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WEARABLE INJECTORS

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Front cover image, "Simulated use of Symbioze® on-body injector prototype.", courtesy Nemera (see this issue, Page 6). Reproduced with kind permission.

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Symbioze®

Smart and sustainable on-body injector platform

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OFFERING A SMART AND SUSTAINABLE ON-BODY INJECTOR FOR CHRONICALLY ILL PATIENTS

In this article, Cécile Gross, Global Category Manager, Parenterals, discusses the unmet drug delivery needs in chronic diseases, and details how Nemera's answer – the Symbioze® on-body injector – fulfils these needs.

When talking about chronic conditions and long-time treatments, diabetes frequently emerges as the first topic of conversation. This is unsurprising as it has been prevalent in medical discussions since the first insulin injection to a human being, which was administered a century ago. However, diabetes is not the only chronic disease that inflicts a cumbersome daily burden on patients' lives. On the drug development side, much progress has been made, with new medicines enabling a broader range of pathologies to be addressed with biologics, while on the delivery side, technical innovations and patient awareness have led to an increased variety of well-accepted devices.

So what's next? According to recent analysis,[1] the two key therapy areas of focus are oncology and immunology, with a compound annual growth rate estimated at approximately 10% through 2026. Oncology will offer new treatments, whereas immunology will benefit from an increased number of treated patients and several new products, before the arrival of biosimilars. Another fast-developing area is neurology, especially with novel therapies being developed for migraine, Alzheimer's disease and Parkinson's disease.

Apart from the rapid and continuous rise in biologics, three other major trends play a prominent role in the drug delivery devices field – home administration, digital connectivity and environmental sustainability. As a device manufacturer, Nemera's goal is to try to square this circle, integrating every constraint put forth both by its pharma partners and patients with chronic conditions.

> "Apart from the rapid and continuous rise in biologics, three other major trends play a prominent role in the drug delivery devices field – home administration, digital connectivity and environmental sustainability."

ADDRESSING THE FULL RANGE OF UNMET NEEDS WITH ONE DEVICE

The idea to offer a smart, sustainable on-body injector to chronically ill patients stems from the unmet need to simultaneously address the challenges of biologics, self-administration, connectivity and sustainability in a single device. The need for high volume delivery and the limitations of current injectable drug delivery devices have already been stated in previous articles.[2] Combined, these factors naturally lead to on-body injectors as the solution. They are ideal for the administration of biologics in general, and more specifically for the drugs used in therapeutic areas such as oncology, immunology, haematology, neurology and immuno-oncology.

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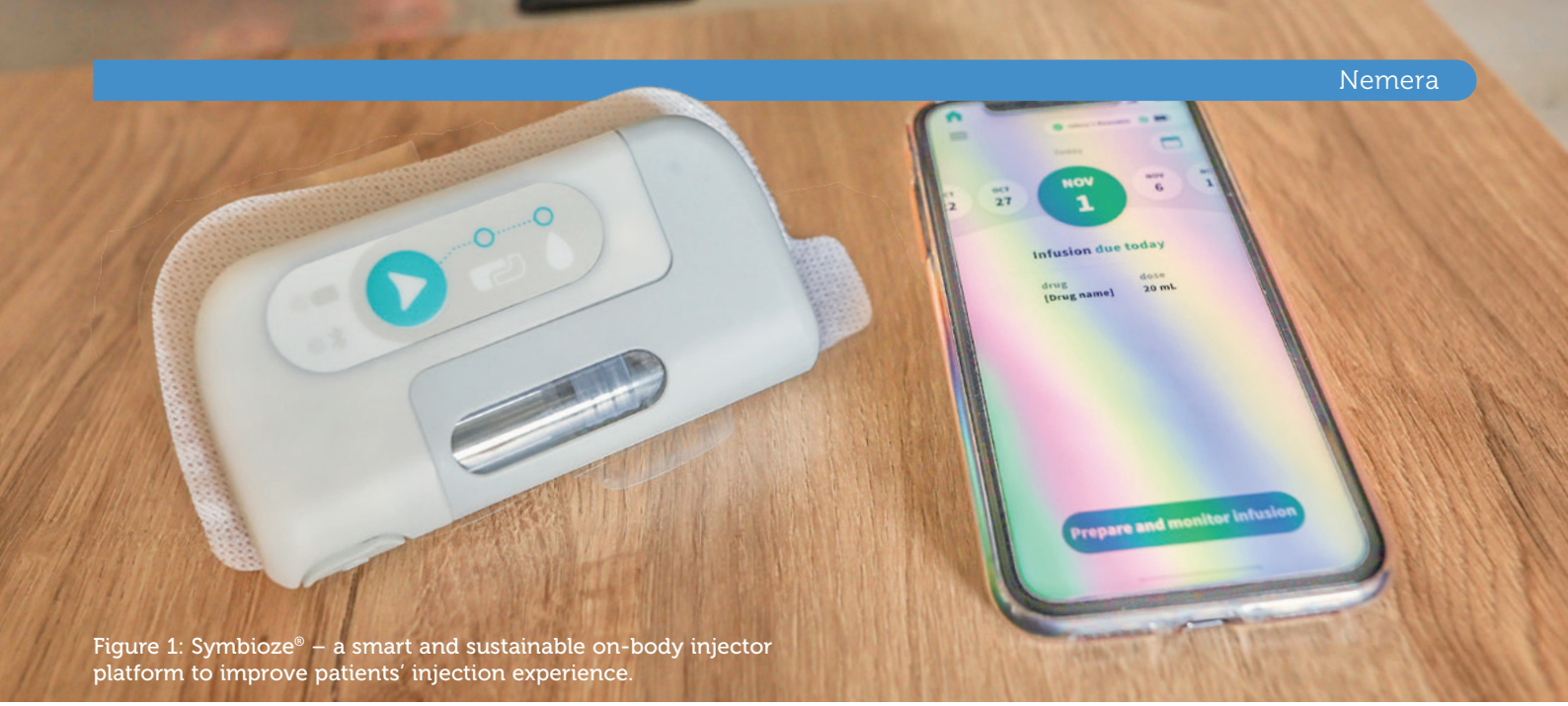

Figure 1: Symbioze® – a smart and sustainable on-body injector platform to improve patients' injection experience.

