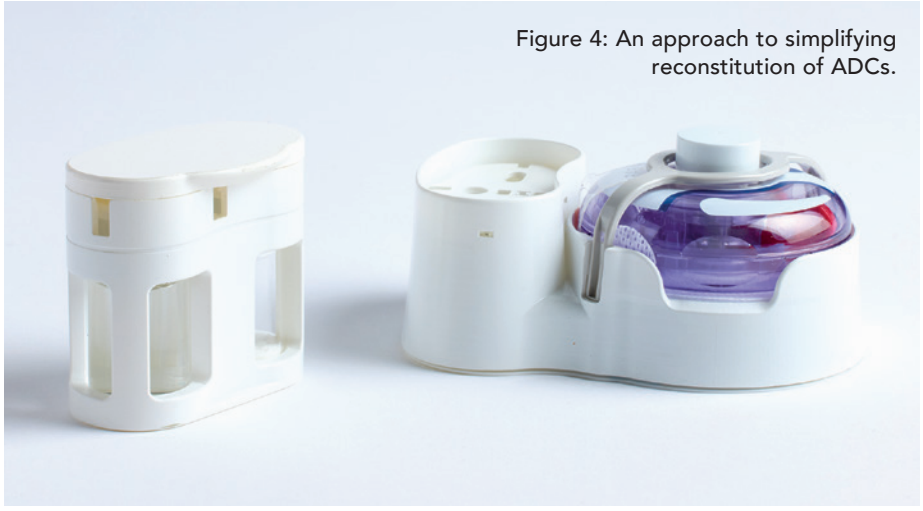

Figure 4: An approach to simplifying reconstitution of ADCs.

LOOKING AHEAD

The transition of ADCs from IV to SC delivery is not a question of if, but when and how. The market drivers are clear: a rapidly growing drug class, increasing use in earlier treatment lines, a strong patient and provider preference for SC administration and a global healthcare system under mounting capacity pressure. The formulation and delivery challenges are real but addressable with current large-volume SC technologies, each offering distinct paths forwards.

For ADCs in particular, the choice of SC delivery strategy deserves careful evaluation beyond simple PK matching. The unique features of ADCs, specifically the presence of cytotoxic payloads connected by protease-sensitive linkers, the reliance on lyophilised formulations and the potential for local tissue toxicity, introduce considerations that are absent from conventional monoclonal antibody IV-to-SC conversions. A device-centric approach that preserves the existing formulation, uses the original container closure system, delivers at a low pressure and accommodates lyophilised products would be particularly well suited to this drug class.

As the ADC pipeline continues to expand, drug manufacturers will increasingly need to evaluate SC delivery options early in their development programmes. The ability to convert directly from an IV vial-based formulation to SC delivery, with minimal reformulation, container closure changes or co-formulation with exogenous enzymes, represents a significant practical advantage that could accelerate time to market and reduce development risk.[26,27]

> "THE TRANSITION OF ADCs FROM IV TO SC DELIVERY IS NOT A QUESTION OF IF, BUT WHEN AND HOW. THE MARKET DRIVERS ARE CLEAR: A RAPIDLY GROWING DRUG CLASS, INCREASING USE IN EARLIER TREATMENT LINES, A STRONG PATIENT AND PROVIDER PREFERENCE FOR SC ADMINISTRATION AND A GLOBAL HEALTHCARE SYSTEM UNDER MOUNTING CAPACITY PRESSURE."

ABOUT THE COMPANIES

Enable Injections is a global healthcare innovation company developing and manufacturing drug delivery systems designed to improve patient experience. Enable's body-worn enFuse® on-body injector delivers large-volume pharmaceutical and biologic therapeutics via SC administration, with the aim of improving convenience, supporting superior outcomes and advancing healthcare system economics.

The Biopharmaceutical Innovation & Optimization Center provides drug delivery, solubilisation and stabilisation services to researchers with the aim of translating innovative research into new medical treatments and technologies. It works with researchers at the University of Kansas and experts around the world to transform new discoveries into products for patients.

WuXi Biologics provides R&D and manufacturing services including chemistry drug contract research, development and manufacturing organisation services; biology discovery; preclinical testing and clinical research services; and cell and gene therapy contract testing, development and manufacturing.

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Early Insight

BEYOND THE BARREL: PREFILLED SYRINGES THAT FOLD IN HALF

Pacto Medical

Ian Speers, **Robert Halvorsen** and **Ryan Stinebaugh** of **Pacto Medical**

discuss the unmet needs in prefilled deployability that led to the development of Slimshot™, a detached plunger rod that nests alongside the syringe, and Slimshot™ Doser, a companion concept designed to reduce the mental load of variable dosing in high-pressure delivery situations, and how these concepts can contribute to improved workflows and logistics throughout the healthcare sector.

Prefilled syringes (PFSs) have earned their place in the healthcare sector by decreasing preparation steps, improving the speed and sterility of drug delivery, reducing overfill requirements and supporting more consistent delivery of injectable medicines.[1–4] However, as injectable products move into a wider range of care environments, it is no longer enough just to ask whether a product can be delivered safely and accurately – it must also be asked whether a product can be stored, transported, staged and used efficiently and effectively wherever it is needed.

This question becomes especially important in channels where space, cold-chain storage capacity, time and training are constrained. In those settings, packaging volume, kit density, secondary packaging burden and workflow complexity are not ancillary considerations – they directly affect whether enough doses can be stocked, carried and used at the point of need. This is the context in which Slimshot™ and Slimshot™ Doser were developed, not as novelty devices, but as attempts to address real operational constraints that conventional PFS formats often leave unresolved.

DEPLOYABILITY IS BECOMING A DESIGN INPUT

Across healthcare, the "performance" of an injectable product is increasingly shaped by more than just the drug and primary container alone. A therapy can be clinically effective and still be difficult to deploy if it

is bulky to store, inefficient to transport, awkward to stage or overly dependent on ideal user conditions and training.

This can be seen most clearly in emergency response, prehospital care, tactical medicine, disaster preparedness and resource-constrained delivery settings, but the same logic applies in well-resourced hospitals and healthcare systems as well. Pharmacy shelves, automated dispensing cabinets, code carts, bedside storage and distribution networks all operate within the constraints of finite space and finite labour. Even in such settings, bulk creates cost, clutter and inefficiency over time.

This is why deployability should be treated as a key design requirement. In practical terms, that means designing a product's presentation not only for manufacturability and regulatory viability but also for packaging density, cold-chain storage efficiency, last-mile transport, kit organisation and fast, reliable use by real clinicians in real environments.

THE PROBLEM BECAME CLEAR IN THE FIELD

Slimshot™ grew out of first-hand experience managing medical logistics and delivering clinical care in low-resource environments around the world. In managing humanitarian and medical supply chains in disaster, emergency, austere and resource-constrained settings, one problem became impossible to ignore: life-saving medicines are only useful if they are affordable and can actually be moved, stored and distributed to where they are needed.

In many of those constrained settings, the issue was not a lack of clinical demand for PFSs. The issue was that traditional PFS formats were often too bulky relative to the number of doses that teams needed to carry and deliver. When every pouch, drawer, kit and cooler matters, even modest reductions in form factor can change what gets stocked and how much of it can travel to the last mile.

Those same constraints show up in other locations and workflows too. Nurses care about having what they need readily accessible in carts, automated dispensing cabinets and bedside storage. Helicopter and ground emergency teams care about kit density. Pharmacy and warehouse staff care about the cumulative burden of secondary packaging, restocking frequency and shelf space. In each case, the format of the PFS becomes part of the proposed value.

WHEN USERS CREATE WORKAROUNDS, THE DESIGN REQUIREMENT REVEALS ITSELF

One of the clearest signals that a product format is mismatched to its environment is when users start creating workarounds. In emergency and field settings, clinicians have historically detached plunger rods to save space, pre-drawn medications into syringes before each deployment or relied on alternative drug delivery presentations simply because existing options do not meet their needs (Figure 1).

Such workarounds solve one problem while creating others. They can add handling steps, increase training burden, introduce more variability and create additional opportunities for error. They also reveal something important: compactness is not cosmetic. It is a functional requirement that users have already been trying to solve for themselves. Therefore, there is an opportunity for product developers to solve that problem deliberately, without giving up the core advantages that made PFSs attractive in the first place.

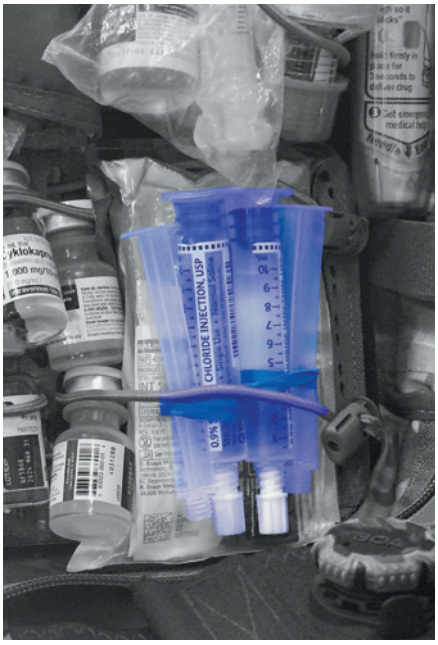

Figure 1: Space constraints lead to dangerous do-it-yourself solutions – many medics remove and/or repackage plunger rods.

SLIMSHOT™ – A PLUNGER ROD NESTED NEXT TO THE BARREL

Slimshot™ is designed to reduce syringe bulk without requiring a wholesale change to familiar PFS workflows. The core concept is a compact plunger rod that nests alongside the syringe barrel during storage and transport and is then attached at the point of use (Figure 2). It is designed to work with standard off-the-shelf barrel, plunger and tip components, in sizes ranging from 0.5 to 60 mL, using all types of barrel materials and in alignment with familiar manufacturing and handling patterns, all while materially reducing stored volume.

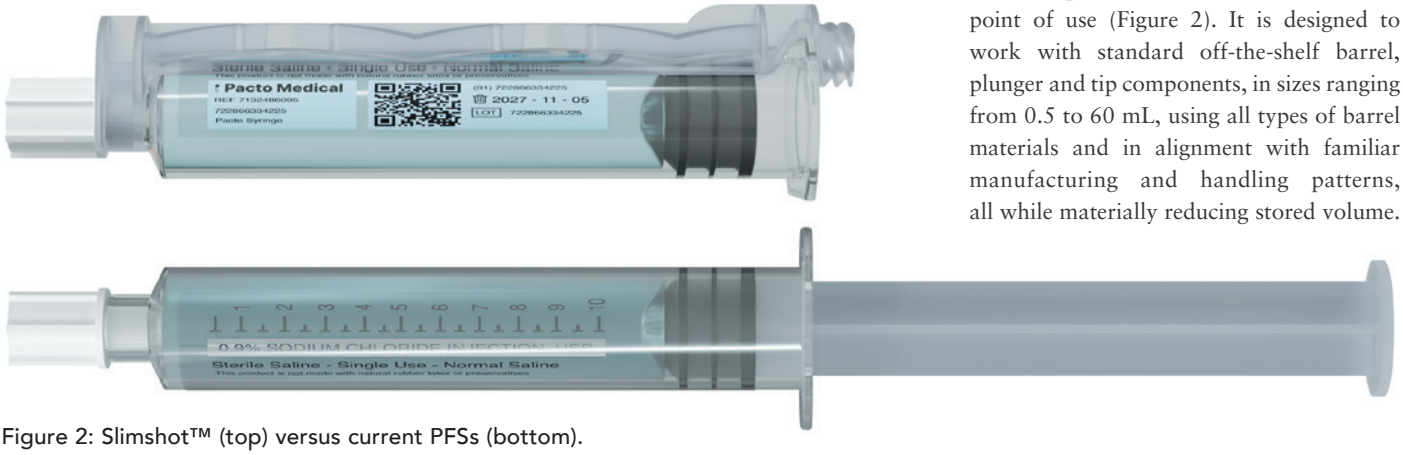

Figure 2: Slimshot™ (top) versus current PFSs (bottom).

The goal of Slimshot™ is not simply to make a syringe look different – it is to improve the economics and practicality of PFSs across the whole value chain, from manufacturing and packaging to transport, storage and use. Slimshot's design can reduce the packaging footprint by up to roughly 40% compared with a standard PFS. In operational terms, that means:

- Approximately 7,000 more 10 mL PFSs per 48" x 40" x 48" pallet
- Approximately 35% reduction in supply chain costs
  - Includes reduced costs associated with terminal sterilisation, packaging, storage, transport and restocking
- Lower storage burden for warehouses and care environments
- More efficient use of cold chain storage
- Denser packing in kits, bags and emergency caches
- Less packaging material associated with each delivered dose
  - For a 10 mL PFS, plastic flow wrap per syringe could be reduced by 0.1 g and cardboard used per syringe could be reduced by 0.5 g
- Reduced carbon footprint and emissions per syringe delivered, due to more efficient sterilisation, packaging, transport and storage.

Those are the kinds of gains that matter to pharmaceutical partners, CDMOs and end users alike; gains that compound across the system rather than staying confined to the device itself.

CLINICAL RECEPTION MATTERS AS MUCH AS COMPACTNESS

Compactness only has value if users can assemble and use the product confidently (Figure 3). Therefore, close attention was paid to early clinician feedback during Slimshot's development. When tested with 50 nurses from around the world, 100% were able to successfully assemble Slimshot™ in an average of 4 seconds.

When surveyed about how easy it was to assemble Slimshot™, 80% of those nurses answered "Very easy", 18% answered "Easy" and the remaining 2% answered "Neutral". When surveyed about how confident they were that they could use Slimshot™ correctly in their day-to-day job, 92% answered "Very confident", 6% answered "Somewhat confident" and the remaining 2% answered "Neutral". When tested with a total of 111 nursing professionals, 92% did not need any type of instructions on how to assemble Slimshot™.

PRECISION DOSING IS A DEPLOYABILITY PROBLEM TOO

Compactness is only one part of the real-world challenge. In many care environments, especially paediatric emergency care, the harder problem is not simply getting a medicine to the bedside or point of injury but getting the right amount into the patient quickly and confidently. Weight-based variable dosing is one of the clearest examples. In high-stress and high-consequence scenarios, clinicians often rely on rapid reference tools such as the Broselow tape to convert patient size into a target dose, to then translate that target into a delivered volume under time pressure.

That process can be cognitively demanding even for experienced clinicians, and the consequences of error are amplified in paediatrics, where small volume differences matter more. This can be viewed as another deployability challenge – a product is not fully ready for demanding environments if it still relies on mental maths, fine visual estimation or perfect technique at the moment of dosing.

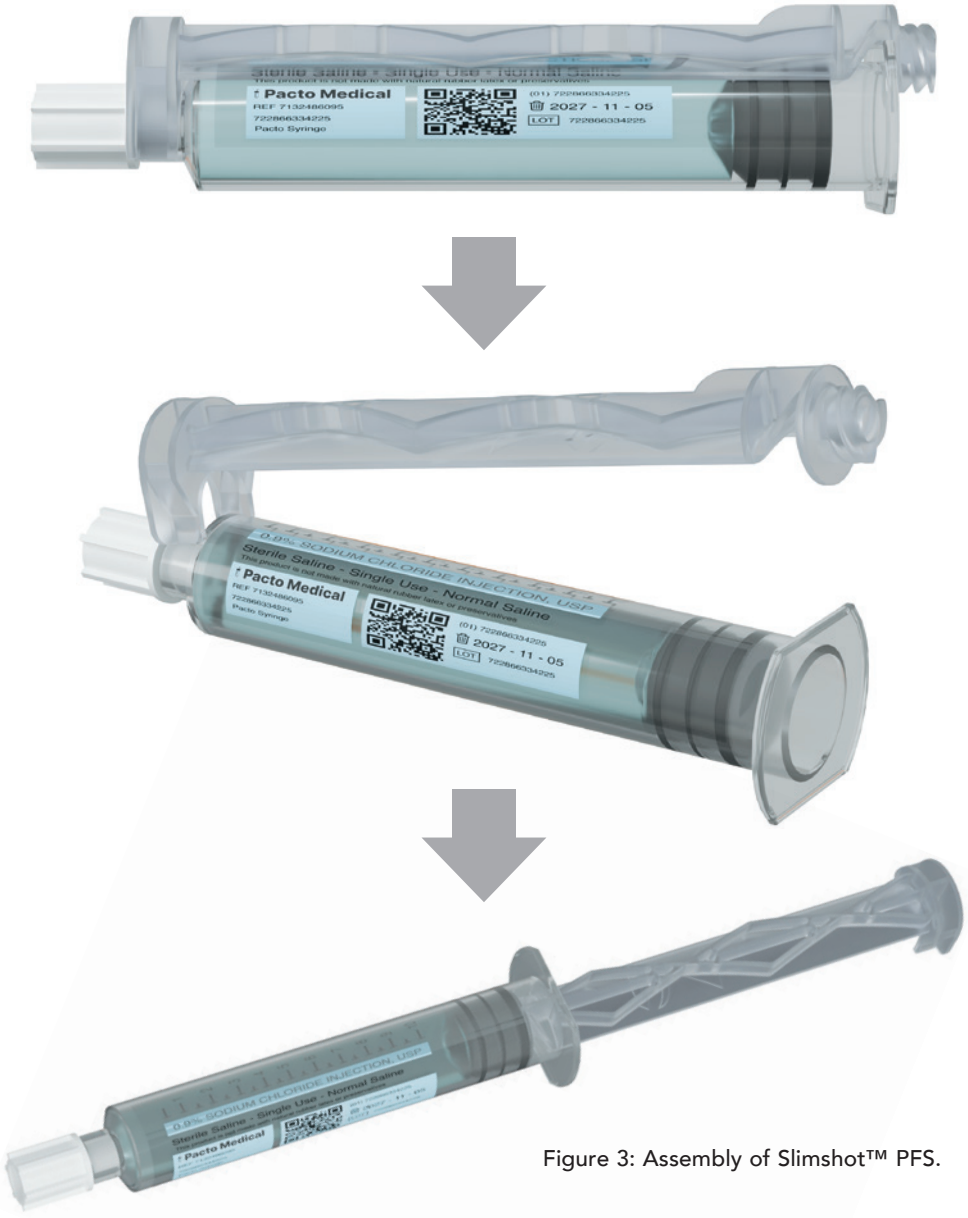

Figure 3: Assembly of Slimshot™ PFS.

For example, in one study, during 118 simulated emergency paediatric resuscitations using conventional syringes, 26% (31 doses) of simulated medication administrations were dosed incorrectly. 65% of those incorrect doses were defined as critical dosing errors (doses administered at less than 90% of the minimum correct dose or greater than 110% of the maximum correct dose).[5] In another study, 14 (70%) out of 20 drug doses prepared with conventional methods during a simulated paediatric cardiopulmonary resuscitation were incorrect.[6]

Slimshot™ Doser is a direct response to these problems (Figure 4). The concept uses a plunger rod with defined notches and an adjustable clip that can be set by the user to a specific position prior to administration. Each notch corresponds to a predetermined dose volume or patient-specific dosing variable, allowing the user to align the clip to the intended target and then dispense that amount of medication with a physical stop built into the device via the secured clip. In effect, the plunger rod becomes both the actuation mechanism and the dosing guide. This can be achieved on either a traditional or compact Slimshot™ plunger rod. The aim is to reduce cognitive load, reduce dependence on barrel-mark readings alone and support more repeatable variable or partial-dose delivery in urgent settings where precise dosing matters most (Figure 5).

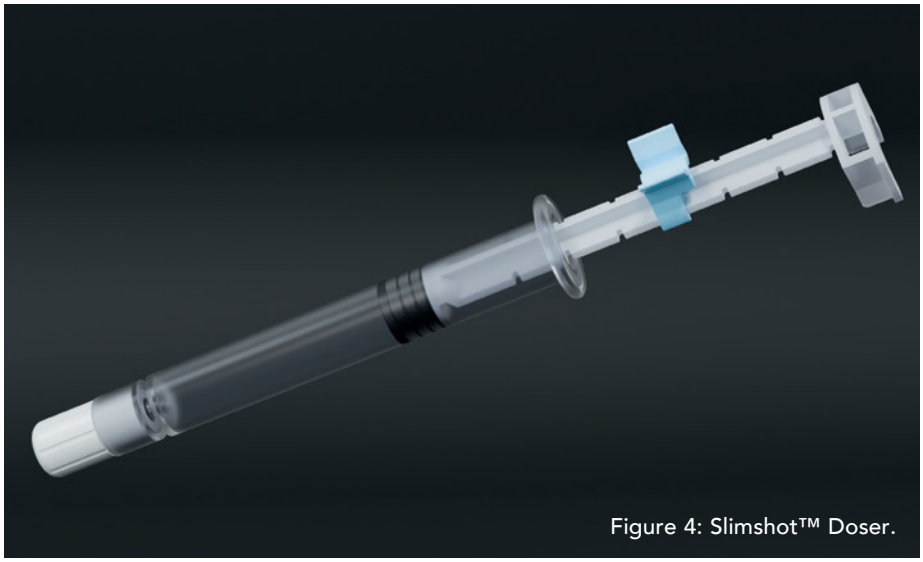

Figure 4: Slimshot™ Doser.