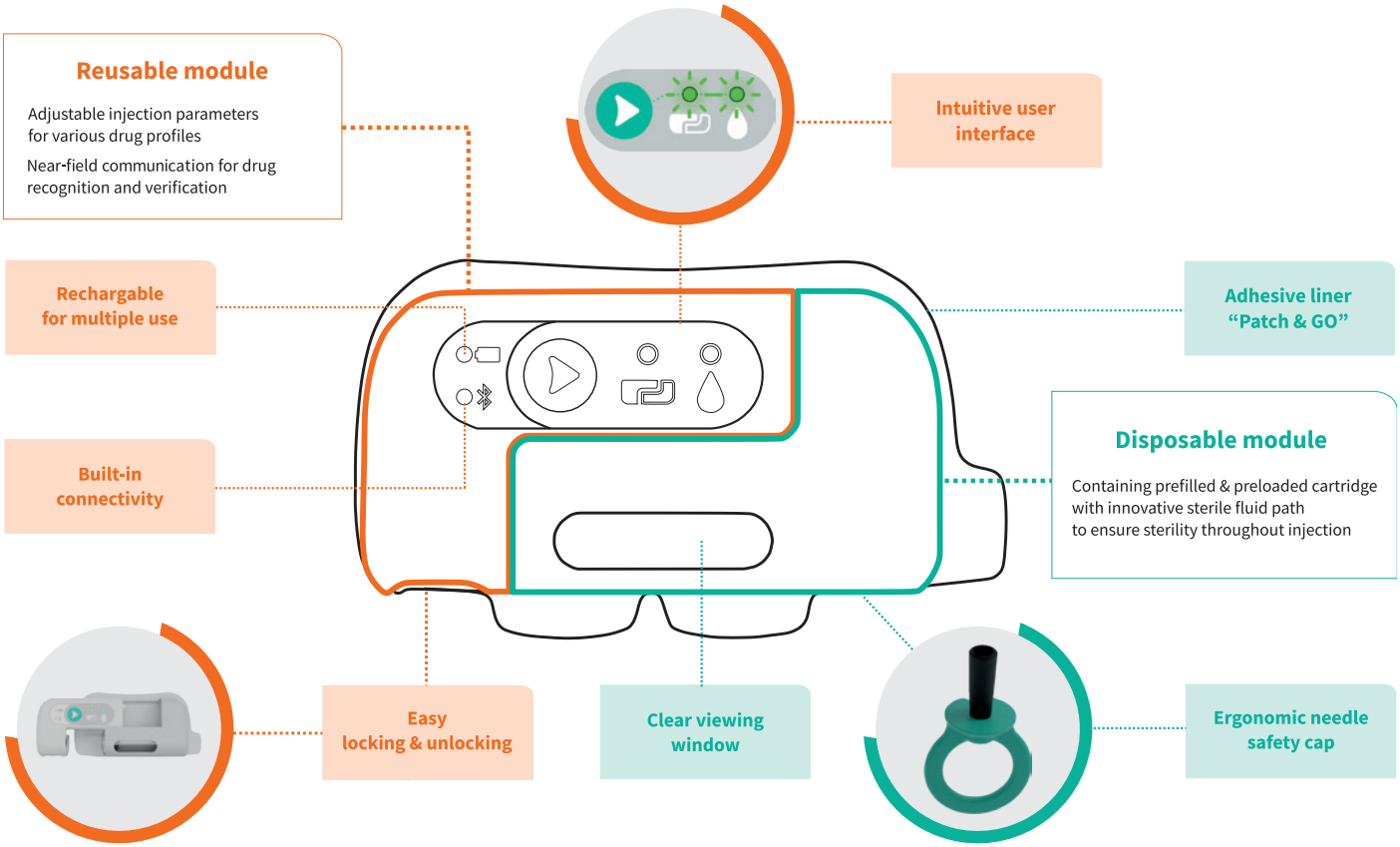

Figure 2: Symbioze® comprises a reusable and a disposable module, offering key benefits to administer complex drugs.

Nemera has chosen its own distinct way to address the challenges of high-volume self-administration. First, by studying the state-of-the-art technology in the field, it became clear that such a device could benefit from miniaturised electronic components. Just taking a look at recently released insulin pumps can provide an insight into what device developers are capable of today. Additionally, reliable large-volume primary drug containers are now available as a standard offering, which makes both in-house integration and compliance to pharma's fill-finish facilities easy.

From a user perspective, an on-body injection device should be ideal for administering multiple drug profiles for multiple uses, so integrating user needs from the start of development is crucial. Nemera has leveraged the expertise of its Insight Innovation Center[3] to map out the patient journey and set out a detailed human factors programme for the different phases of development, including the patient experience from healthcare professionals.

Referring to immuno-oncology, where ease of administration and cost of therapy have been identified as primary unmet needs, Nemera's final device design offers a user-friendly operating protocol and a combination of reusable and disposable modules – a perfect harmony for a device named Symbioze® (Figure 1).

SYMBIOZE®: THE ADDED-VALUE OF A PLATFORM APPROACH

Needless to say, implementing a platform strategy for a high-volume on-body injector has enabled Nemera to leverage baseline knowledge and generated data throughout

the development process. This platform can be tailored to a specific combination product to meet pharma customers' needs.

To be more precise, this added value can be detailed into:

- Broad device versatility
- Delivery and device customisation
- High compatibility with different primary drug container manufacturers
- Controlled development lead-time
- Acknowledged cost-effectiveness.

The main characteristic of the device is the split between a reusable module and a disposable one (Figure 2). The disposable module is totally linked with the drug and its injection. As such, all the features ensure proper, complete and safe administration of the dose.

Symbioze®'s near field communication connectivity feature provides reassurance for both users and pharma companies regarding the administration of the prescribed drug. The transparent window enables a clear visibility of the drug and its container prior to the injection, of the injection progress during the injection and of injection completion once the full dose is administered.

There is no need to load the primary drug container nor to adjust any parameter as the module comes pre-loaded and pre-set. The ergonomic needle shield is highly visible to indicate to the user where to pull the cap from the module. It is also hollow and round to increase the ease of its withdrawal. Removal of the needle shield does not make the needle apparent or increase the risk of needlestick injury, as the insertion and retraction of the needle are automated once the start button is activated.

Last but not least, the adhesive liner is ready to use when the user has the module in hand and, given its shape, the correct way to place the device is naturally obvious. The process could be simply summed up as "Patch and GO" (Figure 3).

The reusable module contains the electro-mechanical part, which needs to be charged. The battery LED indicates device autonomy and the USB connector allows recharging. This connector is protected, as it is placed inside the module, but it stays easily accessible. There is another LED indicator for the Bluetooth connectivity. This connectivity can be used in features that help fight against the decreasing patient adherence rate over the months.

"Offering a high level of ease-of-use facilitates prescription and training from healthcare professionals. The result is a "Click, Patch and GO" device."

The user interface has been improved as a result of insights gained during the first user study performed in-house and is now restricted to a single green button. Once it is activated, the device "wakes up" and the LED that indicates the connection of the two modules lights up. The second LED indicator is related to the injection readiness.

The tricky challenges of the device using two separated modules (one containing the drug and the other containing the necessary electronics for the injection) are related to the integrity of the drug, which is key to achieving the expected clinical outcomes, as well as ensuring the sterility of the primary drug container in a non-sterile environment. Nemera's R&D teams have addressed these challenges successfully and provided an innovative solution that does not compromise the user-friendliness of the device.

Benefitting from Nemera's experience in autoinjectors, special attention has been

Figure 3: Simulated use of Symbioze® on-body injector prototype.

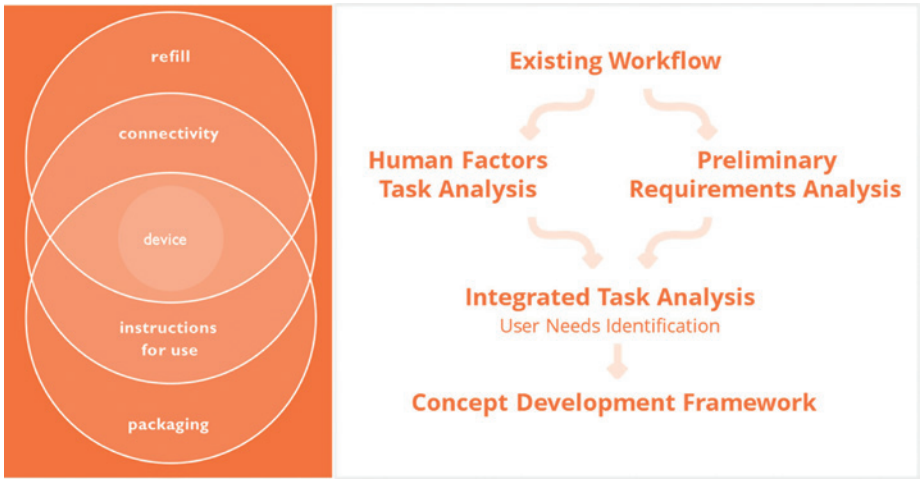

Figure 4: Supporting the combination product ecosystem from the earliest stages of developing a device strategy.

paid to the number of user steps; be it for a patient or a caregiver, a treatment-naïve or an experienced patient. In the same way, offering a high level of ease-of-use facilitates prescription and training from healthcare professionals. The result is a "Click, Patch and GO" device. Once the injection is complete, the two modules can be separated, and the disposable module discarded in a sharps container or biological waste bin.

To follow this user focus and act on Nemera's motto of "patients first" (Figure 4), several studies have already taken place and complementary ones will be performed as the product matures. The latest one was conducted at the company's Insight Chicago location and involved both healthcare professionals and chronically ill patients. The patients were recruited in the following categories:

- Oncology (e.g. multiple myeloma, acute myeloid leukaemia, lung cancer, breast cancer)
- Autoimmune diseases (e.g. rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, atopic dermatitis, psoriasis)
- Haematological immune deficiencies (e.g. Haemophilia A)
- Disorders of the central nervous system (e.g. multiple sclerosis, Parkinson's disease, Alzheimer's disease).

The study was structured in four phases, starting with an introduction to the device, going on to "regular" simulated use, then a deviation from regular simulated use and a post-study interview. The general feedback was good and improvement activities have already started.

Within a continually evolving environment, offering simple care in complex devices is a demanding but exciting challenge. Being part of the adventure with an innovative smart and sustainable on-body injector for chronically ill patients is a key milestone for Nemera. All the company's teams are ready to accompany its pharma partners in the journey to achieve a patient-centric combination product.

ABOUT THE COMPANY

As a world-leading drug delivery device solutions provider, Nemera's purpose of putting patients first enables it to design and manufacture devices that maximise treatment efficacy. The company is a holistic partner and helps its customers succeed in the sprint to market for their combination products. From early device strategy to state-of-the-art manufacturing, Nemera is committed to the highest quality standards. Agile and open-minded, the company works with its customers as colleagues and goes the extra mile to fulfil its mission.

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ABOUT THE AUTHOR

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

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ON-BODY DELIVERY SYSTEMS – NEWS AND TRENDS

In this overview, Tom Oakley, Director of Drug Delivery Device Development at Springboard, discusses the current state of play in the on-body delivery system space, reviews recent milestones and proposes directions for the future.