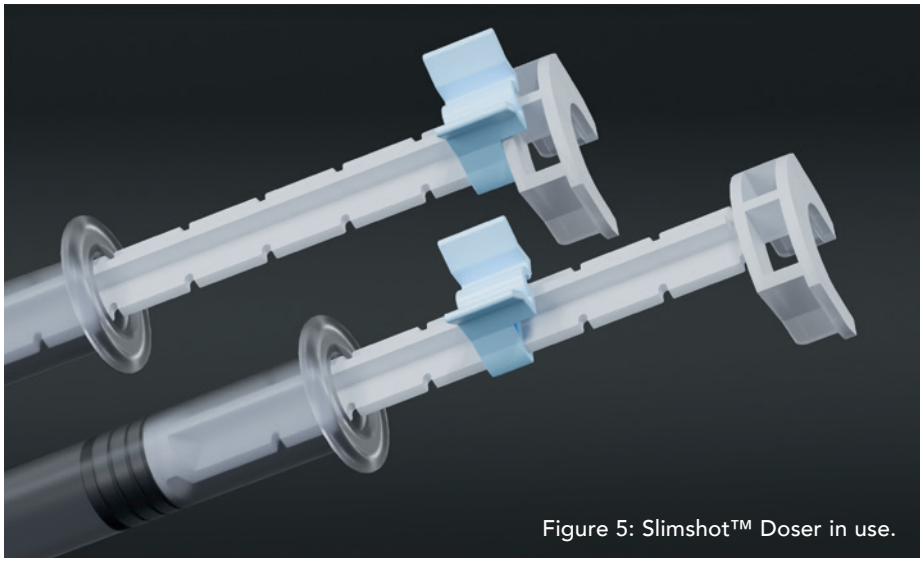

Figure 5: Slimshot™ Doser in use.

MANUFACTURING READINESS HAS TO BE BUILT IN EARLY

For any new syringe architecture to matter commercially, it needs a credible path to scale. This fact has shaped the development of Slimshot™ from the outset. Slimshot™ has been designed as a single-piece plunger rod intended to fit within high-volume injection moulding and practical automated assembly pathways. Partner discussions have focused on Design for Manufacture and Assembly work, scalable materials such as polypropylene and assembly concepts that occur after fill-finish to preserve sterility and minimise disruption to existing processes.

This approach matters because the industry does not need elegant prototypes that break at the factory gate. It needs formats that can be tooled, inspected, assembled and packaged in a commercially viable way. Compact syringe innovation only becomes meaningful when it works simultaneously for the end user, the manufacturing line and the supply chain.

GO-TO-MARKET: START WHERE BULK HURTS MOST

Pacto Medical's go-to-market strategy for Slimshot™ is to begin where the burden of bulk is already visible and commercially meaningful. As such, the initial focus is on medications used in prehospital care, followed by cold chain products, such as vaccines, biologics and other injectable categories where logistical efficiency creates clear value.

Prehospital and emergency care drugs are of strong interest because readiness, portability and speed of use are central

"THE INITIAL FOCUS IS ON MEDICATIONS USED IN PREHOSPITAL CARE, FOLLOWED BY COLD CHAIN PRODUCTS, SUCH AS VACCINES, BIOLOGICS AND OTHER INJECTABLE CATEGORIES WHERE LOGISTICAL EFFICIENCY CREATES CLEAR VALUE."

to the value proposition. Once a compact presentation proves itself in those channels, the broader platform opportunity becomes easier to evaluate. From there, the larger prospect is not confined to one product line – it extends to any injectable presentation where the delivered cost, stocking footprint or deployment model makes conventional bulk an avoidable inefficiency.

PARTNERING OPPORTUNITIES

Pacto Medical believes that compact PFSs will advance fastest with collaboration across the value chain. For pharmaceutical companies, that may start with identifying products whose commercial performance is constrained by packaging density, cold chain storage space or bedside usability. For CDMOs, the focus may be automated assembly, packaging configuration, inspection strategy or manufacturability at scale. For syringe and component partners, it may be compatibility across barrel families, plungers and material systems. In practical terms, the most useful collaborations are likely to include:

- Candidate-product fit assessments
- Design for Manufacture and Assembly development
- Packaging and pallet-density studies
- Channel-specific usability testing.

CONCLUSION

The next important advances in injectable drug delivery will come about by treating deployability as a core part of product design. For many products, especially those used in emergency, stockpiled or logistics-sensitive channels, the key question is no longer only whether a PFS works, but whether it works efficiently enough across the full journey from factory to point of care.

Slimshot™ and Slimshot™ Doser are Pacto Medical's efforts to answer that challenge in two connected ways – by reducing the physical burden of PFS delivery and by supporting more reliable administration workflows where precision matters. The company's broader view is simple: if the industry wants injectable products to reach more settings, serve more users and move more efficiently through the system, then the architecture of the syringe itself has to become part of the conversation.

The technologies discussed in this article are under development and have not been reviewed or approved by the FDA or other regulatory authorities. The inventions disclosed are covered under a variety of patents, including US 12,440,623 B2 and other pending patents in various jurisdictions.

ABOUT THE COMPANY

Pacto Medical is a medical device company developing compact drug delivery device concepts intended for prefilled injectable products. The company's inventions include Slimshot™, a syringe platform concept

"FOR MANY PRODUCTS, ESPECIALLY THOSE USED IN EMERGENCY, STOCKPILED OR LOGISTICS-SENSITIVE CHANNELS, THE KEY QUESTION IS NO LONGER ONLY WHETHER A PFS WORKS, BUT WHETHER IT WORKS EFFICIENTLY ENOUGH ACROSS THE FULL JOURNEY FROM FACTORY TO POINT OF CARE."

with a compact, side-mounted plunger rod designed to reduce the packaging volume of PFSs, and Slimshot™ Doser, a complementary device concept focused on supporting precision dosing and reducing cognitive load when dealing with variable-dose medications. Pacto Medical works with pharmaceutical companies, PFS manufacturers, CDMOs and other partners to evaluate integration of these device concepts into drug-device combination products. Pacto Medical's emphasis is on reducing supply chain costs, increasing equitable access to PFS technology, reducing logistical constraints and reducing waste and carbon footprint in drug delivery.

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AUTOINJECTOR TECHNOLOGY FOR AUTOMATIC MICROPARTICLE SUSPENSION AND INJECTION

Kindeva

Girum Yemane-Tekeste and **Stephen Leslie** share how **Kindeva** is building on its experience and history of innovation to develop an enabling technology for injectable microparticles and then evaluating it through proof-of-principle testing.

As a global leader and CDMO for combination products, Kindeva® has an over 50-year track record of successfully designing, developing and manufacturing devices that solve complex drug delivery challenges. For autoinjectors, Kindeva has designed, developed and manufactured devices for unique applications including but not limited to dual-chamber (reconstitution and sequential co-injection), intramuscular injection, emergency-use and military devices.

A new frontier in drug delivery is on the horizon as advancements in medical technology shift treatment towards more shelf-stable, long-acting and at-home patient care. Microparticle and autoinjector technologies are at the forefront of these advancements, as the application of each seeks to further the development of patient treatment in areas such as pancreatic cancer, meningitis and diabetes.[1]

"A NEW FRONTIER IN DRUG DELIVERY IS ON THE HORIZON AS ADVANCEMENTS IN MEDICAL TECHNOLOGY SHIFT TREATMENT TOWARDS MORE SHELF-STABLE, LONG-ACTING AND AT-HOME PATIENT CARE."

Proteins, peptides and small molecules prepared as microparticles often have a longer shelf-life and reduced cold chain requirements. In addition, preparations involving polymers, such as polylactic acid and polylactic co-glycolic acid in capsule, matrix or sponge forms, can function as long-acting therapies through the slow release of embedded hydrophilic or hydrophobic drugs.[2] This slow release is tuneable and has the potential to revolutionise care for chronic diseases by reducing the frequency of treatments.[3]

For administration by injection, microparticles are commonly suspended in a liquid prior to delivery by lengthy periods of manual shaking or agitation to ensure proper dispersion of the drug and uniform dosage delivery. Autoinjectors are in demand as they allow targeted delivery, efficient dose accuracy and at-home treatment.[4] With the appropriate modifications, autoinjectors can be used for automated microparticle suspension and delivery to drastically simplify the use steps, minimise use errors and enable self-administration at home. Kindeva is currently developing a technology that can automatically suspend microparticles in a liquid medium and deliver the microparticles into an injection site.

Kindeva's new patent-pending technology uses acceleration physics and controlled cavitation. Cavitation is a method used in various applications, including pharmaceutical manufacturing processes, for mixing liquids with other liquids and solids with liquids.[5] Kindeva's technology enables both subcutaneous and intramuscular microparticle injections and works without accelerating the primary container, thereby reducing the risk of glass breakage. It can be deployed in a single- or dual-chamber primary container configuration if isolation of the microparticles and suspension liquid is required for drug stability.

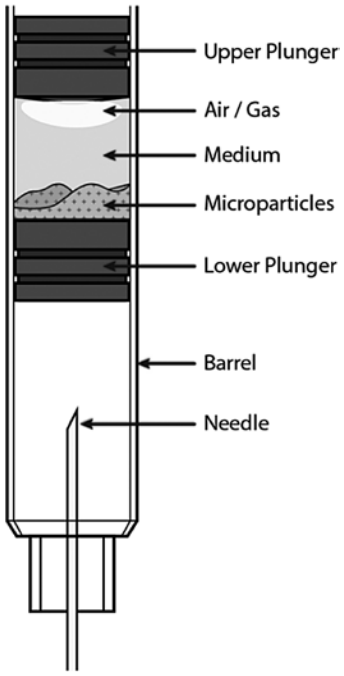

Figure 1: Schematic of the single-cartridge/single-chamber primary container configuration.

CONCEPT OVERVIEW

To illustrate the concept and operating principle for the autoinjector technology, the single-cartridge/single-chamber configuration can be used. The system consists of an upper plunger, air/gas, injection liquid medium, microparticles, lower plunger, barrel and needle in a sterile drug delivery system or autoinjector (Figure 1).

Principles of Operation

The approach and key process steps are as follows (Figure 2):

1. Acceleration force is applied at the upper plunger.
2. Liquid accelerates in the barrel, causing the liquid static pressure to become lower than the vapour pressure. Cavitation is created, causing the air/gas to expand towards the lower plunger in the liquid, displacing, mixing and suspending the microparticles.
3. The lower plunger is stopped, causing the liquid static pressure to exceed the vapour pressure, displacing the air/gas out of the liquid and towards the upper plunger, collapsing the cavitation. This causes additional microparticle displacement, mixing and suspension, and the air/gas is eventually displaced into the upper plunger's cavity. The lower plunger is punctured by the needle.

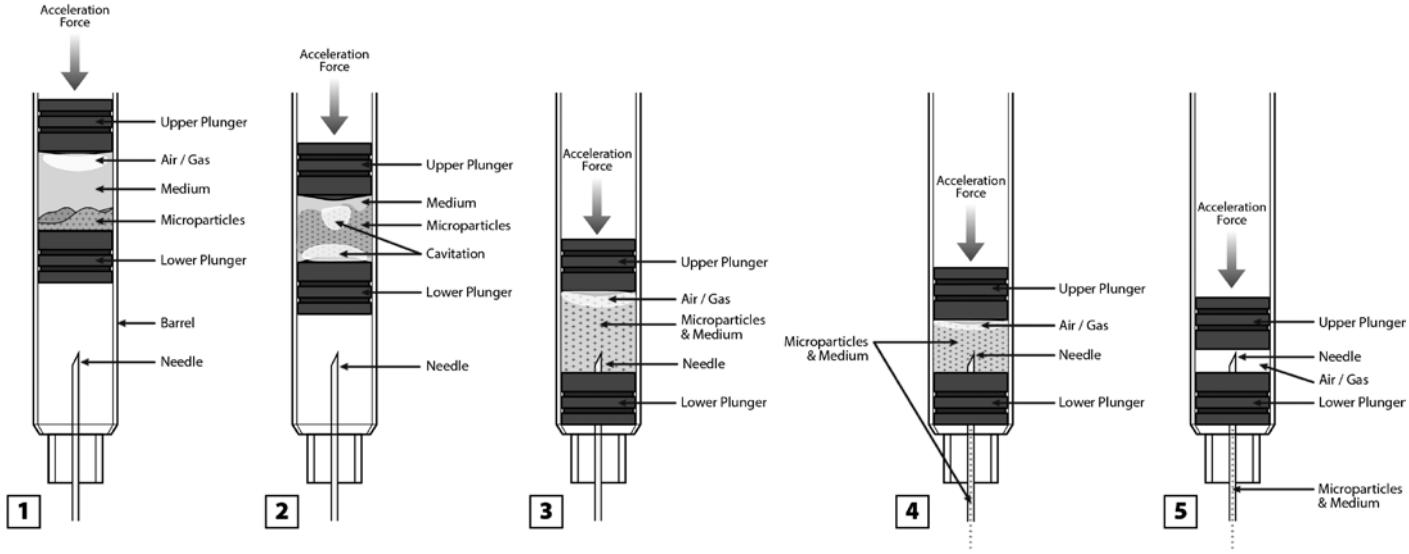

Figure 2: Principles of operation for the acceleration/cavitation-induced microparticles suspension and injection technology (shown for single-cartridge/single-chamber configuration).

4. The upper plunger continues to move, displacing the liquid and the suspended microparticles into the needle.
5. The upper plunger displaces the liquid until the injection is completed. The upper plunger is stopped, and the air/gas remains in the system within the upper and lower plunger cavities.

PROOF-OF-PRINCIPLE STUDY AND RESULTS

Microparticle Suspension and Injection

Efficient suspension occurs through the optimisation of parameters including acceleration, air/gas volume, liquid volume and viscosity, and microparticle mass and size. A high-speed camera was used to record the microparticle suspension and injection (Figure 3). The injected microparticles were collected, and the mass of the microparticles was measured to determine the delivered dose. By using both aqueous and non-aqueous liquid mediums, up to 95% of the microparticles were delivered, with further optimisation possible.

Cavitation Formation

To illustrate the principles of operation shown in Figure 2, a study was conducted to show the creation of controlled cavitation in a liquid medium for optimum suspension and mixing of the microparticles in the system. The high-speed camera images show the formation and the collapsing of cavities (Figure 4).

In addition, the scale and power of cavitation can be controlled by acceleration rate and force, air/gas volume, and liquid

"IN ADDITION TO THE SINGLE-CHAMBER DESIGN KINDEVA HAS ALSO DEVELOPED DUAL-CHAMBER AND DUAL-CARTRIDGE CONCEPTS AND PERFORMED PROOF-OF-PRINCIPLE TESTING."

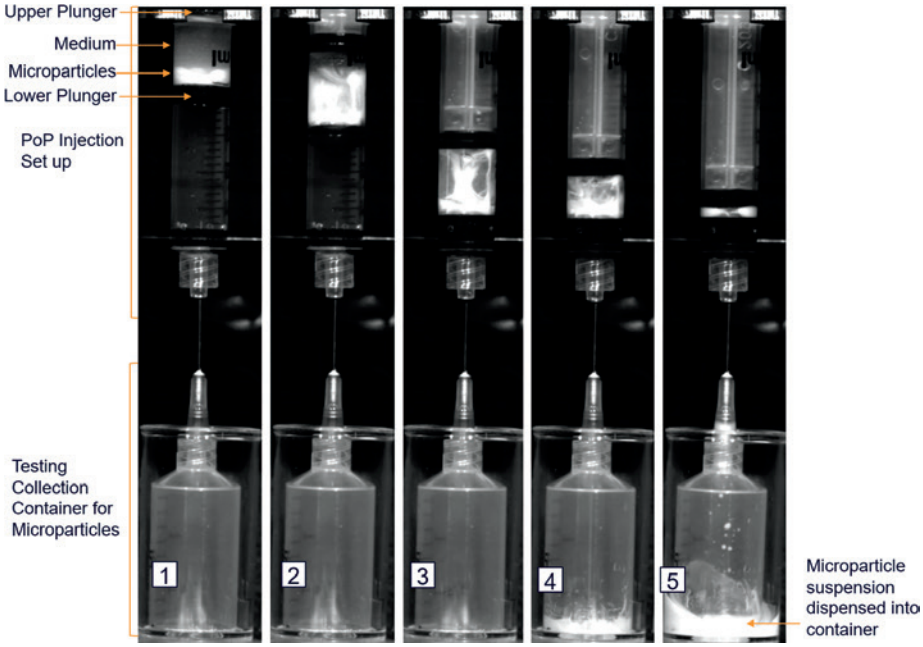

Figure 3: High-speed images during suspension and injection process in proof-of-principle testing. Panels 1–5 correspond to principles of operation steps.

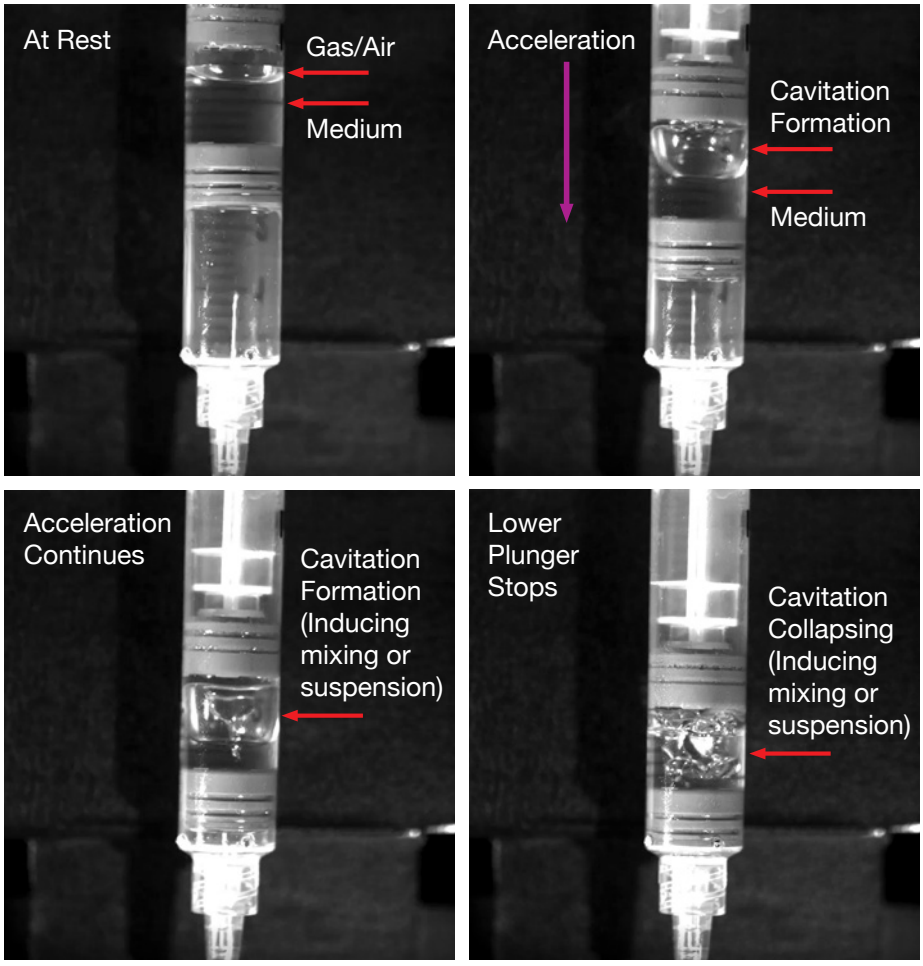

Figure 4: Cavitation formation and collapse in liquid medium using Kindeva's autoinjector technology.