INTRODUCTION

The on-body delivery system (OBDS) market is changing rapidly and it has become clear that these devices are critical to the delivery of some new drugs that are currently in development. The OBDS market is relatively young, which lends itself to exciting innovations and a high potential growth rate.

Before launching into the details, it is important first to clarify which OBDSs are under discussion. By far the largest market for wearable injectors is diabetes; however, ambulatory insulin infusion pumps will be considered out of scope of this article because they deserve an article all to themselves. They are focused on one therapy where the flowrate is clinically relevant and their requirements are covered by IEC-60601-2-24 (if electronic) or ISO 28620 (if non-electronic).

For this article, the focus will be on OBDSs where the flowrate is not clinically relevant (other than avoiding the flowrate being too high, which could cause patient discomfort or a leak) and their requirements are covered by ISO 11608-6:2022. Such OBDSs can be used for a wide, ever-increasing range of indications and drugs, particularly those where the relatively high volume, viscosity or dose timing makes autoinjectors inappropriate. Examples include pegfilgrastim, for reducing infections after chemotherapy; evolocumab, for reducing cholesterol; and various drugs for Parkinson's disease.

> "OBDSs can be used for a wide, ever-increasing range of indications and drugs, particularly those where the relatively high volume, viscosity or dose timing makes autoinjectors inappropriate."

Figure 1: Amgen's Neulasta.

RECENT MILESTONES

The first launch of the modern generation of non-insulin OBDSs was Insulet's (MA, US) Onpro® for Amgen's Neulasta® drug in 2015 (Figure 1).[1] This is a modified version of the Omnipod insulin pump and delivers the injection in one bolus approximately 27 hours after the device is filled from a prefilled syringe by a healthcare professional and attached to the patient's body. Since its launch, over one million patients have used the Onpro OBDS to deliver Neulasta.[2] The drive mechanism uses shape memory alloy ("muscle wire") to reciprocate a lever arm, which rotates a ratchet wheel and leadscrew to push the plunger. The drug container is a custom oval plastic cartridge.

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West Pharmaceutical Services' (see this issue, Page 43) SmartDose 3.5 mL (Figure 2) was launched in 2016 for Amgen's Repatha® and branded "Pushtronex®".[3] In 2019, scPharmaceuticals (MA, US) announced its intent to go to market with West's SmartDose® 10 injector for FUROSCIX®, a proprietary subcutaneously delivered furosemide solution for the treatment of worsening heart failure due to congestion.[4] The platform uses an innovative telescopic plunger rod to minimise device size. The primary drug container is a custom cartridge made of cyclo-olefin polymer.

Figure 2: West's SmartDose 3.5 mL.

Enable Injections (see this issue, Page 18) has supported three clinical studies using its enFuse® pump (Figure 3), one of which is published.[5] Pharmaceutical partners can use their original drug container because the user fills the device just before use, thus inflating an elongated elastomeric drug container. Once on the body and activated, the elastic energy of the drug container expels the drug formulation in "bands" to smooth out the pressure over time. Enable has announced relationships with Lilly, Sanofi, Apellis, Genentech, UCB and CSL Behring, and has received US$215 million (£178 million) in financing as of January 2022.[6]

Figure 3: Enable's EnFuse.

Ypsomed's (see this issue, Page 23) YpsoDose single-use injector is an electromechanical prefilled and pre-assembled patch device for 10 mL glass cartridges (Figure 4). Needle insertion, injection, end of injection feedback and needle safety steps are all performed automatically. The needle remains hidden at all times and is made safe after injection and device removal. Ypsomed is scaling up its manufacturing capability for YpsoDose in Switzerland with first clinical studies starting in 2023.

Nemera (see this issue, Page 6) has completed a formative study on its Symbioze wearable pump (Figure 5) and expects to have new prototypes from rapid tooling by the end of 2022. The design has a reusable subassembly containing the motor and electronics, alongside a disposable subassembly containing the drug path and container. The reusable subassembly checks the identification of the disposable subassembly using near-field communication (NFC) before injection. The reusable electronics allow for additional features with minimal impact on cost or the environment, such as Bluetooth connectivity.

Figure 4: Ypsomed's YpsoDose.

Figure 5: Nemera's Symbioze.

"Pharmaceutical companies continue to see the drug container as a key risk, especially for prefilled devices, because anything that is not a standard glass pharmaceutical cartridge requires a lot more risk management and evidence before being accepted by regulators."

BD has announced two OBDS platforms that are in development:

- BD Evolve™ On-body Injector is a programmable platform supporting injections up to 3 mL. BD has conducted nine pre-clinical and five human factor studies
- BD Libertas™ Wearable Injector supports 2–5 mL or 5–10 mL doses in its two sizes and is fully mechanical (no electronics or software). The drug container is a nearly standard glass cylinder, available in standard nest and tub configurations. In 2021, BD published a clinical study on the 5 mL variant with 52 subjects to test functionality and acceptability with patients.[7]

Gerresheimer (Düsseldorf, Germany) acquired Sensile Medical and now has three OBDSs in its offering:

- SensAir, a pump optimised for delivering large molecules (Figure 6)
- An OBDS based on the SenseCore rotating piston pump for small molecules
- A belt-worn delivery system, currently used by EVER pharma to deliver apomorphine for Parkinson's disease.

Bespak (King's Lynn, UK), now owned by Recipharm (Stockholm, Sweden), is not actively developing its hydrofluoroalkane-powered Lapas wearable injector. Similarly, SteadyMed was acquired by United Therapeutics (MD, US), which took the expanding-battery-driven Patch Pump® out of the running.

CURRENT DEVICE STRATEGIES

Early in development, the team must choose between using a standard or custom drug container. There is frequent temptation to use a custom drug container to improve device layout, enable novel delivery mechanisms and improve usability. As such, it is no surprise that there are numerous OBDSs in development with custom drug containers, and many more that have been discontinued.