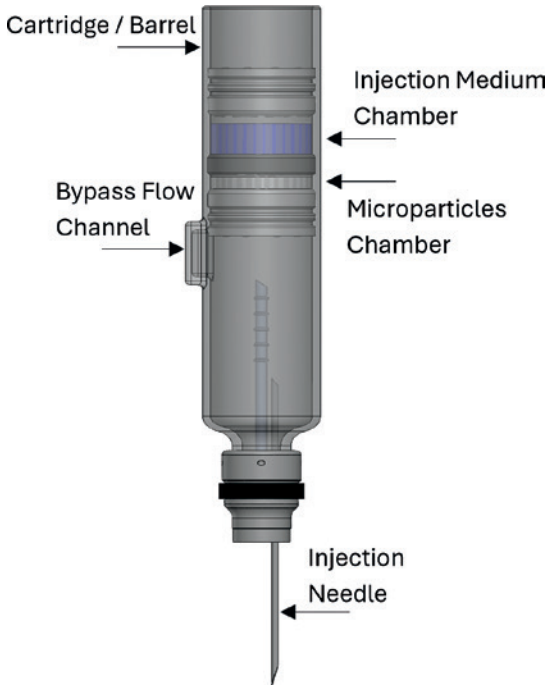

Figure 5: Kindeva's single-cartridge dual-chamber system.

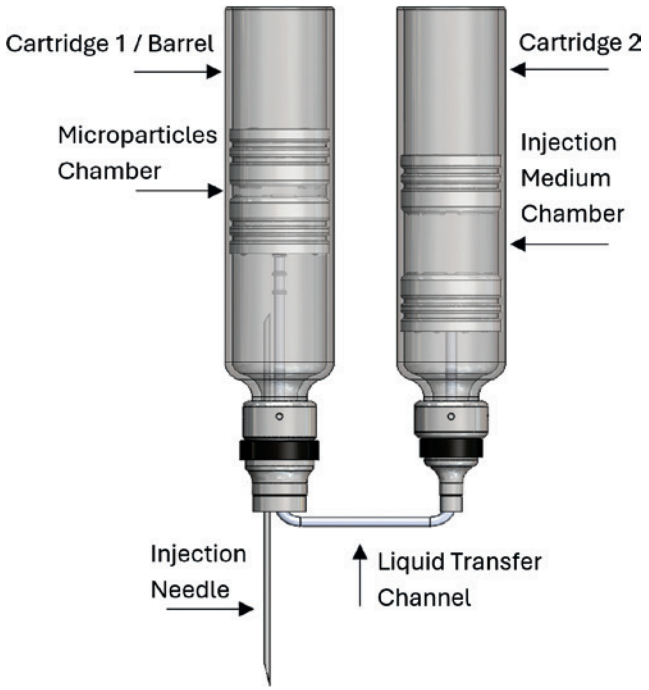

Figure 6: Kindeva's dual-cartridge dual-chamber system.

volume and viscosity. These control features can be optimised and configured based on the drug's sensitivity. Importantly, the container is not accelerated, instead remaining stationary, which helps to mitigate mechanical stress on the primary container.

DUAL-CHAMBER AND DUAL-CARTRIDGE TECHNOLOGY FOR DRUG STABILISATION

In addition to the single-chamber design Kindeva has also developed dual-chamber and dual-cartridge concepts and performed proof-of-principle testing. Dual-chamber/dual-cartridge technology enables a lyophilised drug product to be stored separately from its liquid medium prior to drug administration by suspension or reconstitution. Upon autoinjector activation, the liquid is transferred to the microparticle chamber prior to acceleration for microparticle suspension and injection.

Kindeva's first concept is a single-cartridge system with two separate chambers (i.e. one chamber to store the microparticles and the other to store the liquid medium) (Figure 5). The second concept has two cartridges, where one cartridge stores the microparticles and the other stores the liquid medium (Figures 6 & 7). The principle of operation for driving acceleration and cavitation is the same; however, there are additional design features required to ensure that cavitation is consistently induced for dual-chamber/dual-cartridge configurations.

Figure 7: Kindeva's dual-cartridge autoinjector system for storing microparticles separately from medium before automatic suspension and injection.

CONCLUSION

This proof-of-principle evaluation of Kindeva's autoinjector technology demonstrates that acceleration and controlled cavitation can be used in autoinjectors to automatically suspend and inject microparticles in seconds. This enables the use of microparticles for drug delivery, improving drug stability and patient compliance. With further parameter tuning, Kindeva's autoinjector technology can be extended to the delivery of nanoparticles and other drug formats that require suspension prior to administration.

With more than six decades in the industry, Kindeva's experience in combination product development and manufacturing enables the company to support its partners with an extensive history of innovation and technical know-how that ensures the delivery of high-quality products every time. Backed by a proactive team of industry experts, Kindeva develops solutions that chart new territory while staying firmly grounded in science.

Kindeva has experienced engineers and leaders in its Combination Product Development Center of Excellence, as well as the necessary equipment and infrastructure to complete device development for entire combination product programmes. It also offers à la carte services for smaller projects. Kindeva has a track record for designing and manufacturing autoinjectors performing reconstitution, sequential co-injection, intramuscular injection and emergency-use administration. In addition, Kindeva develops and manufactures other combination products including pulmonary, nasal, dermal and other injectables products, including microneedles.

**The Kindeva cavitation-induced automatic microparticles suspension and injection technology is in development. As such, the technology is subject to various risks and uncertainties.*

Kindeva® is a registered trademark of Kindeva Drug Delivery, L.P. in the United States.

ACKNOWLEDGEMENTS

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Expert View

STERILE DRUG PRODUCTION: AN EVER-EVOLVING MARKET

Dr Norbert Kübler discusses the current state of sterile drug products, considering how advancing technology is changing the field, the role of quality control and the challenges faced during scale-up and manufacturing.

"CHANGING TRENDS IN THE FORMAT OF STERILE PRODUCTS HAVE FOCUSED ON INCREASING THEIR EASE OF USE, PARTICULARLY FOR DRUGS TARGETING CHRONIC DISEASES AND THOSE THAT ARE DESIGNED FOR SELF-ADMINISTRATION BY THE PATIENT AWAY FROM A CLINICAL ENVIRONMENT."

The pharmaceutical industry is always evolving and advancing, with next-generation drugs and a growing range of new modalities to target diseases in the pipeline. Nowadays, patient centricity is a key factor at the heart of drug product design, so the challenge for innovators is to formulate and design dosage forms and delivery methods that are safe, easy to use and improve the overall patient experience and compliance.

In recent years, changing trends in the format of sterile products have focused on increasing their ease of use, particularly for drugs targeting chronic diseases and those that are designed for self-administration by the patient away from a clinical environment. One of the greatest barriers for patients using such medicines is a psychological one, so it is important that they are delivered by simple systems suitable for self-administration.

Currently, there are two principal types of self-injection device in common use. Firstly, there is the single-use injection system, usually containing a prefilled syringe. With these, the patient simply presses the device against their skin and pushes a button to deliver the dose. For safety, these devices should include a way to protect the needle and prevent injury to the patient from the needle after injection.

The second type of self-injection device uses a cartridge that contains multiple doses, usually within a glass or plastic barrel within the autoinjector device. These are very common for patients who are taking insulin or glucagon-like peptide-1 (GLP-1) drugs for diabetes or weight loss. This design allows for flexibility in the number and size of doses that can be administered, and connectivity between the autoinjector and a mobile device can be included to facilitate patient reminders when a dose is due, including which dose size is necessary. Not only does this optimise the delivery of the medicine, it can also be combined with glucose monitoring for insulin, for example. This data can then be monitored by physicians to check not only patient compliance with the drug regimen but also whether the drug is controlling their blood sugar effectively.

"THE MORE WIDESPREAD THE USE OF ADVANCED TECHNOLOGIES, THE CHEAPER THEY WILL BECOME, WHICH WILL MAKE THE BENEFITS MORE ACCESSIBLE TO A GREATER NUMBER OF PATIENTS IN THE LONG TERM."

The natural consequence of increased innovation and connectivity within any device is a greater cost, which will be tolerable in some markets but prohibitive in others. However, the more widespread the use of advanced technologies, the cheaper they will become, which will make the benefits more accessible to a greater number of patients in the long term.

For innovators looking to develop new sterile products, the choice of device is crucial. Incorporating novel technologies into a delivery device, especially for a custom application, increases the cost significantly, but also offers brand differentiation. A standard, off-the-shelf platform device will always come at a reduced cost but, for a novel product, such a device would present less of a barrier to entry for future generic or biosimilar competition.

Historically, the sterile product market has been dominated by glass primary packaging, typically ampoules or bottles. However, traditional glass packaging is now

"SINCE COMING INTO EFFECT IN 2022, ANNEX 1 TO EU GMP GUIDELINES HAS TRANSCENDED ITS EUROPEAN ORIGINS TO BECOME A GLOBAL BENCHMARK FOR STERILE MANUFACTURING."

being increasingly complemented by plastic alternatives. There are potential benefits and disadvantages to this – from a safety perspective, the reduction in the use of glass lowers the risk of breakage, whereas plastic can have unwanted interactions with drug formulations, meaning that specific studies into the potential of extractables and leachables are required.

REGULATORY OVERSIGHT

Since coming into effect in 2022, Annex 1 to EU GMP guidelines has transcended its European origins to become a global benchmark for sterile manufacturing. The regulation introduced stringent new requirements that apply universally across all sterile product forms, from vials and prefilled syringes to cartridges and filled bags. This has elevated the standard of compliance for the entire industry worldwide.

The updated guidelines champion a proactive, risk-based approach to prevent contamination from all sources, including those which are microbial, particulate, pyrogenic and chemical. Central to this is the mandate for a holistic contamination control strategy (CCS). The CCS necessitates the implementation of advanced barrier technologies, such as isolators and restricted access barrier systems, to create a robust physical separation between the product and its environment, thereby minimising human intervention in the manufacturing process.

"LIKE CHANGING PRIMARY PACKAGING FROM GLASS TO PLASTIC, EMPLOYING SINGLE-USE EQUIPMENT RELIES ON A DEEP UNDERSTANDING OF ANY POTENTIAL INTERACTIONS BETWEEN THE MATERIAL AND DRUG PRODUCT."

While the intense focus on CCS significantly expands the role of the quality control department, Annex 1 moves beyond departmental silos by demanding a cross-functional approach to compliance. This requires seamless collaboration between quality control, quality assurance, production and engineering teams. Consequently, operating within a qualified cleanroom is no longer sufficient; a sophisticated, process-centric understanding of technical complexities, such as airflow dynamics and barrier system integrity, is now the fundamental requirement.

MANUFACTURING TRENDS

The sterile filling sector is seeing an increased use of single-use systems within manufacturing, transitioning away from traditional stainless-steel equipment. This reduces process complexity for cleaning and cross-contamination controls, saving time and reducing the risk to product quality. However, like changing primary packaging from glass to plastic, employing single-use equipment relies on a deep understanding of any potential interactions between the material and drug product. Additionally, using single-use equipment significantly increases the amount of waste generated.

Another change in manufacturing is the general shift from bulk components – such as stoppers and vials – that require sterilisation before use to being supplied pre-sterilised. Although there is an increased cost for pre-sterilised components, the use of such items can be justified for smaller runs through lower set-up times, whereas, for very large quantities, in-house sterilisation of items remains more cost-effective.

Process controls and monitoring are now routinely carried out in-line, with advances in digital technology and connectivity having enabled them to be integrated into manufacturing lines. Capturing data and incorporating it into electronic batch records with full protection and integrity allows for seamless generation of verification reports and supporting documentation. That data can also be monitored over time to provide greater insight into process performance and rapidly highlight any variabilities that may occur.

The advancement of new modalities brings about more challenges for the analytical process used to ensure both the efficacy and purity of drugs. The rise in the number of biological drugs being developed and manufactured has highlighted the growing need for advanced analytical techniques. Quality control departments have had to invest in and embrace these advances so that product development is not delayed and patient safety is not compromised.

One of the greatest problems associated with sterile drug manufacturing is the scale-up process, in part due to the impact that it has on so many product parameters. For example, when handling larger batch volumes of temperature-sensitive drugs, the increased processing time can be problematic. Using jacketed vessels can reduce the risk of product degradation in such a situation, allowing products to be held at lower temperatures for prolonged periods of time.

Similarly, increased volumes can impact filling lines. Early stages of development may see a batch being completed in a relatively short time, but commercial batches may see that time multiply manyfold. This introduces further challenges for ensuring that product quality remains consistent throughout.

Looking towards other modalities, there are many specific challenges in manufacturing sterile products. For example, the new generation of autologous cell therapies typically uses much smaller volumes of material, so it is essential to minimise losses in handling and processing, which makes traditional batch approaches inappropriate. Traditional batch sterility testing takes 15 days. However, this is not possible for these products, due to the fact that they must be released for use within 24–48 hours of manufacture.

As such, solutions that can test for sterility and allow for real-time product release, in compliance with current guidelines, are required.

For CDMOs manufacturing drug products, it is vital that the evolving trends within the market are understood, allowing investment to be made ahead of time in technologies and systems that can meet the ever-changing needs of customers, regulators and patients. Speed is crucial within manufacturing; however, this can never be to the detriment of product quality or patient safety. Whether dealing with new devices or technologies that can enable faster, more efficient and accurate production, manufacturers must be in a position to implement changes rapidly and effectively to serve their customers and deliver the next generation of potentially life-changing drugs to patients.

Dr Norbert Kübler

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ABOUT THE COMPANY

Adragos Pharma is a global CDMO headquartered in Munich, Germany, serving clients across Europe, Japan and North America. With a customer-centric approach, the company provides end-to-end development and manufacturing services for small- and large-molecule drug products, including biologics, orphan drugs and clinical trial support. Adragos operates seven facilities worldwide, employs over 1,800 people and brings over 300 years of combined experience to delivering high-quality pharmaceutical solutions.

DEORA™: FILLING THE GAP FOR MULTI-USE, FIXED-DOSE INJECTION SOLUTIONS

Manuela Giacon of **Stevanato Group** explores the evolution of handheld drug delivery devices, leading up to today's challenges, and presents the company's latest addition to its drug delivery portfolio.

THE EVOLUTION OF PARENTERAL SELF-INJECTION

As with many technologies that we now take for granted, injection devices were designed in exceptional circumstances to solve a specific problem before evolving into the widely used solution that we recognise today. It was the need to rapidly self-administer antidotes on the battlefield that led to the development of the first injection kits, starting with "syrettes" during World War II[1] and evolving into autoinjectors in the late 1950s.[2]

Designed for reliable use in unpredictable, high-pressure, conditions, these initial devices were primitive and prone to error but offered a blueprint for the development of self-contained and pre-measured injection instruments. Subsequently, as plastic technologies advanced, sterile and single-use syringes emerged in parallel.

The 1980s heralded the shift from self-injection as a technical task to a practical daily routine, with devices redesigned for real patients rather than trained operators. Device designers now needed to consider "human factors", such as grip strength, dosing clarity and the management of patient anxiety. Between 2005 and 2015, these considerations shaped innovation and industry standards. Concepts such as "intuitive user interface", "concealed needle" and "end-of-dose feedback" became the norm.

Even as designers refined usability, new challenges emerged in the form of biologic

"THE NEXT GENERATION OF DRUG DELIVERY SYSTEMS MUST THEREFORE PRIORITISE SCALABILITY, USABILITY AND SUSTAINABILITY."

drugs requiring subcutaneous injection. These transformational drugs accelerated pen and autoinjector adoption, but their higher complexity formulations demanded further design modifications. As device complexity grew in parallel, industry collaboration naturally followed, with pharmaceutical companies partnering with technology vendors to co-develop drug-device combination products.

RISING VOLUMES, RISING PRESSURES

Despite the significant growth in biologics, annual device quantities remained relatively modest, typically in the hundreds of thousands, up until the late 2010s, with only a few exceptions. This was set to change, as custom, drug-specific devices made way for flexible platform injectors. In recent years, rapidly rising global demand, led by glucagon-like peptide-1 (GLP-1) treatments, has accelerated manufacturing output into the hundreds of millions of units. This further highlights the importance of external manufacturing partnerships and risk mitigation strategies, such as dual sourcing, to ensure continuity and reduce dependency on single suppliers.

Today, growing demand continues to intensify pressure on global logistical and supply chain networks, exacerbated by geopolitical events and policy interventions such as tariffs. The level of demand requires manufacturers to hold substantial inventory, tying up working capital and limiting financial flexibility, while also investing in appropriate manufacturing facilities. To remain competitive, manufacturers must make this investment with minimal delay, while also generating proportional returns. Additionally, environmental objectives now underpin these challenges as the industry seeks to minimise the impact associated with device production.

The next generation of drug delivery systems must therefore prioritise scalability, usability and sustainability. Environmental factors – such as material use, waste generation and emissions – are closely tied to supply chain resilience. A sustainable supply chain minimises impact on people and the planet by optimising the use of resources, considering component availability, inventory requirements, sourcing redundancy and production footprint.

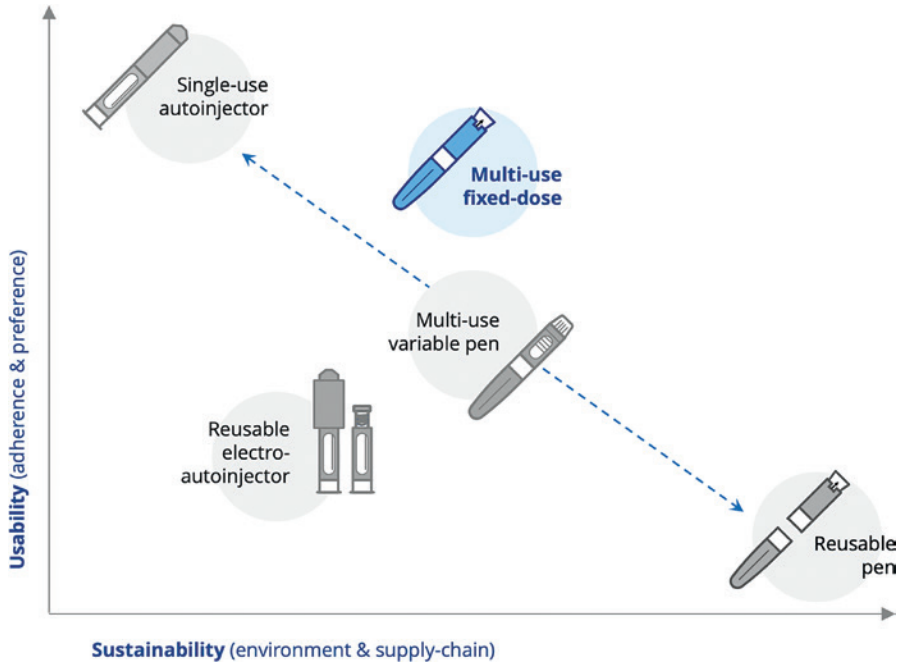

Figure 1: As sustainability increases, usability tends to decrease. Multi-use, fixed-dose pens strike a balance between user needs and sustainability.

THE SUSTAINABILITY-USABILITY CONUNDRUM

A recurring design concern is the inverse relationship between usability – considering both adherence and preference – and sustainability – from both an environmental and supply-chain perspective. Efforts to reduce environmental impact often introduce additional complexity for the user (Figure 1).

Within this context, single-use autoinjectors remain a valuable option as they minimise user steps and support therapy areas with specific injection schedules that may not be compatible with a multi-use device.[3] However, the environmental impact of single-use devices becomes significant at very high volumes. For instance, based on an average weight of approximately 25 g per single-use autoinjector, weekly use over one year corresponds to almost 1.5 kg of waste per patient.[3] At a population level, this results in a significant cumulative waste burden. From a supply chain perspective, scaling production of single-use products to the required capacity is a major undertaking, increasing the risk of shortages if manufacturing cannot keep pace. The need to continuously source multiple components for each dose adds to this vulnerability.

Reusable devices, however, can offer environmental benefits in certain scenarios. One estimate suggests that between a single-use autoinjector and a reusable alternative, the volume and mass of the packaged devices could both be reduced by 50%.[4] By reducing component needs and extending device lifespan, reusable products also lower supply chain stress. However, these gains come with trade-offs, as they may introduce additional engineering hurdles and increase user handling requirements.

Multi-use pen injectors – such as those used for insulin administration – reduce waste while maintaining ease of use. However, while variable-dose pen injectors offer valuable flexibility for many therapies, fixed-dose regimens – such as

certain GLP-1 agonists or monoclonal antibody regimens – sometimes call for device designs specifically tailored to consistent dosing. Legacy fixed-dose pen platforms may not be a suitable solution, as they were never designed for the larger dose volumes increasingly required by modern formulations.

In summary, there is a clear market gap – a need for multi-use systems delivering larger-volume, fixed-dose injections that optimally balance sustainability with usability. This was the rationale for Stevanato Group's Deora™ pen injector.