However, pharmaceutical companies continue to see the drug container as a key risk, especially for prefilled devices, because anything that is not a standard glass pharmaceutical cartridge requires a lot more risk management and evidence before being accepted by regulators. The choice of drug container is particularly important for prefilled devices because they typically have strict requirements for drug stability over two years' shelf life.

Secondly, the device designer must choose between two fundamental methods of delivering the drug to the patient – either pushing the drug out of the container or pulling the drug out

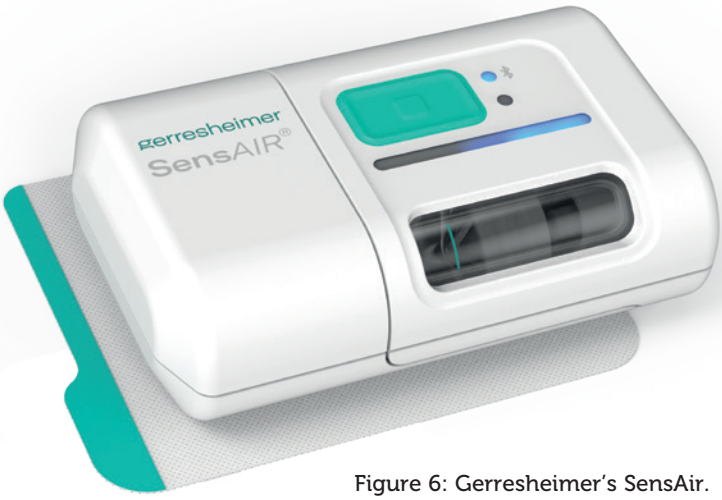

Figure 6: Gerresheimer's SensAir.

Method	Advantages
Push drug out of container	• Minimal drug degradation due to minimising exposure of drug to: – Multiple materials – Hydrophobic surfaces – Agitation – Bubbles caused by air coming out of solution under partial vacuum. • High pressures are possible for delivering viscous formulations through narrow cannulas and needles in reasonable time. Contrast this with "pulling" pumps, where the pressure differential moving the formulation out of the container is limited to atmospheric pressure.
Pull drug out of container	• More options for designing a compact pump layout • More options for changing size or type of drug container without changing pumping mechanism. The volume can be extended to infusions where the only limit on volume is the burden of carrying the size and weight of a large volume or being attached to a remote container • Opportunity to use the pump to fill the drug container as well as empty it. This can be useful for patient-fill and reconstitution scenarios.

Table 1: Advantages of pushing or pulling the drug out of its container.

Method	Standard or near standard drug container	Non-standard drug container
Push drug out of container	• Ypsomed YpsoDose • Gerresheimer SensAir • BD Libertas • Nemera Symbioze • Bespak Lapas.	• West SmartDose • Insulet OnPro • Enable enFuse (drug is in standard container until time of use).
Pull drug out of container	• Eitan Medical Sorrell (see this issue, Page 28) • Gerresheimer SenseCore-based pumps.	• BD Evolve.

Table 2: Publicly announced pumps categorised by push/pull and drug container.

of it. Table 1 lists the advantages of each method; note that the advantages of one method mirror the disadvantages of the other, so listing the disadvantages is unnecessary. Table 2 shows how different companies are providing OBDSs with different strategies with respect to "push" or "pull".

NEW ISO 11608-6 STANDARD

The ISO 11608 family of international standards has been recently updated, with many published in April 2022. ISO 11608 Part 6 is new and covers OBDSs, specifically covering fixed-dose delivery systems where the medicinal effect is measured by the dose volume, not the flowrate. In contrast, delivery systems that are designed to deliver given flowrates are covered by IEC 60601-2-24 and ISO 28620. The standard is designed to cover requirements that are not typically present for handheld injection devices, such as:

- Means of attachments to the body
- Occlusion detection
- Leakage due to worst-case environments, and orientation
- Changes in or periods with vibration, temperature, humidity, atmospheric pressure, light exposure and orientation whilst in use
- Dose delivery over time.

It also defines test methods for adhesion, dose delivery profiles and needle/cannula displacement whilst in the body.

The additional requirements described in the 11608-6 standard should make it clearer to stakeholders why there can be more development work required to bring an OBDS to market compared with a prefilled syringe. At the same time, the clarity brought by the standard should reduce the time that device developers and regulatory affairs people spend trying to work out the requirements and expectations for new OBDSs.

CHALLENGES

Considerable progress has been made on the main challenges for OBDSs in recent years. For example, while many patients, caregivers and healthcare professionals are familiar with autoinjectors, the use scenarios of OBDSs are unfamiliar. As such, the occurrence of certain usability risks could be increased. To combat this, usability (human factors) now needs to be considered early and throughout device development according to the two main regulatory requirements in the area:

- US FDA guidance "Applying Human Factors and Usability Engineering to Medical Devices"
- IEC 62366-1:2015 "Application of usability engineering to medical devices".

However, there are still some companies that prefer not to conduct early formative human factors studies, despite them being critical to determining a meaningful user requirements specification.

Another challenge where progress has been made is the need for parenteral injections to be sterile. The sterility strategy for prefilled syringes tends to be straightforward – the syringe is sterilised with its needle shield in place then filled in a sterile isolator. However, most OBDSs do not use a prefilled syringe as a primary container and therefore need a strategy to both achieve and maintain sterility. This can require some novelty when the drug container is not connected to the needle or cannula before use because there could be a non-sterile region between those two subassemblies. With suitable design, various methods for sterilising the drug path have been used successfully in different devices, such as ethylene oxide, nitrogen dioxide, ultraviolet radiation *in situ* and others.

That said, three challenges have continued unabated and may even have increased recently. First, cold chain distribution presents a challenge to device developers. Most biologics, which are often the target for OBDSs, need to be transported and stored at refrigerated temperatures. Therefore, if the OBDS is prefilled, it must be robust to cold temperatures and condensation, which can be challenging for devices containing electronics and batteries. In addition, the overall size of the device and its packaging must be minimised because cold chain space is finite, expensive and has a significant environmental footprint.