INTRODUCING DEORA

Deora is the newest pen injector in Stevanato Group's portfolio of hand-held drug delivery systems, designed for the delivery of multiple fixed-dose injections of up to 0.75 mL. Unlike variable-dose devices, the user does not need to manually measure each dose. Instead, Deora operates with a simple, two-step, pull push mechanism for dose selection and delivery. The user pulls to set the dose then pushes to inject, receiving tactile and audible confirmation after each step (Figure 2).

The device is engineered to deliver a single predefined dose size, preventing partial or split dosing, whether through use error or intentional user adjustments. This enables accurate delivery of up to seven doses using a single device, rather than multiple single-use injectors. It then automatically locks once the final dose is administered. By combining the multi-use benefits of a pen injector with simplified usability, Deora strikes a balance between variable-dose pens and single-use autoinjectors.

Figure 2: The Deora fixed-dose pen injector operates with a simple, two-step, pull-push mechanism for dose selection and delivery.

Deora functions as a platform product, supporting multiple configurations. Compatible with both 3 and 1.5 mL cartridges, the device's delivered dose volume can be customised so that it changes during a treatment period. For example, monthly dose modifications can be accommodated without affecting the patient experience. The device is engineered for reliable production in large quantities, with a low component count to simplify both production and assembly.

A COHESIVE DRUG DELIVERY ECOSYSTEM

Taking the advantages offered by each device category into account, Stevanato Group's portfolio is intentionally built to span multi-use fixed or variable doses and single-use injection requirements for pharmaceutical partners. The result is a set of optimised and complementary platform products that pharmaceutical partners can more easily and flexibly match to their individual drug programmes. Together, these platforms support a wide spectrum of formulations, patient needs and commercial strategies.

Deora joins a robust handheld device portfolio, alongside Alina®, a variable dose pen injector platform, and Aidaptus®, a two-step single-use autoinjector platform (Figure 3). Alina supports established

"TAKING INTO ACCOUNT THE ADVANTAGES OFFERED BY EACH DEVICE CATEGORY, STEVANATO GROUP'S PORTFOLIO IS INTENTIONALLY BUILT TO SPAN MULTI-USE FIXED OR VARIABLE DOSES AND SINGLE-USE INJECTION REQUIREMENTS FOR PHARMACEUTICAL PARTNERS."

Figure 3: Stevanato Group's handheld drug delivery platforms offer complementary solutions across multi use variable dose, multi-use fixed-dose and single-use injection formats.

regimens as well as emerging treatments that involve multidose delivery, including those for chronic conditions such as diabetes or weight management. To support confident self-injection, Alina features an easy-to-dial mechanism and a clear display.

Aidaptus, developed by Owen Mumford (Oxfordshire, UK) and manufactured in collaboration with Stevanato Group, is a two-step autoinjector ideal for biologics and higher-viscosity formulations. It accommodates both 1 and 2.25 mL prefilled glass syringes in the same base device, with a plunger rod that automatically adjusts to the drug fill volume during assembly.

AGILE AND SCALABLE MANUFACTURING

Stevanato Group's handheld injection platforms – including Alina, Aidaptus and the new Deora pen – are designed and developed with manufacturing efficiency and scalability in mind. This shared design approach ensures compatibility with standard final assembly processes used for handheld drug delivery devices, creating opportunities to use common final assembly assets across the three platforms, despite differences in device architecture and functionality. This can help to minimise equipment footprint on the factory floor and enable continuous operational improvements, ultimately enhancing efficiency and supporting faster production.

A further advantage is that the required final assembly equipment can be sourced directly from Stevanato Group, enabling pharmaceutical partners to streamline technology transfer and simplify operational planning. By combining device platforms, final assembly capabilities, glass primary packaging and analytical services within a single framework, Stevanato Group offers an integrated solution that can help accelerate industrialisation and reduce supply chain complexity.

Today's pharmaceutical companies are operating under unprecedented pressure, being required to advance sustainability, deliver innovation, address patient needs, manage regulatory complexity and maintain resilient supply chains. In this context, Deora – a fixed-dose multi-use injection device – can help address these challenges. Its ability to support multiple therapies, reduce waste and streamline production workflows position it as an optimal response to current challenges in drug delivery.

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Manuela Giacon

Manuela Giacon, Product Manager for Pen Injectors at Stevanato Group, brings over a decade of expertise in the parenteral primary packaging and medtech sectors. She conducts thorough analyses of new markets, growth areas, current trends, various customer segments, potential partnerships and services. Through close collaboration with development teams, Ms Giacon guarantees finely tuned bespoke solutions to meet customer demands within the ever-evolving market environment. Ms Giacon holds a degree in economics and, prior to her current role, she was part of the Strategic Marketing and Communication department.

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DELIVERING ON GLP-1 DEMAND
ROBUST DEVICE PORTFOLIO AND SCALABLE SUPPLY STRATEGY

At Stevanato Group, we combine a robust product portfolio with global manufacturing reach to support pharmaceutical partners with an end-to-end approach at scale.

For multi-dose pen injector applications, the **Alina®** platform delivers market-ready solutions for variable dosing, while the **Deora™** platform enhances usability for fixed-dose treatments. In the single-use autoinjector segment, **Aidaptus®**, offered in collaboration with Owen Mumford Pharmaceutical Services, provides a flexible platform designed to simplify market entry.

Stevanato Group

MANAGING COMPLEXITY, DELIVERING VALUE

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IMPORTANCE OF BEING PATIENT-CENTRIC IN CARDIOVASCULAR-KIDNEY-METABOLIC CARE

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Cécile Gross and **Mark Tunkel** of **Nemera** discuss the company's substantial portfolio of user-friendly, effective injectable devices available to meet the needs of patients with diverse chronic conditions.

Until recently, chronic conditions such as obesity, Type 2 diabetes mellitus, atherosclerotic cardiovascular disease, heart failure, chronic kidney disease and metabolic dysfunction-associated steatotic liver disease have been managed through separate treatments. Recent evidence reveals that these conditions share overlapping pathophysiological mechanisms and, therefore, treatment strategies. Today, they are recognised as interconnected disorders.

In November 2023, the American Heart Association was the first to define cardiovascular-kidney-metabolic (CKM) syndrome as a "health disorder attributable to connections among obesity, diabetes, chronic kidney disease and cardiovascular disease (CVD), including heart failure, atrial fibrillation, coronary heart disease, stroke and peripheral artery disease. CKM syndrome includes those at risk for CVD and those with existing CVD".[1] As a result, the framework has expanded and can be called the Cardiovascular-Renal-Hepatic-Metabolic (CRHM) syndrome.[2]

In parallel, new medications have demonstrated benefits across multiple similar conditions, improving both quality of life and clinical outcomes. Over the past five years, clinical trials have shown promising results for these therapies, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs), dual glucose-dependent insulinotropic polypeptide/GLP-1 RAs, sodium-glucose cotransporter 2 inhibitors and finerenone. More clinical

"THE COMPANY'S SOLUTIONS ADDRESS SOME OF THE MAIN CHALLENGES WITH GLP-1 RA PRODUCTS: DESIGNING DEVICES THAT LIMIT UNDERDOSING RISK AND INCREASING PATIENT ADHERENCE THROUGH A POSITIVE USER EXPERIENCE."

trials are underway to further expand the indications of novel agents and to provide additional insight where current evidence is lacking.

These significant advances in therapeutic approaches aim to expand treatment options and improve outcomes across the intertwined conditions that define the aforementioned syndromes. They also have the potential to transform the future of CKM/CRHM treatment moving towards patient-centred interdisciplinary care.

GLP-1 RAs have become frontrunners in treating CKM/CRHM because they improve insulin resistance and glycemia, as well as reducing weight and CVD mortality. As obesity is a major driver of CKM syndrome, prevention and management of this condition is a clinical and public health priority. The WHO recognised the importance of this priority in its guideline on the use of GLP-1 medicines in treating obesity.[3]

Beyond public health, public spending is also at stake. In the US, the total cost of chronic diseases due to obesity and being overweight has been assessed by the Milken Institute at 9.3% of GDP. Obesity is by far the greatest contributor to chronic disease burden, accounting for 47.1% of the total cost of chronic diseases nationwide.[4]

Drawing on over two decades of expertise in high-volume manufacturing of injectable devices, and by incorporating well-established pen injector platforms, Nemera now provides a broad portfolio of proprietary products. Developed in-house to meet the needs of diverse patient populations and global markets, these solutions enable users to benefit from:

- **Easy and Comfortable Use:** Low activation force, smooth injection, ergonomic design and intuitive handling improve patient comfort.
- **Accurate and Safe Dosing:** Precise dose delivery and easy adjustments reduce dosing errors and incorrect dosage selection.
- **Clear Feedback:** Visual indicators confirm injection status and full dose delivery, increasing confidence.
- **Improved Adherence and Access:** Simplicity, reduced training needs and lower cost per injection support better treatment adherence and wider access.
- **Versatility and Reliability:** Compatible with a wide range of drugs and based on proven, patient-accepted technology.

As a GLP-1 RA device manufacturer and combination product service provider, Nemera has an opportunity to become a key player in CKM/CRHM care. The company's solutions address some of the main challenges with GLP-1 RA products: designing devices that limit underdosing risk and increasing patient adherence through a positive user experience.

SECURING CLINICAL OUTCOMES

A pharma company must integrate many factors into its delivery device selection to create a patient-centric and clinically effective drug delivery experience. Obese patients are defined by their BMI, but other comorbidities, patient education, engagement with treatment, therapy preferences, lifestyle, previous interactions with medical devices, geographical factors and costs should also be taken into consideration when selecting a drug delivery device.

Some of the most important factors in securing a positive clinical outcome are limiting the risk of underdosing and increasing patient adherence. Nemera has designed several pen injector platforms with unique features to achieve this.

Limiting Underdosing Risks

Underdosing is one of the largest risks to ensuring positive clinical outcomes, which is why it is specifically addressed with the newest platforms in Nemera's pen injector portfolio: PenDIA and PenSET (Figures 1 & 2).

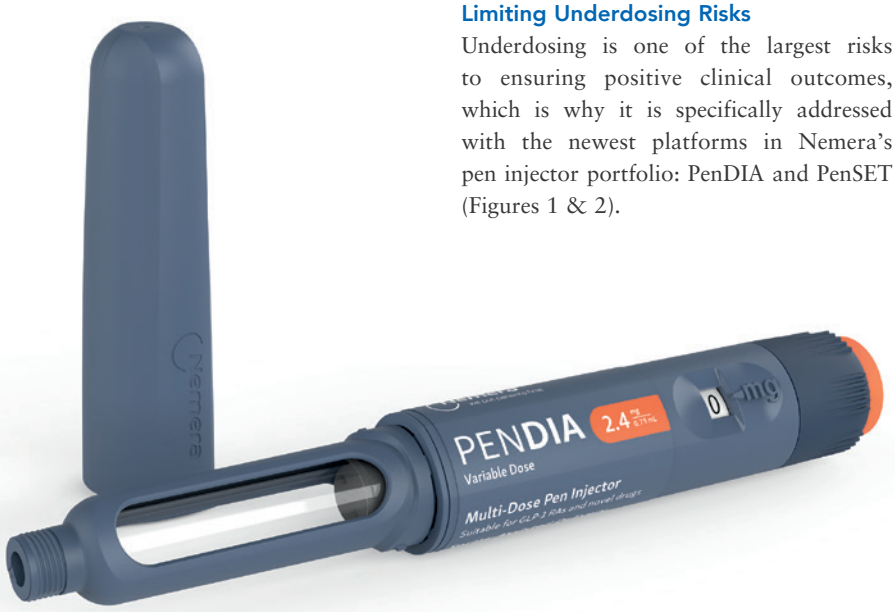

Figure 1: PenDIA pen injector platform with the ability to limit underdosing risk.

Figure 2: PenSET pen injector platform with full fixed-dose possibilities.

PenDIA is a spring-assisted, variable multidose pen injector platform, which is the basis for PenDIA Step, a variant that allows pharma companies to pre-select the dose increments that patients must use to administer a dose. This prevents potential underdosing by requiring patients to dial the pharma companies' pre-selected doses before administering. In order to use PenDIA Step, patients must dial their appropriate dose and cannot inject unless the previously defined dose increment is selected on the pen dial. There is no possibility to dial "in-between" dose increments. The pen can also be fully reset or dialled back if a user makes an error or dials before they are ready to administer.

PenSET is a spring-assisted, fixed-dose pen injector platform, that combines the advantages of a pre-set dose as in autoinjectors alongside multidose capabilities as in conventional pen injectors. Again, patients can only dial the dose the pharma company has pre-set.

Offering a Positive User Experience and Increasing Patient Adherence

Adherence challenges are common among patients with obesity and poor adherence rates must be improved to secure clinical outcomes.[5] When selecting a delivery device, pharma companies focus on its ease of use to foster the greatest patient acceptance.

The aforementioned PenDIA and PenSET platforms are designed with a spring-assisted injection, which provides patients with a constant dosing rate and reduced injection force, elevating the user experience. They also clearly indicate the injection status to reassure patients that they have fully administered their treatment.

The PenDURA platform is a reusable, spring-assisted, variable multidose pen injector platform. On top of spring-assisted delivery, it has an ergonomic design that offers more comfortable drug delivery, reinforced by a clear visual feedback system that allows patients to inject confidently (Figure 3). The sliding injection button acts as a safety feature to stabilise the pen onto the skin before, during and after the injection.

Figure 3: Clear indication of injection status to enhance patient adherence with PenDIA, PenSET and PenDURA pen platforms.

For manual, variable multidose pen injectors, the PenVARIO platform was designed with a large window and optimal contrast to enable patients to read the dose they have selected easily. For each of its GLP-1 RA variants (i.e. liraglutide, semaglutide and tirzepatide), it also integrates an active last dose stop that prevents incomplete administration of the last dose left in the pen.

Connectivity features related to medication management have been helping patients with diabetes and other conditions to monitor their treatment and increase adherence.[6,7] This technology can also be applied for obese patients. Nemera has developed an add-on device that does not modify the way the pen injector is used. Patients can receive information related to their injections directly from the add-on device to an app on their smartphone.

"PENDIA AND PENSET PLATFORMS ARE DESIGNED WITH A SPRING-ASSISTED INJECTION, WHICH PROVIDES PATIENTS WITH A CONSTANT DOSING RATE AND REDUCED INJECTION FORCE, ELEVATING THE USER EXPERIENCE."

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

For specific customer applications, Insight by Nemera – the independent development and consulting team within the company's services business unit – can support pen-platform-based combination products from registration through to commercialisation. Nemera provides this support through a suite of consulting services designed to address every aspect of combination product development. With a proven track record in helping customers achieve regulatory approvals in over 50 countries with a wide variety of device types and suppliers, they define customised strategies to meet the unique needs of each programme. Nemera's services include:

- **Functional/Analytical Lab Testing and Design Verification**: State-of-the-art facilities and customised methodologies ensure that products meet safety, quality and compliance standards. Nemera supports performance and functionality testing, analytical testing (stability, biocompatibility/biological risk assessments, etc.) and design verification for final combination

products. Their processes align with ISO and US FDA requirements.

- **Human Factors Management and Design Validation:** Nemera ensures that devices and combination products are safe and effective for target users while enhancing the patient experience and adherence. The areas supported include human factors strategy development, risk analyses, usability testing (formative and summative) and preparation of regulatory documentation for global regulatory authorities.

- **Instructional Materials and Secondary Packaging Development:** Nemera creates tailored instructions for use, value-added packaging and integrated digital assets that improve the user experience, increase adherence, boost engagement and support specific combination product applications.

- **Quality/Regulatory Strategy and Registration Support:** Nemera's team can help partners navigate the complexities of global regulatory processes and standards from strategy and pre-market activities to registration and post-market support. This includes developing strategies, engaging with regulatory bodies and preparing submission-ready materials to ensure compliance with global requirements including the management of Essential Drug Delivery Outputs.

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

To provide fully automated industrial capability to its partners, Nemera has invested in two of its European plants in Poland and Germany (Figures 4 & 5), expanding its pen injector manufacturing capabilities. Able to produce prototypes, small series for clinical batches and large-scale volumes, these plants are equipped with state-of-the-art machines from moulding to assembly activities, including quality control testing.

Figure 4: State-of-the-art facility dedicated to pen injector manufacturing in Szczecin, Poland.

Figure 5: Extended facility for pen injector manufacturing in Neuenburg, Germany.

"TO PROVIDE FULLY AUTOMATED INDUSTRIAL CAPABILITY TO ITS PARTNERS, NEMERA HAS INVESTED IN TWO OF ITS EUROPEAN PLANTS IN POLAND AND GERMANY TO EXPAND PEN INJECTOR MANUFACTURING CAPABILITIES."

Nemera provides comprehensive service offerings with global manufacturing facilities and a commitment to sustainability. Its holistic approach ensures that every aspect of combination product development is seamlessly integrated.

BENEFITS OF PARTNERING WITH AN INTEGRATED PRODUCT AND SERVICE PROVIDER

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

By working with Nemera, the need to co-ordinate multiple specialised partners is eliminated. This simplifies the process and reduces complexity and risk, while accelerating regulatory approval and market access. This agile and integrated approach

allows customers to focus on their core business while Nemera manages the details of combination product development, ensuring that the result is safe, effective and differentiated.

In conclusion, the expansion of therapeutic indications will broaden the patient population, meaning that the adoption of a patient-centric approach in CKM/CRHM care will no longer be optional – it will be essential for improving both clinical outcomes and patients' quality of life. CKM/CRHM conditions are deeply interconnected; by placing the patient – not just the disease – at the centre of care, Nemera can foster stronger engagement, leading to improved adherence to therapies. Prioritising patient empowerment, education and common understanding across industry ensures that care is not only clinically sound but also meaningful and responsive to the lives of those it serves.

"CKM CONDITIONS ARE DEEPLY INTERCONNECTED; BY PLACING THE PATIENT – NOT JUST THE DISEASE – AT THE CENTRE OF CARE, NEMERA CAN FOSTER STRONGER ENGAGEMENT, LEADING TO IMPROVED ADHERENCE TO THERAPIES."

Cécile Gross

Cécile Gross serves as Global Category Marketing Manager at Nemera, where she leads the strategy, development and lifecycle management of the Parenteral Devices portfolio. Her scope includes advanced delivery platforms such as safety systems, pen injectors and on-body injectors, ensuring they meet evolving market and patient needs. With over 20 years of experience in the medical device industry, she brings deep expertise in marketing of high-technology solutions and driving effective product lifecycle strategies across diverse device categories. Ms Gross holds a degree in International Business and a Master's in Marketing and Management in the Healthcare Industry from the IMIS Institute in Lyon (France), equipping her with both global business insight and sector-specific leadership capabilities.

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Mark Tunkel

Mark Tunkel is Services Strategy & Marketing Director at Nemera. He was previously a partner at Insight Product Development, which was acquired by Nemera in 2019 and became the Insight Innovation Center. With more than 20 years of global business development experience and a deep understanding of the marketplace challenges and trends impacting the pharma industry, Mr Tunkel has advised many of the world's leading companies on their product development and innovation strategies, with an emphasis on driving realisation and highly favourable business outcomes.

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ONE PEN AT A TIME

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DELIVERABILITY, ACCEPTABILITY, AVAILABILITY: ASSESSING THE EVOLVING STRENGTHS OF MICRONEEDLE-BASED DRUG DELIVERY

Dr May Pidding of **LTS** explores the growth and future potential of microneedle technology and its suitability for a broad range of drug delivery applications, specifically presenting the case for the accelerated uptake and wider adoption of Microneedle Array Patch (MAP) technology.

There is a paradox at the heart of medical science. Viewed from one angle, it is a world rooted in evidenced ideas; viewed from another, it is driven by a belief that truths are not absolute and that knowledge is, at best, provisional.

This acceptance of uncertainty acknowledges the vast complexity of human biology, an evolving understanding of optimal medical approaches and the difficulties associated with discovering, developing and delivering therapies that make a difference to patients. Perfect solutions are rare. More often, variables must be accommodated and compromises accepted in the interests of outcomes. An example of this is covid-19 vaccines, which, although developed at incredible speed, demanded an unprecedented investment of resources.

When it comes to more traditional, default methods of drug delivery, unavoidable compromises are widely evident, whether it is the requirement for medicines to be distributed and stored in cold chain conditions, the need for patients to travel to healthcare facilities for supervised administration, or for undesirable delivery forms to be accommodated by those with either needle phobias or problems swallowing. However, innovative alternatives are now available that address legacy delivery shortcomings and offer additional new benefits.

An example of this is microneedle technology, specifically microneedle array patch (MAP) technology, which is now proven and available for customised projects in the form of the proprietary AccuTip MAP platform from LTS (Figure 1).

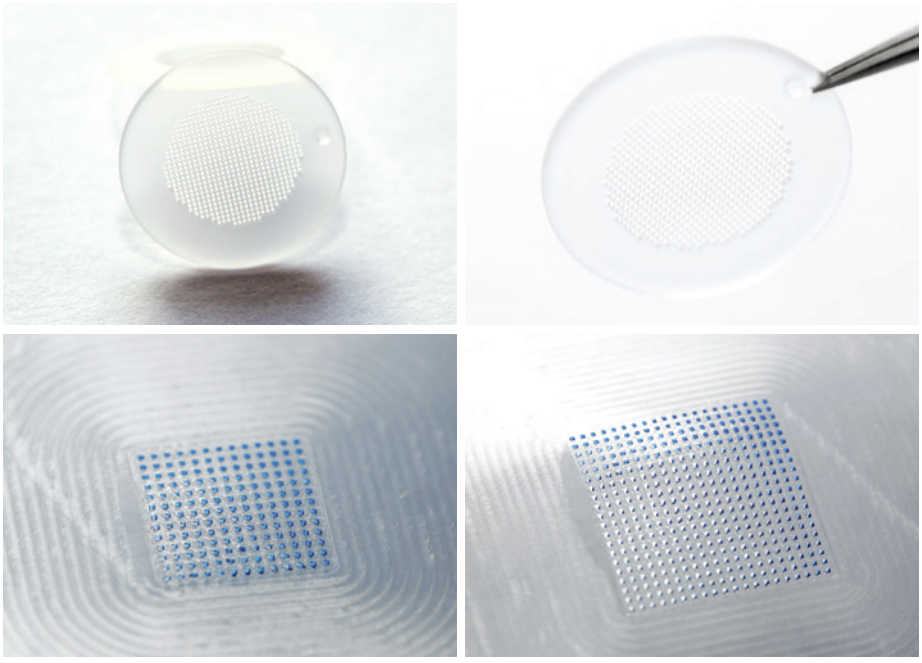

Figure 1: Different microneedle array patch designs.

MAPs leverage the skin's unique properties, enabling minimally invasive, pain-free drug delivery with the potential to enhance therapeutic outcomes and improve patient comfort and compliance, while fundamentally changing how and where patients can access treatments and vaccines. This transformative technology has displayed effectiveness in proof-of-concept trials, as well as suitability for a wide variety of molecules including biologics, vaccines and small molecules. The flexibility and configurability of MAPs may allow them to overcome the limitations of legacy injection systems.

THE SKIN: A GATEWAY TO SYSTEMIC DELIVERY

While the skin is easily accessible and immunologically active, to date it has been underutilised as a route for systemic drug delivery. Largely, this has been because drug delivery options have been limited to the delivery of small molecules at relatively low doses.

However, scientific advances in intradermal therapeutic systems, such as MAP technology, can overcome these limitations. Microneedle patches, typically consisting of arrays of hundreds of microscopic needles per patch, can painlessly penetrate the outer layers of the skin and deliver APIs directly to the viable epidermis or dermis. Here, substantial immune cell populations, capillary networks and microvascular structures enable efficient uptake while avoiding deeper tissue penetration and the pain associated with intramuscular or subcutaneous injections. Additionally, because the route of delivery bypasses the gastrointestinal tract and liver, MAPs avoid the reduction of drug efficacy caused by the first-pass effect.

Crucially, MAPs are not a singular design concept but a versatile platform. Modern systems typically use dissolvable polymer microneedles that encapsulate the API within the needle tips themselves.

"MAPs ARE NOT A SINGULAR DESIGN CONCEPT BUT A VERSATILE PLATFORM."

Upon application, the needles dissolve in the skin, delivering the drug in alignment with the dosing protocol. Their versatility is underlined by the fact that the rate of release of a particular molecule can be controlled through formulation with either slow or quick-release polymers, depending on the target profile of the drug product.

From a patient perspective, the experience is simple and largely pain free. In terms of healthcare infrastructure and investment, it removes many of the restrictions associated with traditional delivery methods, avoiding the involvement of trained healthcare professionals (HCPs), eradicating injections and, in many cases, curtailing the need for deep-freeze cold chain logistics.

FROM CONCEPT TO CLINIC

Microneedle technology has been in existence since the 1970s but, for many years, it has remained largely confined to academic research. Manufacturing complexity, dosing precision and scalability have posed significant challenges, and the absence of a clear regulatory and commercial pathway reinforced the perception of MAPs as an emerging, perhaps even speculative, technology.

However, today, the picture is very different (Figure 2). Significant advances in materials science, precision manufacturing

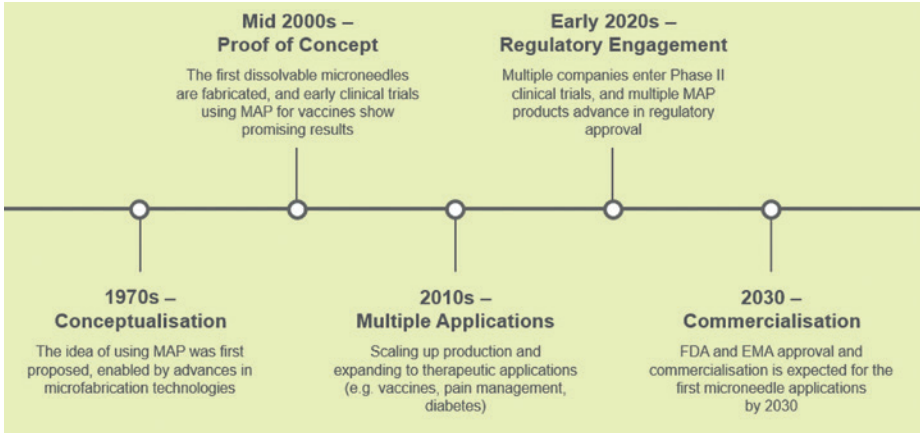

Figure 2: The evolution of microneedle-based drug delivery.

and process automation in recent years have transformed MAPs into a credible, clinically validated delivery platform.[1] A total of 128 registered clinical trials using microneedle technology for therapeutic and diagnostic purposes have been registered globally, covering applications ranging from vaccines and biologics to high potency small molecules.[2]

These trials support a growing body of evidence that demonstrates the capabilities of MAPs in achieving comparable results to established delivery routes in terms of efficacy, safety and dose consistency, with many studies evidencing improved tolerability among patients.[3]

One such example is a Phase I investigator-initiated clinical booster study conducted by LTS on a licensed hepatitis B vaccine, which compares delivery via MAP with the traditional intramuscular injection (Figure 3). The results showed that MAP delivery generated a stronger immune response, both with and without the use of an applicator. Notably, unlike the licensed vaccine, this enhanced response was achieved without adjuvants and using a delivery method that is inherently pain free. As such, the ability of MAPs to maintain or improve efficacy of vaccines in a patient-friendly form has direct and significant advantages for large-scale programmes – such as global vaccination initiatives – in terms of lower cost, greater supply resilience and wider reach.

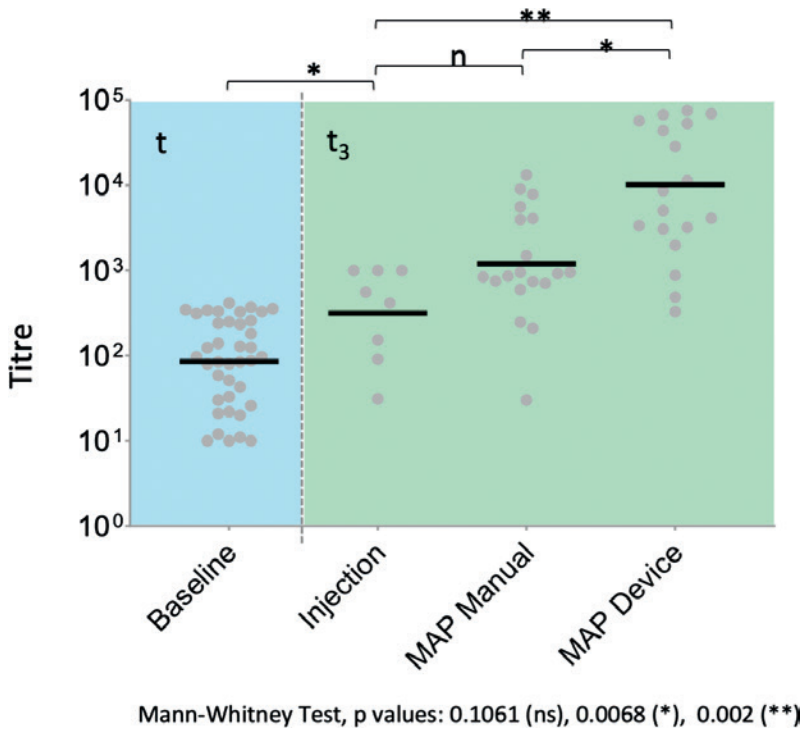

Figure 3: Phase I investigator-initiated clinical booster study.

MITIGATING COMPROMISE: MAPs VERSUS CONVENTIONAL DELIVERY ROUTES

Every drug delivery system incorporates a degree of compromise, leading to crucial questions regarding the level and nature of the trade-offs required and whether they can be accepted. Oral delivery is convenient but unsuitable for most biologics and vaccines, and problematic for patients with difficulty swallowing. Injections offer broad applicability but bring pain, anxiety, the need for trained administrators or patients proficient with self-administration and the risk of needlestick injury and infection, all of which can converge to impair adherence and compliance. In many cases, clinical resources might also be required to support drug delivery, placing a burden on healthcare providers and inconveniencing patients, with the impact felt disproportionately by those with limited mobility or access to care. For the healthcare payers, such burdens can be associated with considerable financial cost.

MAPs resolve some of these key points of friction. By enabling simple, self-administered, pain-free delivery, they remove many of the practical and psychological barriers that prevent patients from fully engaging with and adhering to their treatment regimens. For individuals with needle phobia, children and the elderly, this represents a transformative shift – particularly in the context of managing chronic conditions at home. Indeed, LTS's recent study on multiple sclerosis treatment demonstrates that MAP technology has great potential to provide an alternative to injectable therapy systems.[4]

From a wider healthcare ecosystem perspective, MAPs can reduce reliance on HCP time, lower the burden on clinical facilities and support decentralised care models. These benefits extend beyond convenience for individuals; they contribute to more resilient, inclusive and affordable healthcare systems that work better for patients of all ages and physical capabilities.

Application by MAPs enables patients to maintain their regular lifestyles, ensuring that daily life is not dictated by their disease or treatment regimen. In addition, better adherence due to ease of application leads to significant reductions in hospitalisation rates due to non-compliance to treatment.

"THE ABILITY OF MAPs TO MAINTAIN OR IMPROVE EFFICACY OF VACCINES IN A PATIENT-FRIENDLY FORM HAS DIRECT AND SIGNIFICANT ADVANTAGES FOR LARGE-SCALE PROGRAMMES – SUCH AS GLOBAL VACCINATION INITIATIVES – IN TERMS OF LOWER COST, GREATER SUPPLY RESILIENCE AND WIDER REACH."

ONE PLATFORM, MANY POSSIBILITIES

One of the most compelling attributes of MAP technology is its flexibility. The same underlying platform can be adapted to deliver a wide range of molecules, including vaccines, biologics, mRNA formulations and small molecules. The needle geometry, matrix composition, dose loading and release kinetics can all be tailored to the specific requirements of a given API and indication. This configurability supports applications ranging from mass vaccination to more targeted treatments, where smaller batch sizes and precise dosing can be accommodated in a GMP-compliant and economically viable way. As such, patients are not forced to adapt to delivery systems that are optimised for scale but, rather, can receive medicine via convenient delivery systems that are suited to their specific treatment regimens and personalised medicine needs.

There are few barriers to equitable drug access as pervasive as cold chain requirements. For many biologics and vaccines, maintaining stability from manufacture to administration can demand ultra-low temperature storage. In regions with limited infrastructure, or in emergency response scenarios, this requirement alone can determine whether a therapy can be made available at all. MAP technology has demonstrated real potential in addressing this challenge.

In a study conducted by LTS using a lipid nanoparticle (LNP) formulated mRNA rabies vaccine, doses delivered with MAPs achieved protective antibody titres comparable with intramuscular injection (Figure 4). Importantly, these results were obtained with storage conditions of 2–8°C for the MAPs – far less demanding than those associated with the original bulk material, which was stored at -80°C.[5]

Taken together, these findings suggest that MAPs could significantly reduce – or even eliminate – cold chain dependency for certain therapies. In doing so, they directly address one of the most persistent structural inequalities in global drug delivery.

> "MAPs COULD SIGNIFICANTLY REDUCE – OR EVEN ELIMINATE – COLD CHAIN DEPENDENCY FOR CERTAIN THERAPIES. IN DOING SO, THEY DIRECTLY ADDRESS ONE OF THE MOST PERSISTENT STRUCTURAL INEQUALITIES IN GLOBAL DRUG DELIVERY."

MANUFACTURING, REGULATION AND THE MYTH OF "EARLY ADOPTER RISK"

While the positive momentum around MAPs as an innovative drug delivery method has continued to build over time, adoption has been hindered to a certain extent by hesitancy surrounding manufacturing complexity, regulatory uncertainty and the comparative costs of individual products. It should be acknowledged that these concerns were not without foundation in the earlier stages of MAP development. However, they have subsided as the technology has evolved and matured.

Through a combination of process optimisation, automation and modular manufacturing design, MAP production can now be scaled in a controlled, cost-effective manner. Modern approaches focus on optimising small-scale processes and then replicating them through modular expansion. This strategy reduces upfront capital investment while preserving flexibility and regulatory control, providing a managed pathway for a technology that is readily available for development and clinical studies.

Regulatory engagement has evolved in parallel. As a manufacturing authorisation holder in Germany, LTS operates in continuous dialogue with healthcare authorities, clarifying any perceived points of uncertainty while ensuring that MAP development aligns with expectations around dosing consistency, materials compliance and patient safety. This proactive approach de-risks clinical progression and shortens time to market for pharmaceutical partners.

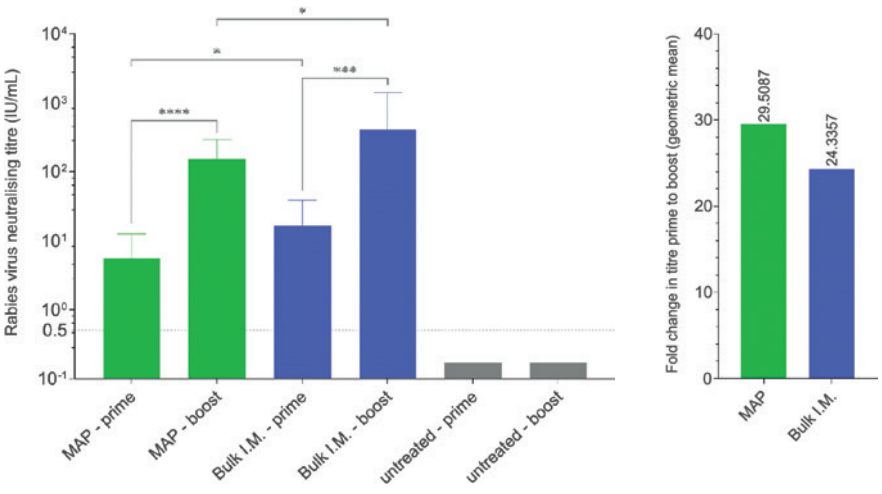

Figure 4: mRNA-LNP rabies vaccine preclinical trial in guinea pigs.

MATCHING DRUG DELIVERABILITY AND PATIENT ACCESSIBILITY TO COMMERCIAL AVAILABILITY

Equality in accessibility does not mean offering everyone the same solution. It means ensuring that everyone can access treatment in a way that works for them physically, psychologically and practically. MAP technology represents a meaningful step towards that goal. By removing needle-related pain, reducing cold chain dependence, enabling self-administration and supporting a broad range of APIs, MAPs challenge long-accepted norms in drug delivery and expand the options available.

The conclusion is clear: access to life-enhancing medicines will only become more equitable by designing drug delivery solutions that adapt to patients, wherever they are and whatever their circumstances. Having long progressed beyond experimental early stages, MAPs are now proven as a market-ready technology that offers first-mover advantage to forwards-thinking organisations focused on overcoming the challenges associated with legacy delivery routes. Through a combination of API deliverability, patient acceptability and clinical availability, MAPs today are helping establish tomorrow's new era of patient centric medicine.

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Expert View

TRANSDERMAL DRUG DELIVERY: ENHANCING PERMEABILITY AND *IN VIVO* TRANSLATION

Dr Leo Pan of WuXi AppTec provides insights into the field of transdermal drug delivery and investigates the two primary approaches being taken to advance the sector – enhancing the ability of drugs to permeate through the skin barrier and translating *in vitro* data to an *in vivo* reality.

"TRANSDERMAL DRUG DELIVERY ALSO MAINTAINS A CONSTANT, EFFECTIVE BLOOD DRUG CONCENTRATION, SO THAT PATIENTS DO NOT SUFFER FROM FLUCTUATIONS IN BLOOD DRUG LEVELS WHICH CAN OCCUR WITH ORAL ADMINISTRATION, REDUCING ADVERSE EFFECTS AND PEAK-TROUGH FLUCTUATIONS."

Transdermal drug delivery is among the oldest methods of administering medications in human history. The Ancient Egyptians used oils, fats, perfumes and other ingredients to make cosmetic and dermatological products; in Ancient Greece, the physician Galen developed something similar to modern cold cream; and precursors of modern transdermal patches were found in Ancient China.

Today, these drugs, which are administered through the skin rather than via injection, inhalation or oral ingestion, offer many benefits to drug developers. This form of drug delivery enables the API to enter the bloodstream for systemic distribution, with developers constantly seeking ways to improve their delivery further. To this end, researchers tend to focus on two areas in particular: enhancing permeability and *in vivo* translation.

THE BENEFITS OF TRANSDERMAL DRUG DELIVERY

Transdermal drug delivery products include transdermal patches, creams, sprays, gels, ointments, foams, films, microneedle systems and more. Transdermal patches are the most established format, the first of which, a three-day patch to treat motion sickness, was approved in the US in 1979.[1] Since then, the transdermal drug delivery market has expanded to the fields of pain management, hormonal applications, central nervous system disorders, cardiovascular diseases and other applications, such as nicotine patches to help patients quit smoking.

Transdermal drug delivery offers several advantages over other methods. It avoids the first-pass effect in the liver and degradation in the gastrointestinal tract, which reduces the interindividual variability in the drug response and improves the effective bioavailability for some drugs. This also means there is reduced formation of toxic or inactive metabolites. Also, doses can be lowered, which is especially valuable for drugs that are primarily metabolised orally.

Transdermal drug delivery also maintains a constant, effective blood drug concentration, so that patients do not suffer from fluctuations in blood drug levels which can occur with oral administration, reducing adverse effects and peak-trough fluctuations. This feature makes transdermal patches widely suited for pain reduction, hormone therapy and cardiovascular drugs.

Above all, transdermal drug delivery is a convenient route of administration for patients. It is non-invasive, straightforward and often requires less frequent dosing. This makes this form of delivery particularly useful for treating chronic conditions and even essential for patients who struggle with swallowing or managing injections. It is also often the best option for long-term treatments due to their ease of use.

The sustained-release properties of this type of delivery make it suitable for drugs with short biological half-lives that require frequent oral or non-gastrointestinal administration. This can reduce dosing frequency, extend the duration of delivery, enable flexible administration and improve patient compliance, particularly for those who struggle with oral medications. For developers, transdermal delivery can also extend product lifecycles and differentiate existing drugs, as well as enable reformulation of drugs with poor oral tolerability.

"CHEMICAL METHODS ARE THE MOST COMMONLY EXPLORED MEANS OF ENHANCING TRANSDERMAL DRUG PERMEATION, AS THEY ARE RELATIVELY AFFORDABLE, EASY TO PRODUCE, OFFER DESIGN FLEXIBILITY AND ALLOW PATIENTS TO SELF-ADMINISTER THEIR DRUGS."

ENHANCING THE PERMEABILITY OF TRANSDERMAL DRUG DELIVERY

To be effective, transdermal drugs must penetrate the skin's outermost layer: the stratum corneum. This is the skin's primary barrier and is composed of dead cells surrounded by a lipid matrix. It is highly lipophilic and extremely resistant to diffusion. The structure of the stratum corneum resembles a brick wall and is around 10–20 µm thick. Only very small lipophilic molecules, such as nicotine, can naturally cross this barrier.