Second, demands from patients, payers and pharmaceutical companies to reduce environmental impact are increasing. Some devices have been selected on their environmental credentials. Compared with prefilled syringes or autoinjectors, wearable injectors tend to:

1. Require more plastic
2. Need an adhesive patch
3. Need soft cannula insertion (and perhaps retraction)
4. Need electronics and batteries.

To address this, some wearable injectors employ strategies such as:

1. Splitting the device into reusable and disposable subassemblies
2. Increasing the number of possible times a patient can reuse a given device
3. Collecting a used device from one patient, reconditioning it and sending it to another patient to use.

Thirdly, the intellectual property space around OBDSs has become increasingly crowded. As such, freedom to operate is a key issue.

FUTURE DIRECTIONS

It is possible to speculate on future directions of development for OBDSs. Looking forward, the major themes are likely to be:

- Rationalisation of requirements and designs. That is, requirements and designs will simplify according to which user experiences are discovered to be most successful on the market and, in turn, which user experiences become expected by patients, carers, healthcare professionals and payers. For example, autoinjectors seem to have moved from "automatic needle insertion with button activation" to "manual needle insertion with push-onto-body activation". These changes may lead to simpler and smaller devices
- Tension between adding functionality, such as connectivity, versus optimising for environmental sustainability
- Connection with companion diagnostics. This will be the subject of a panel discussion at the Partnerships on Drug Delivery (PODD) conference in Boston in October 2022

- In time, rationalisation of wearable device suppliers in the marketplace. As a relatively new device category, there is a lot of innovation and competition. Like any other disruptive industry or device category, a handful of players may come to dominate the market over the coming years because pharmaceutical customers may prefer proven technologies, tooling and production costs might become amortised for devices already on the market, and some device manufacturers will gain early-mover advantage.

SUMMARY

More than at any other time, in 2022, the world recognises the need for high-quality, accessible and sustainable healthcare. The OBDS market is in an exciting and pivotal phase, with some devices on the market, many more devices racing to clinical studies and some falling by the wayside. However, pressures from environmental sustainability, ever-increasing usability requirements and the demand for new features mean that the race is far from over.

If you have questions or would like to discuss any points, please do not hesitate to contact the author.

ABOUT THE COMPANY

Springboard specialises in developing devices from concept to manufacture for regulated markets. The company is expert at creating innovative yet robust designs and solving difficult technical problems quickly. Springboard does not have internal projects, so it is as fast and cost effective as possible, and the intellectual property belongs to its clients.

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"The OBDS market is in an exciting and pivotal phase, with some devices on the market, many more devices racing to clinical studies and some falling by the wayside."

ABOUT THE AUTHOR

Tom Oakley leads engineering and scientific teams developing new injection devices, pumps and inhalers. He has been the named inventor on dozens of patents throughout his 20 years' experience in industry. Mr Oakley is a regular speaker at various international conferences on innovation and medical device development, and mentors engineering and MBA students on innovation and device development at the Cambridge University Engineering Department and the Judge Business School (Cambridge, UK). He read Engineering at the University of Cambridge before becoming the Choate Fellow in Human Physiology and Pathology at Harvard University (MA, US).

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FLEXIBLE CARE – ENABLE WEARABLE DELIVERY

Here, Jennifer Estep, Senior Director, Global Marketing & Commercial Strategy, and Mehul Desai, PharmD, Vice-President of Medical Affairs, both at Enable Injections, discuss the benefits for patients and healthcare providers of innovative subcutaneous delivery.

Anne heard the news from her physician at a young age – she had a chronic disease, one for which there is no cure. She had few options – she could either ignore her diagnosis and live confined to the full progression of her disease or she could aim for remission and learn to live with needles, nurses, an infusion chair and a rigid infusion schedule. Anne did not feel as if she had a choice.

After a few years of intravenous (IV) therapy, Anne found out she was in remission, and was elated. To stay in remission, she continued her therapy, but a change in policy by her insurance company meant she could no longer receive her IV infusions in the clinic. She had to move to home health for her IV infusions. Even though getting IV therapy at home is good news for many patients, as they no longer have to commute, Anne felt as though it was one more thing that she could not control.

The home infusions did not go as planned. The first scheduled home infusion day came, but the medicine and supplies didn't arrive until the next day. The rescheduled first home infusion day also did not work out, as a different home health nurse got lost and never arrived at her home. The third try was a success, but Anne had new concerns. What happens when the nurse is different every time? And what about the risk of covid-19 exposure by allowing a nurse who had visited other patients that same day and week? Was she comfortable having a stranger in her home every time she needed her infusion?

She realised that, as an immune-compromised patient, she did not want to be exposed to health risks like covid-19 in her home or share her couch and TV shows with a stranger while she received her IV treatment. It was such a concern that Anne informed the insurance company she wanted to go back to the IV clinic because she had more control. The insurance company refused the request, and Anne compromised by agreeing to receive her infusions in the home health company office building. The room where she received her IV therapy was a remote, unfriendly cinder block room. It was not what she wanted, but she felt she did not have a choice. Was there an alternative?

GAP IN CURRENT CARE

For patients and healthcare providers (HCPs), the subcutaneous (SC) option is a strong one. However, many drugs are not available for SC delivery, for a variety of reasons.

Parenteral Administration

Many drugs must be administered parenterally, specifically biologics, and a common parenteral route is via IV administration. IV administration requires an HCP to initiate and monitor the infusion, usually takes several hours and involves an exposed needle.