By increasing the permeability of the skin before or as the drug is delivered, researchers can raise the flux – the rate at which it passes across the skin. This enables therapeutically meaningful doses to reach systemic circulation or local tissues and expands the range of drugs suitable for transdermal delivery.

Chemical and physical permeation enhancers are frequently used to improve drug permeability. Chemical methods are the most commonly explored means of enhancing transdermal drug permeation, as they are relatively affordable, easy to produce, offer design flexibility and allow patients to self-administer their drugs.

TOXICOLOGICAL RISKS OF PERMEABILITY ENHANCERS

The toxicological risks associated with high solvent concentrations are numerous. Developers must avoid certain pitfalls when aiming to increase permeability; for example, harsh penetration enhancers, such as dimethyl sulfoxide (DMSO), can damage the skin, and chronic use of enhancers can disrupt the skin barrier and increase the risk of infection. To evaluate the toxicological liabilities of permeability enhancers, developers should assess acute irritation, sensitisation, phototoxicity and systemic toxicity using *in silico*, *in vitro*, *ex vivo* and *in vivo* models. Early screening can help to avoid costly late-stage failures.

Irritation and Barrier Disruption

High concentrations of solvents can cause skin erythema, oedema and desquamation, while chronic exposure can lead to hyperkeratosis, dermatitis or eczema. Some ionic liquids may disrupt keratinocyte membranes at high doses. To address this issue, developers should define and respect no-observed-effect levels (NOELs) using dose-response irritation data, demonstrate the reversibility of barrier effects, use repeated-dose toxicity studies and structure toxicity optimisation for ionic liquids.

Sensitisation and Allergic Reactions

Solvents can promote contact dermatitis, and ionic liquids may trigger T-cell-mediated hypersensitivity. To address this, researchers can exclude or strictly limit skin sensitisers, apply a weight-of-evidence sensitisation strategy and use conservative exposure margins.

Phototoxicity

Some solvents are photo-reactive, causing oxidative stress under UV exposure. Phototoxic hazard identification can identify whether solvents or ionic liquids generate reactive oxygen species (ROS) under UV or visible light. Developers should set toxicological thresholds that consider worst-case UV exposure and apply risk-based exclusion to the development strategy.

Systemic Toxicity

Solvents can also increase the penetration of drugs and toxins, such as residual impurities and leachables. High concentrations and doses of solvents or ionic liquids (if absorbed) may result in specific organ toxicity. To mitigate the risk of systemic toxicity, researchers should apply strict toxicology thresholds, evaluate co-transport risks and perform organ risk assessments.

IMPROVING *IN VIVO* TRANSLATION

In vivo translation is essential for transdermal drug development because it relies on dynamic, living skin physiology that cannot be fully captured *in vitro*. Without effective translation, developers risk misjudging dose, efficacy, safety and regulatory acceptability. Key gaps between *in vitro* permeation and irritation models and living organisms include the lack of physiological complexity and homeostatic regulation, simplified tissue architecture and limited cell-to-cell interactions. *In vitro* models also lack systemic and immune response mechanisms, which are crucial for predicting whole-body toxicity.

In vitro systems also often fail to accurately predict long-term or chronic effects because of their static, short-term nature. In contrast, *in vivo* studies offer advantages such as dynamic homeostasis, complete detoxification and clearance mechanisms, fully layered tissue structures with functional barriers and the ability to capture immune responses and systemic effects.

"*IN VIVO* STUDIES OFFER ADVANTAGES SUCH AS DYNAMIC HOMEOSTASIS, COMPLETE DETOXIFICATION AND CLEARANCE MECHANISMS, FULLY LAYERED TISSUE STRUCTURES WITH FUNCTIONAL BARRIERS AND THE ABILITY TO CAPTURE IMMUNE RESPONSES AND SYSTEMIC EFFECTS."

To improve translation, developers should focus on integrating *in vivo* and *in vitro* data into project disciplines and design experiments. They should also use predictive pharmacokinetic and pharmacodynamic models, ensure that they are using the most useful biomarkers and surrogate endpoints, and place emphasis on collaboration and data sharing.

Ex vivo models, such as reconstructed skin, can act as a bridge between *in vitro* and *in vivo* testing. However, they have variable reliability in predicting human safety, depending on the endpoint assessed. Models such as EpiDerm (Mattek, Ashland, MA, US) and SkinEthic (EPISKIN, Lyon, France) show high reliability, exhibit correlations with human data and are validated for regulatory use.

To enhance physiological relevance, full-thickness reconstructed human skin models incorporate a collagen dermal layer containing human fibroblasts, thereby better mimicking the structure and function of natural skin. However, in practice, reconstructed skin models often underestimate permeation, particularly for lipophilic and small molecules, owing to the absence of a functional dermis and skin appendages.

NAVIGATING REGULATORY CONCERNS

Regulators focus primarily on the following items when evaluating the safety of transdermal drug delivery systems:

- Local skin toxicity
- Systemic exposure and toxicokinetics
- Enhancer and excipient safety
- Long-term and cumulative effects.

Global regulation of transdermal drug products is only partially harmonised through ICH guidelines and OECD test methods. Some of the core scientific principles apply across multiple regions, but implementation, evidentiary thresholds and review emphases differ between agencies, including product classification, local tolerability expectations and evidentiary thresholds for combination products and novel excipients.

As such, sponsors must design transdermal programmes to a globally conservative standard, using harmonised scientific principles while anticipating region-specific regulatory interpretation. Developers should treat transdermal systems as combination products. For example, in the US, patches must comply with both device and drug regulations.[2] Regulators assign the primary mode of action to these products, which determines which centre reviews them.

One of the more common mistakes when assessing the toxicology of a transdermal drug candidate for submission is only to evaluate acute irritation and not the long-term barrier impairment. This can be avoided by conducting repeated-dose studies with histopathological evaluation. Another mistake is failing to consider that while the API may not be phototoxic, the enhancer may be. This can be managed by conducting phototoxicity studies with the full formulation.

A FINAL WORD ON TRANSDERMAL DRUG DELIVERY

The global transdermal drug delivery system market size is projected to reach more than US$136 billion (£101 billion) by 2030, rising from $62 billion in 2023, according to a report from Grand View Research.[3] This is partly due to the increasing incidence of chronic diseases, but also because these systems are improving through research on permeability and *in vivo* translation.

"FURTHER ADVANCES IN TRANSDERMAL TECHNOLOGY HOLD GREAT PROMISE, INCLUDING TECHNOLOGICAL INNOVATIONS AND 3D BIO-PRINTED SKIN WITH IMMUNE COMPONENTS."

Further advances in transdermal technology hold great promise, including technological innovations and 3D bio-printed skin with immune components. Advanced microneedle technologies are also being explored, with the hope that they will enable routine transdermal delivery of biologics, while smart and connected transdermal systems could move the field towards precision medicine. As with many medical research areas, machine learning is being touted as a possible accelerant to progress.

As these technologies move forwards, the number of applications for transdermal drug delivery will increase dramatically, providing new treatment options for patients around the world. Developers seeking to carve out a share of that expanding market can significantly increase the impact of their products by focusing on enhancing both permeability and *in vivo* translation, thereby changing the lives of countless patients.

ABOUT THE COMPANY

WuXi AppTec is a partner and contributor to the pharmaceutical and life sciences industries, providing R&D and manufacturing services that help advance healthcare innovation. With operations across Asia, Europe and North America, WuXi AppTec offers integrated, end-to-end services through their unique CRDMO platform. WuXi AppTec works alongside nearly 6,000 partners across over 30 countries, supporting their efforts to bring breakthrough treatments to patients. Guided by a vision that every drug can be made and every disease can be treated, they are committed to advancing breakthroughs for patients – one collaboration at a time.

Dr Leo Pan

Leo Pan, PhD, is the Senior Director of Toxicology at WuXi AppTec. He earned his PhD in developmental biology and, since graduating in 2008, has dedicated his career to chemical and drug safety evaluation. Prior to joining WuXi AppTec, Dr Pan served as a Study Director at Intertek, where he specialised in reproductive toxicity testing for chemicals. Throughout his career, he has contributed to a wide array of preclinical programmes for pharmaceuticals, many of which have been submitted to regulatory agencies such as the US FDA and NMPA for Investigational New Drug and New Drug Application approvals.

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CLOSING THE SAFETY GAP: WHY PHARMA-DEDICATED LABELS MATTER

Paavo Sillanpää of **UPM** discusses why pharma-dedicated labels matter for more challenging labelling applications as well as how to avoid potential label failure and brand risk.

PACKAGING FORMAT EVOLUTION AND CHALLENGES

Pharmaceutical packaging is undergoing a transformation as continued growth in injectables, biological drugs and self-administered therapies is driving the adoption of prefilled syringes, injection pens, autoinjectors, wearable devices and on-body injectors.

In the pharmaceutical industry, there is growing interest in moving away from traditional glass packaging formats to plastics, such as polypropylene, cyclo-olefin polymer and cyclo-olefin copolymer. At the same time, technologies such as blow-fill-seal, traditionally used for large volume parenterals and ophthalmics, are being used for select applications, such as single-dose vaccines. As packaging formats evolve, regulatory scrutiny intensifies. Authorities are paying closer attention to potential compound migration from packaging into drug products, as well as the biocompatibility of medical devices such as prefilled syringes, injection pens and inhalers.

A Sophisticated Industry with an Avoidable Weak Link

Pharmaceutical development and manufacturing have become increasingly sophisticated. Biologics, highly potent compounds and targeted therapies demand precise control over every aspect of the product lifecycle. At the same time, modern delivery formats, such as prefilled syringes, autoinjectors, infusion systems, inhalers and ophthalmic products, are bringing drug

"MANY PHARMACEUTICAL PRODUCTS ARE STILL LABELLED WITH STANDARD-GRADE MATERIALS DESIGNED FOR GENERAL INDUSTRIAL OR CONSUMER USES. THIS MISMATCH IS WHERE THE SAFETY GAP OPENS."

substances into direct contact with complex packaging and device components. In this environment, every material choice matters.

Regulators, such as the US FDA and EMA, set clear expectations for how container closure systems must be designed, qualified and controlled. However, despite the increasing complexity of delivery systems, many pharmaceutical products are still labelled with standard-grade materials designed for general industrial or consumer uses. This mismatch is where the safety gap opens.

LABELLING CHALLENGES FOR INJECTABLES

Injectable products illustrate this mismatch particularly clearly. Containers with diameters below 23 mm – especially those between 7 and 12 mm – require adhesives engineered for tight mandrel hold and cold chain performance. When general-purpose label materials are used instead, risks such as edge lifting, peeling or loss of legibility become far more likely. In addition, injectable applications demonstrate how this compliance gap manifests operationally. Materials proven adequate for standard conditions may fail when exposed to cold chain, moisture and curved surfaces, resulting in visible label failure on finished drug products.

Standard Label Materials Create Unnecessary Hazards

Labels are an integral part of pharmaceutical packaging and medical devices: they carry the critical information that patients and healthcare professionals rely on (Figure 1). However, what is less visible – and also often underestimated – is that labels can also contribute to extractables and leachables (E&L). When the wrong label materials are used, unwanted substances may appear in E&L studies or ISO 10993 biocompatibility testing. This can trigger retesting, raise costs, delay approvals and, in the worst case, interrupt supply.

Standard-grade label materials are fit for purpose in many non-regulated applications. However, when applied to certain pharmaceutical packaging scenarios, they can introduce risks that can become costly. This is because standard materials are typically not tested for sterilisation resistance, extreme temperatures/cold chain conditions or validated on pharmaceutical packaging formats. Furthermore, they are not produced under controlled raw material sourcing and change management processes, supported by documentation aligned with FDA and EMA expectations or prioritised in supply chains during raw material shortages.

Figure 1: Labelling across pharmaceutical packaging types.

Label Failure and Brand Risk

The gaps caused by using standard labels in pharmaceutical applications leave brand owners with an unattractive choice: generate additional data themselves or accept a higher level of risk. In regulated environments, neither option is ideal. So, what are the risks?

If a label fails – whether through migration, loss of adhesion, print degradation or instability during sterilisation or cold storage – the malfunction is visible on the final product to regulators, healthcare professionals and patients. The reputational and financial impact typically lands on the brand owner, whose product appears unsafe or non-compliant, and the converter, who supplied the labels. Even if the root cause is the selection of a standard material for a high-risk application, the damage is shared throughout the value chain.

E&L and Migration: Why Labels Matter

Three concepts are crucial for understanding the relevance of low-migration labels – extractables, leachables and migration. First, extractables are compounds that can be extracted from materials under

aggressive laboratory conditions, such as with elevated temperature or strong solvents. These represent a worst-case scenario. Second, leachables are compounds that migrate into drug products under normal or accelerated storage conditions and are directly relevant to patient safety and product quality. Finally, migration is the process by which substances move from packaging or label materials into the product, driven by factors such as contact, temperature, solubility and storage time.

Labels can contribute to E&L risk in several ways. All label components must be considered, including the material, adhesive chemistry, inks and top coats. If plastic vials or syringes are used, there is always a potential risk for migration as the label adhesive is in direct contact with the packaging surface and the label-to-container surface area is large. This is where low-migration adhesives differ from standard adhesives. Low-migration adhesives are designed by selecting polymer structures that have higher molecular weight without residual monomers – minimising potential mobile additives and components with low molecular weight is essential.

Controlled selection of raw materials and locked formulations, which have strict change management, allow low-migration adhesives and constructions to address E&L risks. Risks are further minimised by using defined standard operating procedures to avoid cross-contamination from other adhesives, alongside detailed risk analyses, ensuring that the product is identical to previous versions if manufacturing is moved to another line or production location. Although low-migration adhesives and label constructions do not eliminate the need for E&L studies, they provide a safer starting point and support more efficient, risk-based evaluations.

"ALTHOUGH LOW-MIGRATION ADHESIVES AND LABEL CONSTRUCTIONS DO NOT ELIMINATE THE NEED FOR E&L STUDIES, THEY PROVIDE A SAFER STARTING POINT AND SUPPORT MORE EFFICIENT, RISK-BASED EVALUATIONS."

Pharma-Dedicated Label Materials

So, what are pharma-dedicated label materials and why is it important to use them for injectable packaging? Pharma-dedicated label materials are designed to withstand sterilisation and cold chain conditions, perform across common pharmaceutical packaging types and comply with relevant regulatory expectations. They are particularly important for use with injectable products, as these are sensitive to uncontrolled material changes. As a result, adjustments intended to address adhesion, printability or supply substitutions can cascade into expanded testing, updated filings or delayed releases due to heightened scrutiny of container closure components.

Hidden Costs Associated with Standard Materials

The choice between standard and pharma-dedicated labels often appears, at first, to be a simple cost comparison. In reality, the true economic picture looks very different. This is because standard materials are not the best choice for high-risk or demanding applications, such as injectables, and can in fact have a raft of hidden costs attached to their use. These can include the need for additional E&L studies and analytical work, extended stability tests to investigate unexpected interactions and delays in marketing authorisation due to packaging questions.

The choice of standard labelling materials can also lead to product holds or batch rework caused by label performance issues, costly revalidation activities when suppliers alter formulations and follow-up actions during audits and potential recalls. Even if such events are relatively rare, the impact when they do occur is high. A single significant delay or recall can outweigh the marginal savings made when using standard materials across many production runs.

VALUE GENERATED BY PHARMA-DEDICATED LOW-MIGRATION LABELS

Pharma-dedicated label materials deliver a wide range of benefits to converters and pharmaceutical brand owners. These include the reduction of uncertainty in E&L studies, the ability to have more targeted, risk-based testing and support for smoother interactions with regulatory agencies. Pharma-dedicated materials also provide more stable performance under demanding conditions and support change management across the product lifecycle.

Essential for brand owners, pharma-dedicated label materials bring performance designed for stress conditions such as sterilisation, low temperatures and real-world handling, as well as consistent adhesion and durability across plastics, glass and small-diameter containers or medical devices. The materials are also aligned with regulatory expectations, simplifying internal quality and risk assessments. This minimises the risk of manufacturing disruptions and unexpected issues with stability studies. Overall, pharma-dedicated materials provide built-in risk mitigation that protects both patients and product supply.

"PHARMA-DEDICATED LABEL MATERIALS BRING PERFORMANCE DESIGNED FOR STRESS CONDITIONS SUCH AS STERILISATION, LOW TEMPERATURES AND REAL-WORLD HANDLING, AS WELL AS CONSISTENT ADHESION AND DURABILITY ACROSS PLASTICS, GLASS AND SMALL-DIAMETER CONTAINERS OR MEDICAL DEVICES."

Figure 2: The supplier-converter-brand owner triangle.

WHY COLLABORATION MATTERS: THE SUPPLIER-CONVERTER-BRAND OWNER TRIANGLE

Pharma packaging risk management works best when all three parties collaborate, and the earlier the collaboration, the better (Figure 2). An experienced pharmaceutical label material supplier will bring formulation stability, regulatory awareness, documented test data and global supply consistency to the triangle. The right converter will bring converting, printing excellence and process control, as well as guidance on the label material selection. The brand owner brings their product knowledge, quality requirements and regulatory compliance needs. When it comes to the label application to pharmaceutical packaging, experienced label material suppliers will also be able to provide their support and expertise.

When the three parties collaborate early, correct material recommendations will be made right from the start. As a result,

label validation becomes smoother and change management prevents repetitive validations. Also, product launches face fewer surprises and supply continuity becomes more resilient. However, these collaboration benefits are not met when converters use standard materials from suppliers who cannot deliver regulatory documentation, do not prioritise formulation stability or frequently shift raw materials without controlled notification.

CHANGE MANAGEMENT: THE HEART OF PHARMA-DEDICATED MATERIALS

One of the most important benefits of choosing pharma-dedicated label materials from a reliable supplier is pharma-grade change management. Pharmaceutical products have long lifecycles and unplanned material changes can be highly disruptive. Thus, the stability window required by pharma companies must span several years.

A case in point is UPM, one of the leading suppliers of pharma-dedicated label materials, which commits to stabilising formulations over extended periods, formalised change notification frameworks that align with pharmaceutical requalification needs and detailed documentation of modifications, their potential impacts and rationales.

MATERIAL INTEGRITY SUPPORTED BY EXPERIENCED PARTNERS

Converters play a critical role in how labels are applied, processed and printed, but the foundation of reliable performance begins with the materials themselves. That foundation is only as strong as the materials, quality systems and manufacturing discipline behind the label stock.

When brand owners and converters choose label materials from trusted suppliers with a long history in regulated markets, they benefit from the stability and transparency that underpin dependable pharmaceutical packaging. Although there are many advantages to working with an experienced supplier such as UPM, the most important ones are: controlled formulations that remain unchanged over long product lifecycles, an extensive support package with data for E&L studies and regulatory submissions, and robust systems to provide consistent quality and traceability to the label coil level if needed. An additional benefit is having a resilient global supply that reduces the risk of shortages or disruptions affecting label availability.

Figure 3: Pharma-dedicated label materials are backed by testing and documentation required for patient safety.

By partnering with an experienced pharma-dedicated label materials supplier, brand owners ultimately gain confidence not only in the label itself but in the expertise, processes and diligence behind it (Figure 3). Think of the importance of supplier choice like this: a label may cover only a few square centimetres, but the trust behind it must span continents, decades and regulatory boundaries.

The pharmaceutical packaging landscape is evolving and further highlighting the case for pharma-dedicated labels as non-negotiable risk-mitigation tools. By choosing pharma-dedicated label materials, converters and brand owners can reduce performance and compliance risks, avoid requalification caused by uncontrolled material changes and build greater confidence throughout the product lifecycle.

Paavo Sillanpää

Paavo Sillanpää, Senior Advisor for Pharma & Healthcare at UPM Adhesive Materials, has more than 25 years of experience in the label industry, covering labelling needs across multiple sectors. He currently focuses on developing solutions for pharmaceutical and healthcare labelling applications and supporting brand owners in label material selection and qualification processes. Based in Europe, Mr Sillanpää has gained a global understanding of market requirements both by living and working in Asia and the US.

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ADVANCING AUTOINJECTOR PLATFORMS FOR EVOLVING DRUG AND PATIENT NEEDS

MGS Healthcare Manufacturing

Martin Høier Thomsen of **MGS** introduces the company's A.i.r. Platform™ within the broader context of the evolution of autoinjector platforms towards more adaptable, customisable solutions. He considers how next-generation autoinjector platforms can address increasingly complex and changing demands, while helping to mitigate risk and prioritise usability.

Platform-based autoinjectors have enabled efficient and scalable device development, but evolving drug and patient needs are testing the underlying design assumptions. By using established off-the-shelf autoinjector platforms, pharmaceutical companies have been able to reduce technical risk, streamline regulatory pathways and accelerate development timelines. Compared with bespoke device development, such platform approaches can offer advantages in cost and speed, establishing them as a widely adopted solution across the industry.

Within this landscape, the pace and complexity of drug development are reshaping expectations for device innovation. Pipelines are increasingly being defined by advanced biologics, higher-viscosity formulations and more specialised delivery requirements that, in some cases, extend beyond the capabilities of existing autoinjector platforms. At the same time, there is a constant focus on improving the use of autoinjectors and minimising risks of misuse as part of the overall treatment experience. There is also a greater focus on differentiation, with devices viewed not only as delivery mechanisms but as integral components of the overall patient experience and as extensions of the brand that can help to distinguish the product.

However, many existing autoinjector platforms are designed within fixed technical parameters, which limits their flexibility to address the specific needs of niche patient populations and drug specifications outside of typical use scenarios. This can force trade-offs where either the drug must be adapted to fit the device or the device cannot

fully support the intended therapeutic profile. Addressing these new requirements will depend on close collaboration between pharmaceutical companies and drug-device development partners.

In response, the next generation of drug delivery platforms is being designed to expand capabilities to accommodate increasingly complex therapies and evolving delivery requirements. These systems need to be built for adaptability, enabling devices to be configured around the specific needs of the therapy and patient. Combining a core technology with flexible, modular design, means that these platforms can enable more comprehensive customisation across a broader set of drug, device and patient variables.

ALIGNING DEVICE PERFORMANCE WITH USER EXPECTATIONS

While autoinjector designs continue to improve, usability challenges remain, especially in how patients interpret – or misinterpret – audible feedback during injection. This continues to be a key focus for regulatory authorities when evaluating new device iterations.

Existing autoinjectors often rely on a two-click feedback system to signal dose progression. However, there can be a delay of up to two seconds between the final audible click and actual dose completion. To mitigate this, the instructions for use direct patients to count several seconds after the final click before removing the device. This introduces variability in interpretation and execution, and regulatory bodies have raised concerns that such instructions can be misunderstood during real-world use. This creates a persistent risk of early lifts, which can result in potential underdosing, with patients perhaps perceiving this as device failure and raising complaints with the pharmaceutical company (Figure 1).

These challenges highlight the need for closer alignment between device behaviour and user expectations, particularly in how device feedback reflects dose progression and completion. Early lift and incomplete dosing are often driven by this misalignment, as patients may rely on audible clicks rather than visual cues and therefore may not observe the full depression of the plunger rod that indicates dose completion.

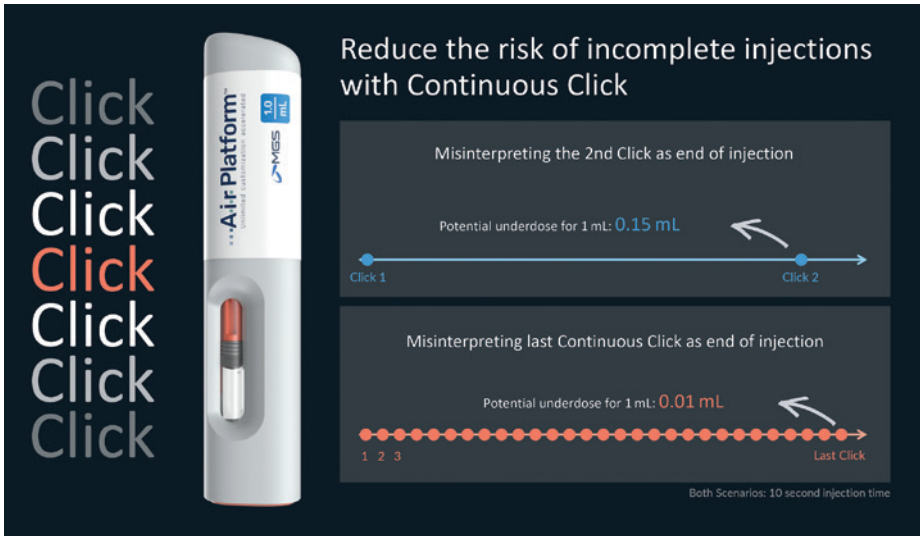

Figure 1: Continuous audible feedback throughout the injection process improves alignment between perceived and actual dose completion.

One way to address these challenges is to implement a continuous audible feedback system throughout the injection process to completion. By minimising the gap between perceived and actual dose completion, this approach can mitigate the risk of underdosing while improving user confidence, adherence and training simplicity.

User experience must also account for variability across patient populations. The requirements for a caregiver administering a paediatric dose differ significantly from those of an adult self-administering a chronic therapy, where limited dexterity may impact use. These differences influence how the device is handled, understood and trusted.

Addressing this requires greater flexibility in how key aspects of device performance are defined. A more adaptable platform enables customisation of key performance parameters, including activation force, hold force, needlestick depth and injection time, helping to ensure that all aspects of the device are designed to fit specific patient needs and expectations.

ADAPTING TO THE DRUG PROFILE

As drug formulations evolve, delivery devices must accommodate a broader range of therapeutic requirements. Drug pipelines now span a wider range of viscosities, concentrations and delivery volumes than those which many existing platforms were designed to support.

Historically, autoinjector platforms were optimised for a narrow range, often centred on a 1 mL fill volume and moderate viscosities. Today, requirements are expanding in both directions. Lower-volume injections, typically 0.2–0.5 mL, are common for highly potent therapies as well as paediatric applications. At the other end, for higher-volume delivery – up to 2.25 and even 5 mL – prefilled syringes are increasingly common for biologics.

Viscosity profiles are also shifting, with many emerging biologics exhibiting higher viscosities that increase injection force requirements, extend injection times and place greater demands on device performance. A more adaptable platform can enable devices to be configured around the therapy, supporting a wider range of

"THE REQUIREMENTS FOR A CAREGIVER ADMINISTERING A PAEDIATRIC DOSE DIFFER SIGNIFICANTLY FROM THOSE OF AN ADULT SELF-ADMINISTERING A CHRONIC THERAPY, WHERE LIMITED DEXTERITY MAY IMPACT USE."

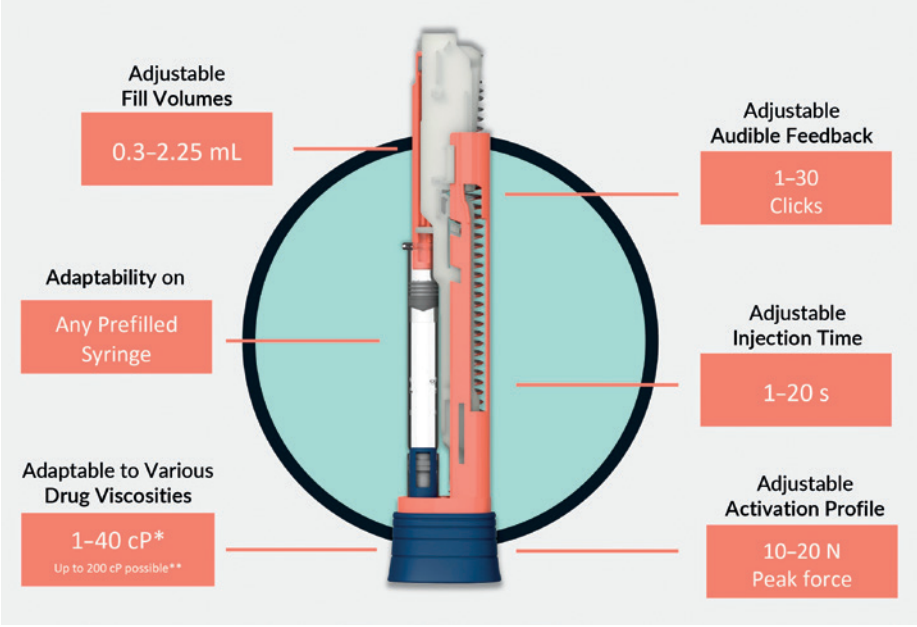

Figure 2: Core technology adaptability across key parameters. *For a 27G with a Special Thin-Wall needle and accepting up to 11 s injection time. **For a 25G needle with an Ultra Thin-Wall needle and accepting up to 16 s injection time.

viscosities and volumes while remaining compatible with virtually any prefilled syringe configuration. This adaptability reduces the need for reformulation driven by device limitations, preserving drug integrity while minimising development complexity, cost and risk (Figure 2).

DESIGNING FOR PATIENT EXPERIENCE AND PRODUCT DIFFERENTIATION

As more therapies enter highly competitive markets, the delivery device is becoming a critical point of distinction, influencing how patients engage with, adhere to and perceive the therapy. As a result, pharmaceutical companies are placing greater emphasis on differentiation at the device level.

For therapies that require frequent or long-term self-administration, the device becomes part of the patient's daily routine. Factors such as ease of use, perceived reliability and emotional response can directly influence patient confidence and adherence. Differentiation is not only a commercial objective but also a clinical one, supporting correct use and reducing anxiety to improve patient outcomes.

The increasing complexity of drug formulations and delivery requirements is driving greater variability in device design. Differences in injection time, activation force, injection volume, use environment and user capabilities often necessitate changes in device configuration, size and user interface. As these functional elements evolve, they create an opportunity to align device design more closely with the therapy and intended patient population.

A customisable platform enables this alignment by providing control over both visual and structural design elements. This includes colours, surface textures and material finishes that support brand identity, as well as the ability to adapt device geometry, proportions and interface features. Rather than addressing branding as a late-stage design consideration, these elements can be integrated from the outset.

Pharmaceutical companies are increasingly managing pipelines that span multiple therapies and patient populations. Flexible platforms enable consistency in device design and user interaction across a product portfolio, while allowing differentiation where needed. Variations in size, ergonomics, colour and interaction cues can distinguish patient populations and therapies, while supporting usability and maintaining overall brand cohesion.

These design decisions must be grounded in real-world use. For example, devices for paediatric patients may require softer geometries, simplified interfaces and more reassuring visual cues, while those for adult or chronic use may prioritise discreteness, portability and consistency. In both cases, visual and tactile elements shape how the device is understood and trusted by the user.

ADVANCING SUSTAINABILITY THROUGH DESIGN EFFICIENCY

Increasingly, sustainability is being integrated into autoinjector platform design, as regulatory signals, corporate environmental, social and governance commitments, and lifecycle considerations begin to shape development priorities.

Design efficiency plays a central role in this shift. Reduced part count and the integration of multiple functions into fewer components enable simpler assembly, improved manufacturing efficiency and lower overall material usage. Optimising device size and design further supports these efforts without compromising performance or safety, reinforcing the need for platform designs that can balance efficiency with the flexibility required for therapy-specific customisation.

Material selection is also evolving, with increased use of lower-emission polymers aimed at reducing environmental impact across the product lifecycle. For autoinjector platforms, these materials must balance performance and cost while meeting regulatory and safety requirements for biocompatibility and consistent manufacturing.

"INCREASINGLY, SUSTAINABILITY IS BEING INTEGRATED INTO AUTOINJECTOR PLATFORM DESIGN, AS REGULATORY SIGNALS, CORPORATE ENVIRONMENTAL, SOCIAL AND GOVERNANCE COMMITMENTS, AND LIFECYCLE CONSIDERATIONS BEGIN TO SHAPE DEVELOPMENT PRIORITIES."

End-of-life considerations also remain a key challenge for autoinjector platforms. Due to the complex mix of components, including needles, glass, multiple plastics and biohazardous materials, many devices are currently directed to incineration rather than recycling. In response, pharmaceutical companies are exploring take-back programmes to enable more sustainable disposal. While these initiatives depend on sufficient return volumes, they represent an important step towards more sustainable solutions. In parallel, there is growing interest in design approaches that could reduce the overall CO_2 footprint by enabling safe, user-guided separation of select components, while ensuring patient safety.

A CUSTOMISABLE PLATFORM APPROACH TO AUTOINJECTOR DEVELOPMENT

As drug formulations and delivery requirements continue to diversify, closer collaboration between platform owners and pharmaceutical companies is becoming essential to accommodate more complex and specialised use cases, including high-viscosity formulations, larger volumes and lower production scales.

The A.i.r. Platform™ developed by MGS is a prime example of this approach. This modular autoinjector platform accelerates combination product development while enabling comprehensive customisation across drug, device, patient and brand requirements. The platform is built around an adaptable core technology that provides a mechanical foundation, enabling co-development with MGS to tailor devices for different applications without redesigning the underlying system.

By using the A.i.r. Platform™'s core technology as a starting point and focusing development on configurable platform elements, pharmaceutical and biotech companies can reduce device development timelines by up to three years compared with bespoke devices. To support early-stage decision-making, the platform incorporates a structured feasibility model in which moulded, functional prototype devices can be delivered within 12 weeks.

MGS developed the A.i.r. Platform™ using insights from 14 therapeutic areas within subcutaneous drug delivery, informed by feedback from clinicians and patients along with regulatory guidance and US FDA observations. These insights highlighted ongoing challenges in existing systems, including early lift, incomplete injections and uncertainty during administration, all of which can negatively impact patient confidence and adherence. As pharmaceutical companies develop new therapies in these areas, the pre-developed documentation by MGS can be readily adapted, enabling more efficient device development and accelerated timelines.

FLEXIBLE DESIGN TO SUPPORT DIVERSE FORMULATION, USER AND BRAND NEEDS

The A.i.r. Platform™ supports extensive customisation across key performance parameters. Injection time, activation profile and delivery force can be adapted to accommodate a wide range of formulations, including higher-viscosity biologics. Fill volumes ranging from 0.3 to 2.25 mL allow developers to tailor delivery profiles for different dosing requirements, while compatibility with any prefilled syringe configuration needed provides flexibility in primary container formats.

> "A KEY FEATURE OF THE A.i.r. PLATFORM™ IS ITS CONTINUOUS AUDIBLE FEEDBACK MECHANISM, WHICH PROVIDES UP TO 27 CLICKS THROUGHOUT THE INJECTION PROCESS."

A key feature of the A.i.r. Platform™ is its continuous audible feedback mechanism, which provides up to 27 clicks throughout the injection process. Unlike two-click systems where the final signal may precede dose completion, this continuous feedback closely tracks dose progression through to completion. This design improvement reduces the gap between the perceived and actual end of injection, which mitigates underdosing. As not all patients visually monitor the device during injection, continuous audible feedback is critical.

Beyond performance, the platform enables customisation of device size, ergonomics and appearance, including cap and needle shield design, body geometry, surface textures, colour systems, window configuration and brand embossments. This allows devices to align with both patient needs and brand strategy while supporting clear differentiation within the market. These capabilities are particularly important across patient populations (Figure 3).

Figure 3: Customisation enabled by the MGS A.i.r. Platform™.

Underlying this flexibility is a streamlined device design that also enables more efficient and sustainable development. The platform uses just seven plastic parts and two springs, reducing material usage and device size, while incorporating optional material separation to enable partial end-of-life recyclability.

REDEFINING PLATFORM-BASED DEVELOPMENT TO ACCELERATE DE-RISKING AND CUSTOMISATION

The evolution of autoinjector platforms towards more adaptable, customisable solutions reflects a focused approach to address and mitigate persistent development risks. Early-stage autoinjector designs inherently carry uncertainty, making it critical to rapidly de-risk concepts and establish confidence in device performance and usability. Platforms such as A.i.r. Platform™ enable this by allowing pharmaceutical and biotech companies to move quickly from concept to a moulded, functional autoinjector with prototypes available in as little as 12 weeks. This enables early user testing, informed stakeholder engagement and a tangible understanding of the device, accelerating decision-making and reducing reliance on purely conceptual development.

Next-generation autoinjector platforms must address increasingly complex and evolving demands. Meeting these challenges requires new approaches to device design that prioritise usability, reliability and risk mitigation with the flexibility to support diverse patient populations, advancing therapies and regulatory expectations. Close collaboration between pharmaceutical companies and platform owners will be essential to establish a new standard for how combination products are developed and delivered in practice.

Martin Høier Thomsen

Martin Høier Thomsen is a Device Platform Manager on MGS' Design & Development team where he plays an integral role in advancing early-phase medical device solutions from concept through realisation. He is widely recognised for his ability to translate concepts into market-ready products and his commitment to sustainable, patient-centric innovation. Mr Høier Thomsen has been instrumental in the development of MGS' new customisable autoinjector A.i.r. Platform™, drawing on his deep technical expertise and human-centred approach to guide the design from concept to functional reality. Before joining MGS, he served as a line manager at LEO Pharma, where he built in depth knowledge of product development and what matters most to pharma innovators.

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Early Insight

EXCIPIENT LANDSCAPES: HIGH-THROUGHPUT SCREENING TO SOLVE VISCOSITY BOTTLENECKS FOR BIOLOGIC THERAPEUTICS

AEMS
Formulation Engineering

Dr Scott Compel and **Dr Alex Hendricks** of **AEMS Corp** discuss the company's automated, microscale screening platform that enables viscosity reduction, using innovative approaches to test excipient combinations effectively.

Next-generation therapeutics, from small interfering RNAs (siRNAs) to antibody-drug conjugates, are moving towards subcutaneous (SC) self-administration. Viscosity remains a persistent bottleneck. Today's excipient-based approaches to solving viscosity problems leave the vast majority of the formulation space uncharted.

AEMS has introduced an automated, microscale screening platform that draws on tools from materials science and machine learning (ML) to navigate the multicomponent excipient space to identify optimal formulation components that conventional methods can miss. The platform provides development teams with the data they need to reduce viscosity, de-risk device pairing and advance stalled programmes while making efficient use of scarce drug substances.

THE VISCOSITY BARRIER IN NEXT-GENERATION THERAPEUTICS

The shift from clinic-based intravenous (IV) infusion to SC self-administration is well established. SC biologics account for more than half of the global biologics market, exceeding US$250 billion (£185 billion) in annual drug revenue out of a total sector valued at roughly $487 billion.[1,2] The advantages are clear: patients gain autonomy, clinical burden drops and adherence improves.[3]

However, SC delivery for high-dose therapeutics comes with hard physical constraints. Standard prefilled syringes (PFSs) and autoinjectors hold fluid volumes of 1–2 mL, which correlates to the maximum volumes that can conventionally

be injected into SC tissue.[3] Fitting a full therapeutic dose into that volume often means pushing API concentrations above 100 mg/mL.[3] At these concentrations, molecular crowding and drug-drug (or drug-excipient) interactions cause viscosity to rise steeply and non-linearly (Figure 1).[4,5]

Once viscosity exceeds roughly 20 cP, a commonly cited threshold for SC delivery through 27G needles,[5] the downstream problems multiply: injection forces climb, administration takes longer, patient discomfort increases and the mechanical load on injection devices can lead to stalling or syringe failure. If the viscosity problem cannot be solved, drug programmes stall. In many cases, programmes may abandon the SC route and default to IV administration, or alternatively may never reach the market.[4]

This is not just a monoclonal antibody (mAb) problem.[6] For other high-concentration biologics, viscosity, stability and excipient interactions become critical constraints. Peptide therapeutics – a sector valued at $50 billion in 2025 and projected to nearly double by 2034[7] – face growing viscosity and stability challenges as formulations push towards higher concentrations for SC delivery.[8] siRNA therapeutics face analogous hurdles. While all six US FDA-approved siRNA drugs currently target the liver via N-Acetylgalactosamine conjugates, the push towards broader tissue delivery is introducing new formulation complexity regarding stability, excipient compatibility and delivery vehicle optimisation.[9] The siRNA sector was valued at $2.7 billion in 2024 and is projected to reach $12.6 billion by 2033.[10] As viscosity is governed by the physical interactions between molecules and excipients rather than by any single drug class, insights gained for one modality translate directly to others. AEMS's screening platform is agnostic to the biomolecules being studied: the same combinatorial methods and ML models that optimise a mAb formulation generate transferable knowledge about excipient behaviour that accelerates screening for peptides, siRNA and other emerging modalities.