SC administration, another parenteral route of administration, requires a fraction of the time of IV administration. However, SC administration has traditionally faced limitations, such as drug volume limitations,

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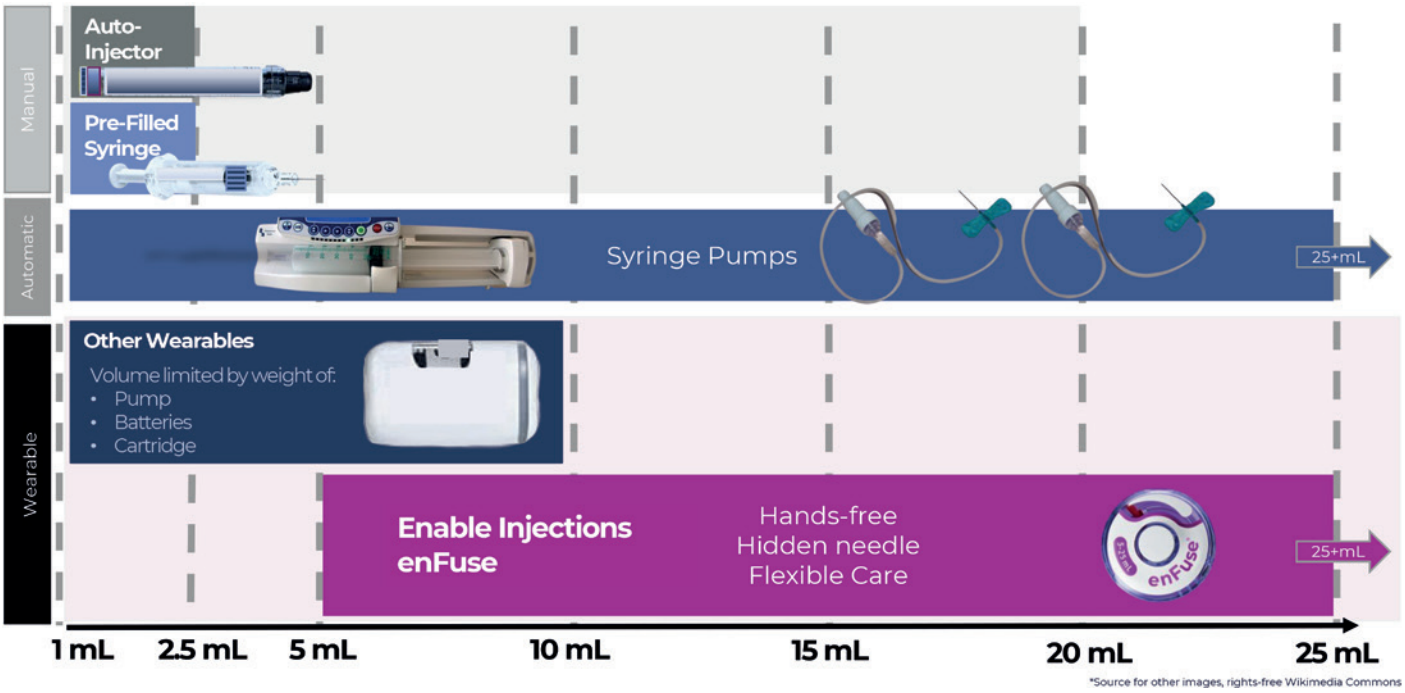

Figure 1: Overview of subcutaneous drug delivery system technology by delivery volume capacity, by type of administration for manual systems and wearable systems.

safety concerns due to exposed needles, hands-on administration and lack of mobility during administration.

Drug Volume Limits

SC administration has historically only involved small volumes (<5 mL) of drug delivered by a device through a needle – such as prefilled syringes and autoinjectors. To reach larger delivery volumes (>5 mL), dosing regimens would have to include multiple injections by a syringe or autoinjector per dosing time.

For pharmaceutical formulation teams, volume restrictions are an impediment. By allowing formulations to be delivered in larger volumes by using modern large-volume SC delivery technology, the development time may be reduced (Figure 1).[1]

Exposed Needle Safety Concerns

Dislike of exposed needles is an issue that affects much of the population. In research conducted in a validation study with kidney failure patients receiving treatment, 26% reported feeling afraid, 41% reported feeling nervous and 33% reported feeling worried the "moment the nurse comes to insert the needle".[2]

Studies report that approximately 25% of the adult population has a fear of needles, and this percentage is higher among children and adolescents.[3] A 2021 review of management of needle fear in adults with chronic disease discusses a study in which 35% of patients reported delaying treatment because of needle phobia due to fear of pain.[2]

Hands-Free Needs

For small- and large-volume delivery via syringe, the medicine must be delivered to the patient using a hands-on approach. For current large-volume SC delivery via syringe, an HCP sits inches from a patient's body, actively pushing the barrel of a large-volume syringe. This syringe delivers therapeutics through an exposed needle stuck into the subcutaneous tissue of the patient's stomach, and typically requires 5-10 minutes of pushing. The focused effort required for this type of injection limits the HCP's time, and the physical rigour required to administer this type of large-volume injection limits the number of times an HCP can repeat the process in a single day.[4,5,6]

Large-Volume Delivery Alternatives

One alternative to the large-volume delivery with a syringe is a syringe pump. A large-volume syringe pump removes the need for an HCP to manually inject the medication into the SC tissue. However, the pump does not eliminate exposed needles, tubing sets or the need for the patient to sit immobile throughout the infusion.[7]

Improvements in Large-Volume Delivery

On-body delivery device volumes are usually limited by device weight, size and container. Current on-body delivery devices are limited to volumes of 10 mL and below. These devices deliver volumes that may also be administered by several self-administered prefilled syringes, autoinjectors or large-volume syringes administered by an HCP.

IMPROVEMENTS THROUGH INNOVATION

Innovations in healthcare are imperative for improving access to medicines and the delivery of therapeutics for patients, caregivers and providers. For patients seeking flexible, convenient care that saves

"Innovations in healthcare are imperative for improving access to medicines and the delivery of therapeutics for patients, caregivers and providers."

Figure 2: The enFuse is a novel, wearable drug delivery system that can deliver large volumes of large- and small-molecule therapeutics (5–25 mL).