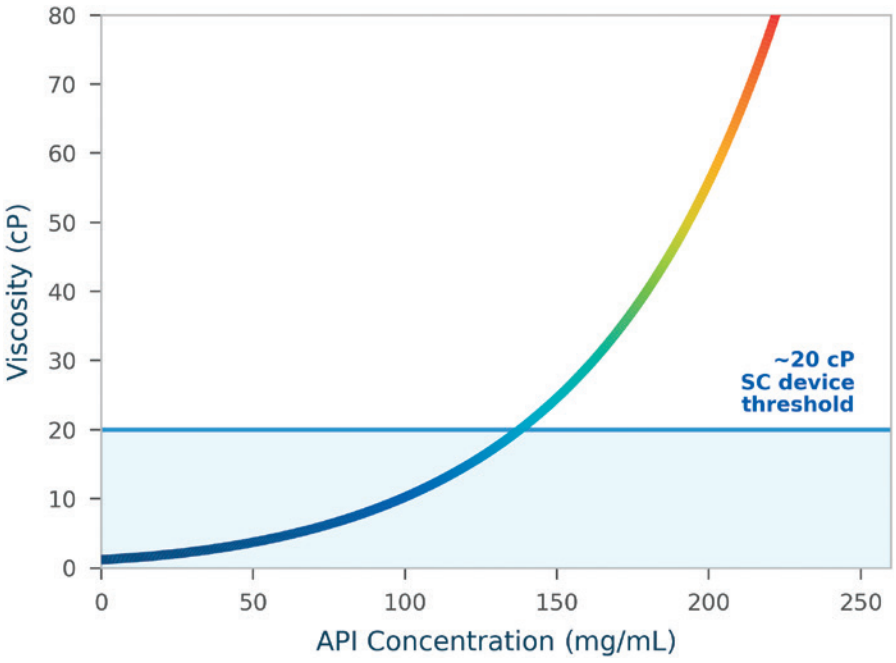

Figure 1: Relationship between biologic API concentration and formulation viscosity, illustrating the device-feasibility threshold for standard SC delivery.

CURRENT APPROACHES LEAVE MOST OF THE FORMULATION SPACE UNEXPLORED

The most advanced viscosity-reduction technologies currently on the market operate in a two-component space. Merck's (Darmstadt, Germany) Viscosity Reduction Platform, for example, offers curated excipient pairs: one excipient selected from a first group and another from a second group, yielding a small set of predefined binary combinations.[11] This is a real advantage over single-excipient strategies, as these platforms have shown that paired excipient synergies can reduce viscosity more than either component alone.

The issue is scale. Pharmaceutical formulators routinely work with around 40 FDA-approved excipients for parenterals. Pairwise combinations of those 40 excipients yield roughly 780 unique pairs. Step up to three-component systems and the number jumps above 9,800. Once varying ratios and concentrations are factored in, the number of accessible formulation conditions becomes essentially limitless. This is both the opportunity and the problem. A space this large offers countless levers to tune towards a desired viscosity target, but no established tools exist in pharma to systematically explore it beyond two components.

AEMS's work solving complex formulation problems has repeatedly shown that the best viscosity outcomes often hide in the three-, four- or five-component space. Small changes in excipient selection, buffer concentration or surfactant ratio can evoke large, non-linear effects. Two-component screening methods cannot detect these multi-parameter synergies. Sequential trial-and-error cannot reach them without burning months and large amounts of API.

The problem is clearest in early development, when SC-versus-IV decisions must be made at pilot manufacturing stages when limited drug substance is available

"THE PUSH TOWARDS BROADER TISSUE DELIVERY IS INTRODUCING NEW FORMULATION COMPLEXITY REGARDING STABILITY, EXCIPIENT COMPATIBILITY AND DELIVERY VEHICLE OPTIMISATION."

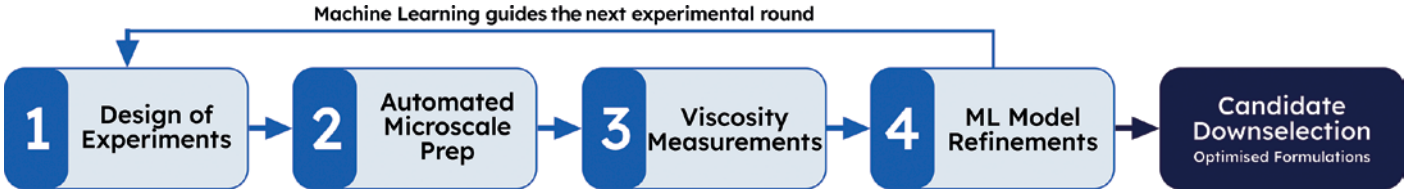

Figure 2: The AEMS iterative formulation workflow. Every experiment feeds a ML model that sharpens the next round of screening. Custom software automates the full cycle, from design of experiments through preparation, measurement and model update, enabling hundreds of experiments per week with minimal hands-on time.

for formulation experiments. When the material runs out before the formulation space has been adequately explored, teams default to suboptimal formulations based on incomplete data, embedding stability and manufacturing risks into the programme that are costly to correct later.[12,13]

THE AEMS APPROACH: MATERIALS SCIENCE MEETS PHARMACEUTICAL FORMULATION

Navigating an effectively limitless formulation space requires tools that the pharmaceutical industry has not traditionally used. AEMS brings expertise from materials science, where researchers have spent decades developing systematic approaches to engineer multicomponent systems. The study of metallic alloys and composite materials in particular has produced well-established methods for mapping property landscapes across three or more interacting components. These methods are high-throughput combinatorial screening, phase-diagram construction and statistical models for multicomponent optimisation.[14,15]

AEMS adapts these methods for pharmaceutical formulations, combining them with ML trained on formulation screening data. The ML models identify molecular trends that guide each round of experiments towards the most productive chemical choices, rather than exhaustively testing every possible combination. This iterative, model-guided approach (Figure 2) is what makes it practical to work with three or more components, using FDA-approved excipients favoured by industry.

The ML capability is not speculative. In a Small Business Innovation Research (SBIR)-funded collaboration with the University of California (UC), Davis, (US) AEMS used its ML-guided screening platform to develop novel antimicrobial seed coatings from mixtures of food-grade, Generally Recognized As Safe organic acids. The models identified multicomponent formulations whose synergistic effects achieved 100-fold pathogen reductions on alfalfa sprouts, outperforming any single acid while simultaneously improving germination rates and sprout mass relative to the industry-standard chlorine treatment.[16]

The underlying problem was the same one AEMS now addresses for injectable biologics: navigating multicomponent formulations to find combinations whose collective performance exceeds that which any individual ingredient can deliver. The tools that discovered synergistic antimicrobial coatings are the same tools now screening excipient combinations for viscosity reduction.

Two operational parameters make AEMS's approach viable for early-stage programmes:

- **Microscale Capability**: AEMS runs formulation experiments at volumes as low as 20 µL per experiment. This allows for broad, multidimensional screening while consuming only a small fraction of the drug substance that other methods would need. When early-stage API is expensive and scarce, this matters.
- **Throughput**: The automated pipeline supports over 600 unique experiments per week. Paired with ML-guided experimental design, this throughput turns what would normally take months of iterative screening into weeks of structured, data-rich exploration.

EVIDENCE OF EXECUTION

AEMS has applied its screening platform to formulations spanning mAbs, peptides and siRNA therapeutics. Figures 3 and 4 show representative ternary- and triangular-prism excipient maps generated from these campaigns. Each point represents a formulation screened at microscale (20 µL), with the resulting viscosity mapped across the combinatorial landscape. The diagrams reveal regions where specific excipient combinations produce viscosity reductions that no single component achieves alone – clear signals of synergistic interaction. These are not theoretical projections; they are experimental measurements drawn from AEMS's automated screening infrastructure, running over 600 formulations per week using exclusively FDA-approved excipients.

The temperature-dependent prism in Figure 4 illustrates a further advantage of high-throughput mapping. By screening the same excipient landscape at 4°C, 20°C and 40°C, AEMS can identify formulation regions where low viscosity persists, independent of temperature. Rather than optimising for a single condition and subsequently testing thermal robustness, the platform selects for thermal stability from the outset. The result is a formulation that performs under cold-chain storage, ambient handling and accelerated stability testing without requiring re-optimisation at each stage.

> "THE STUDY OF METALLIC ALLOYS AND COMPOSITE MATERIALS IN PARTICULAR HAS PRODUCED WELL-ESTABLISHED METHODS FOR MAPPING PROPERTY LANDSCAPES ACROSS THREE OR MORE INTERACTING COMPONENTS."

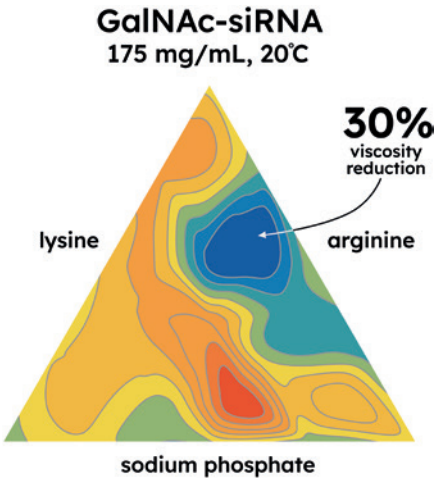

Figure 3: Ternary diagram showing relative viscosity of GalNAc-siRNA (175 mg/mL, 20°C) across combinations of three excipients. Synergistic low-viscosity regions (blue) emerge at specific multicomponent ratios that are not predicted by a single excipient's individual performance.

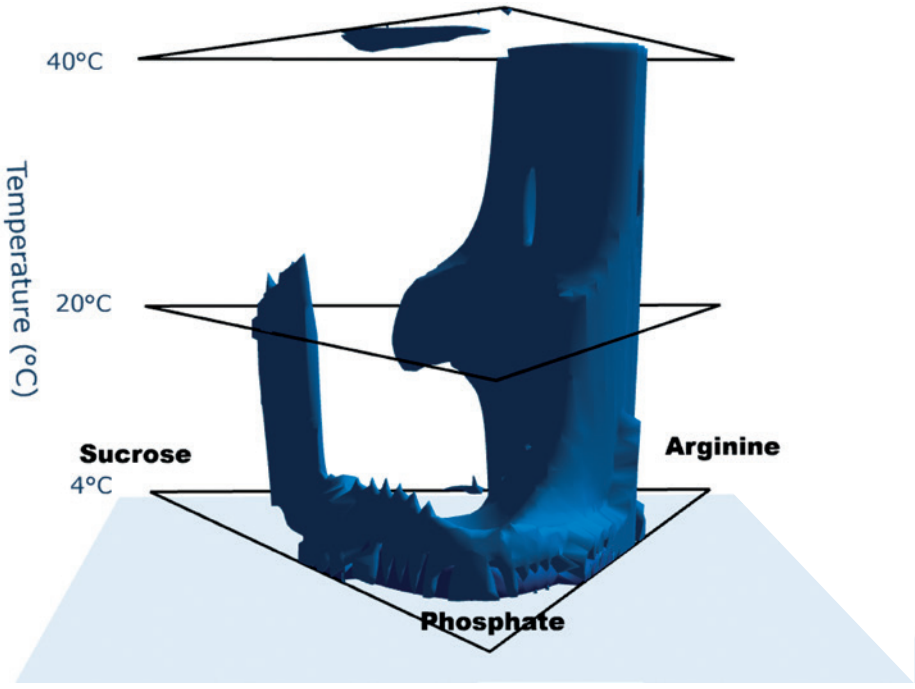

Figure 4: Temperature-dependent ternary prism showing relative viscosity of 175 mg/mL Immunoglobulin G across combinations of three excipients at 4°C, 20°C and 40°C. By overlaying the three temperatures, the platform identifies formulation regions (blue) where low viscosity is maintained independent of temperature. This approach selects for thermal robustness during primary screening rather than verifying it downstream, reducing the risk of late-stage reformulation.

IMPLICATIONS FOR DEVICE AND COMBINATION PRODUCT DEVELOPMENT

Solving viscosity early changes device development entirely. When device engineers receive an optimised, low-viscosity formulation, the hardware picture simplifies. Viscosity below the standard SC threshold means commercially available PFSs work, and finer-gauge needles (27G or thinner) become an option, improving patient comfort.[17]

For teams evaluating SC feasibility for high-dose siRNA or biologic programmes, AEMS provides the viscosity data needed to make a confident route-of-administration call early, before committing to a specific device architecture or regulatory pathway. Furthermore, because the platform works exclusively with FDA-approved excipients, optimised formulations carry no additional excipient-related approval risk.

The practical result is not a single "magic excipient". It is a systematic, data-driven navigation of chemical combinations that locates multicomponent interactions, while preserving flexibility for manufacturing, compatibility and regulatory requirements. Early screening data suggest that certain excipient combinations reduce viscosity across structurally distinct biologics, pointing towards underlying interaction principles that may reach beyond any single molecule. As the dataset grows, AEMS expects these recurring patterns to coalesce into reusable formulation starting points that accelerate development timelines for new candidates, regardless of modality.

> "SOLVING VISCOSITY EARLY CHANGES DEVICE DEVELOPMENT ENTIRELY. WHEN DEVICE ENGINEERS RECEIVE AN OPTIMISED, LOW-VISCOSITY FORMULATION, THE HARDWARE PICTURE SIMPLIFIES."

CONCLUSION

- **The Viscosity Barrier is Real and Growing:** High-concentration biologics routinely hit viscosity limits that block SC delivery and standard device compatibility.
- **Two-Component Screening is Not Enough:** Current approaches cover only a tiny fraction of the available excipient combinations. Finding the most effective formulations often requires screening three or more components.
- **Materials Science and ML Tools Show the Way:** AEMS applies combinatorial screening methods and ML, validated in a published, SBIR-funded collaboration with UC Davis.
- **Insights Transfer Across Modalities:** Early data suggest that excipient combinations effective for one biologic class reduce viscosity in others, pointing towards reusable formulation starting points that accelerate future campaigns.
- **Microscale Precision Preserves Scarce Material:** Performing over 600 experiments per week at 20 µL volumes enables comprehensive, multi-dimensional screening using only FDA-approved excipients, without depleting early-stage drug substance.

- **The Platform Screens for Thermal Robustness from the Start:** By mapping viscosity across temperature simultaneously, AEMS identifies formulations that hold up under cold-chain storage, ambient handling and accelerated-stability conditions, reducing the risk of late-stage reformulation.

ABOUT THE COMPANY

AEMS Corp offers automated, microscale formulation screening for injectable biologics. The company maps multicomponent excipient space using combinatorial design and machine learning to identify low-viscosity formulations suitable for subcutaneous delivery. Their services span monoclonal antibodies, siRNA and peptides, using only FDA-approved excipients.

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Alex Hendricks, PhD, is Co-Founder and Chief Innovation Officer of AEMS Corp. With a background in chemistry and biology, he translates AEMS's core screening and modelling technologies into market-ready service offerings. His work centres on identifying where the platform creates the most value for formulation partners and shaping new product lines around those opportunities.

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Kaléo is a global drug-delivery device company, providing innovation in the field of autoinjector technology. Kaléo's patented Aerio™ platform, with a novel configuration and extensive human factors engineering, powers its portfolio of autoinjector products, as well as products under development for third parties.

See **Page 09**

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KERN LIEBERS is a medium-sized family business headquartered in southwestern Germany. Its Smart Springs and Smart Parts are intelligent functional components developed to meet the highest technical requirements and deliver maximum functionality. Each spring and each part not only fulfills a specific task – it also assumes responsibility for the functionality and reliability of the entire system at over 40 locations worldwide.

See **Page 05**

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Kindeva Drug Delivery is a global CDMO focused on drug-device combination products. The company develops and manufactures products across a broad range of drug-delivery formats, including pulmonary and nasal, injectable and transdermal. Its service offerings span early-stage feasibility through to commercial-scale drug product fill-finish, container closure system manufacturing and drug-device product assembly.

To learn more, see **Page 76**

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Lifecore is a CDMO specialising in the development, fill/finish and commercialisation of sterile injectables, biologics, medical devices and combination products. With an over 40-year regulatory track record and more than 20 commercial products, Lifecore offers end-to-end services including formulation process development, aseptic fill/finish, analytical, packaging and stability studies. Capabilities include expertise with highly viscous products.

To learn more, see **Page 38**

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LTS develops and manufactures drug delivery systems for pharma partners, with a focus on transdermal therapeutic systems, oral thin films, micro-array patches, wearable injectors, nasal and sterile dosage forms. Its systems are applied in more than 40 marketed products.

To learn more, see **Page 96**

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MGS is a global healthcare CDMO dedicated to transforming its clients' challenges into innovations that improve lives. With deep expertise and vertically integrated global capabilities, MGS accelerates innovation for leading pharma, diagnostic and medtech innovators, bridging the gap between imagination and realisation with precision, quality and efficiency.

To learn more, see **Page 111**

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

To learn more, see **Page 90**

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PCI Pharma Services is a global contract development and manufacturing organisation that provides integrated end-to-end drug development, manufacturing and packaging solutions to increase product speed to market and opportunities for commercial success. PCI's experience includes more than 90 successful product launches each year and over five decades in the delivery of supply chain healthcare services.

To learn more, see **Page 50**

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Phillips Medisize, a Molex company, collaborates with leading medical technology, pharmaceutical and *in vitro* diagnostic companies to design, engineer and manufacture lifesaving innovations. As a CDMO, the company leverages 60 years of expertise and capabilities and a global presence to help millions live healthier, more productive lives.

To learn more, see **Page 45**

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

To learn more, see **Page 85**

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Syntegon is a packaging solutions provider for the global pharmaceutical and food industries. In the pharma sector, the company offers solutions for the processing, filling, inspection and packaging of liquid and solid pharmaceuticals. Syntegon has a comprehensive service portfolio that covers the entire machine lifecycle from spare parts management to digital line optimisation.

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UPM Adhesive Materials provides high-performance, innovative self-adhesive products, including label materials for pharmaceutical packaging and medical devices such as prefilled syringes and injection pens. When brand owners and converters choose materials from UPM – which has a long history in regulated markets – they benefit from the stability and transparency that underpin dependable pharmaceutical packaging.

To learn more, see **Page 106**

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With over 40 years of experience, **Ypsomed**'s comprehensive drug delivery device platforms consist of autoinjectors for prefilled syringes, disposable pens, reusable pen injectors, ready-to-use prefilled wearable patch injectors and injection devices for drugs in dual chamber cartridges. Ypsomed is well equipped to tackle digital healthcare challenges and has strategically invested in the development of connected solutions and therapy-agnostic digital device management services.

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More Spotlights overleaf

SHL MEDICAL

OUTSTANDING SPONSOR

SHL Medical designs, develops and manufactures self-injection solutions, such as autoinjectors, pen injectors and specialty delivery systems for large-volume and high-viscosity formulations. By partnering with leading pharma and biotech companies, SHL Medical will continue to develop and supply products and services to support, engage and oversee patients whose quality of life relies on innovative self-treatment therapies.

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To learn more, see **Page 10**

gerresheimer
innovating for a better life

KEY SPONSOR

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. Gerresheimer ensures the safe delivery and reliable administration of drugs to the patient. With around 13,600 employees and over 40 production sites in 16 countries, Gerresheimer has a global presence and produces locally for regional markets.

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To learn more, see **Page 22**

Quvara Medical

KEY SPONSOR

Quvara Medical is a UK-based CMO specialising in precision medical devices for injectable drug delivery. With over 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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To learn more, see **Page 16**

BD
Advancing the world of health™

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As a partner of choice for pharmaceutical and biotech companies across the globe, **BD Medical – Pharmaceutical Systems** provides a broad range of parenteral drug delivery systems including prefillable syringes, safety and shielding systems as well as advanced drug delivery solutions that help ensure pharma meets its drug delivery goals while considering drug complexity, viscosity and dosing volume.

To learn more, see **Page 30**

CREDENCE MEDSYSTEMS

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Credence MedSystems solves challenges in parenteral drug delivery. Its philosophy of Innovation Without Change® preserves existing processes and primary package components. The Companion platform includes needle-retraction, reuse prevention and usability features. The Dual Chamber platform simplifies delivery requiring reconstitution or sequential delivery. The Metered Dosing lineup enables precise microdosing in ophthalmics and aesthetics.

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More Spotlights overleaf

2026/27 Editorial Calendar

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

JUN Oral Drug Delivery DEADLINE: **May 21, 2026**	**JUL** Industrialising Drug Delivery DEADLINE: **May 28, 2026**	**SEP** Wearable Injectors DEADLINE: **Aug 6, 2026**
SEP/OCT Dual Chamber Delivery Systems DEADLINE: **Aug 20, 2026**	**OCT** Prefilled Syringes & Injection Devices DEADLINE: **Sep 3, 2026**	**OCT/NOV** Sustainability in Drug Delivery DEADLINE: **Sep 17, 2026**
NOV Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 1, 2026**	**DEC** Delivering Gene & Cell Therapeutics DEADLINE: **Nov 5, 2026**	**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**	IN WHICH ISSUE SHOULD ***YOUR*** COMPANY APPEAR?

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