Figure 3: Throughout the enFuse injection, the needle is hidden from the user and allows for a hands-free injection.

time and fits into their schedules, SC delivery has that potential with large volume, on-body delivery technology that is truly innovative in size, shape and wearability. As one key opinion leader said at the American Society of Clinical Oncology congress in June 2022, "SC administration by on-body delivery systems is well tolerated, requires short duration of injection and provides a convenient hands-free option."[8]

Innovation benefiting patients and providers has the potential to increase flexibility and:

1) Reduce needle exposure
2) Allow ease of treatment and hands-free administration
3) Allow potential flexibility in the location of the administration – in the clinic or at home, based on the patient and provider needs and preferences.

ENFUSE INNOVATION

Enable Injections is an investigational-stage company developing and manufacturing the enFuse wearable delivery system, designed with the patient in mind. The enFuse (Figure 2) is a novel, wearable drug delivery system capable of hands-free delivery of large volumes of large- and small-molecule therapeutics (>5 mL). Its design simplicity includes using a standard container-closure system and a hidden needle, and its mechanical simplicity eliminates the need for a motor, electronics, batteries or sensors. Its flexibility allows administration in a clinic or hospital, at a pharmacy or at home via self-administration by the patient or by an HCP. Its patient-friendly appearance is smaller and lighter because of its unique technology.

For the enFuse user, a simple single click of a vial into the enFuse transfer base initiates the transfer of medication into the enFuse. Once the transfer is completed, the user removes the enFuse from the transfer base, places the enFuse onto the abdomen and presses the button to initiate injection. The needle is never exposed to the user and allows a hands-free injection (Figure 3).

enFuse EnywhereCare™ flexibility allows in-clinic or at-home self-administration, based on patient and provider needs. enFuse EnyVolume, with flexibility in volumes from 5-25 mL in a single enFuse device, allows for greater clinical efficiencies for providers. Pharma developers may benefit from EnyVolume with greater flexibility and potentially reduced development time.

Constant Pressure Delivery Advantages

The enFuse constant pressure mechanics promote greater flexibility surrounding the speed of the injection and responsiveness to the pressure in the SC tissue. This responsive constant pressure delivery has several advantages, including the potential to increase patient comfort and potentially reduce pain, leakage and backpressure, as well as potentially eliminating the need for the inclusion of a chemical additive to allow SC absorption, such as hyaluronidase.

CONCLUSION

For patients like Anne, the enFuse may offer more than flexibility and simplicity. SC administration of large-volume therapeutics with enFuse technology has the potential to allow patients like Anne to achieve their goals of staying healthy and in remission by continuing their treatments, but with the discretion and flexibility that would allow them to regain control over their calendar and healthcare. For Anne, this could mean thinking of herself less as a patient and more as a human being able to live, thrive and achieve her dreams.

ABOUT THE COMPANY

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

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Jennifer Estep serves as Senior Director, Global Marketing & Commercial Strategy for Enable Injections, leading marketing strategy for Enable and its partner portfolios. She has more than 20 years of experience with marketing in the media, electronics and pharmaceutical industries. Ms Estep has a BSc in Mechanical Engineering from Purdue University (West Lafayette, IN, US).

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ON drugDELIVERY

2022/23 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
October 2022	Prefilled Syringes & Injection Devices	Deadline passed
Oct/Nov	Drug Delivery & Environmental Sustainability	Deadline passed
November	Pulmonary & Nasal Drug Delivery	Oct 13, 2022
December	Connecting Drug Delivery	Nov 3, 2022
January 2023	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Dec 1, 2022
February	Prefilled Syringes & Injection Devices	Jan 12, 2023
March	Ophthalmic Drug Delivery	Feb 2, 2023
April	Pulmonary & Nasal Drug Delivery	Mar 2, 2023
April/May	Drug Delivery & Environmental Sustainability	Mar 16, 2023
May	Delivering Injectables: Devices & Formulations	Apr 6, 2023
June	Connecting Drug Delivery	May 4, 2023
July	Novel Oral Delivery Systems	Jun 1, 2023
August	Industrialising Drug Delivery	Jul 6, 2023
September 2022	Wearable Injectors	Aug 3, 2023

YPSOMED
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WEARABILITY AND USABILITY OF THE YPSODOSE 10 mL PATCH INJECTOR

In this article, Jakob Lange, Senior Director Delivery Systems at Ypsomed, discusses the results of a recently published study into the usability and wearability of the YpsoDose 10 mL patch injector, providing a summary of the insights acquired during the study.

INTRODUCTION

The YpsoDose is a large-volume patch injector that delivers a single-dose volume of up to 10 mL from a cartridge-based primary container, developed in response to the significant increase in demand for new large-volume subcutaneous therapies. These new therapies are usually antibody based and have payloads of up to 1000 mg, requiring a 5–10 mL fill volume. These therapies include treatments for autoimmune diseases, and orphan and rare diseases, as well as immuno-oncology drugs.

In various comparative studies, it has been confirmed that patients and healthcare providers (HCPs) prefer a prefilled and preassembled device, in large part due to the increased convenience. Beyond the immediate advantages of convenience, safety, assurance of the correct dose and time saved, pharma companies particularly like that the user is unable to manipulate the drug container before or after the injection event. Ypsomed has drawn on its experience with prefilled pens and autoinjectors to develop a modular and customisable platform to speed up time-to-clinic, lower up-front investment and lower project risk for pharma partners.

> "Ypsomed conducted a study to examine the feasibility and user perceptions of patch injector self-injections using an YpsoDose prototype."

As there is little information publicly available on the usability and patient perceptions of large-volume patch injector technologies such as the YpsoDose, Ypsomed conducted a study to examine the feasibility and user perceptions of patch injector self-injections using an YpsoDose prototype. Specifically, data on usability (i.e. overall handling) and wearability

Disease	Cancer	Multiple sclerosis	Rheumatoid arthritis	Psoriasis
Number of patients	5	2	7	2
Disease	Crohn's disease	Asthma/COPD	Cardiovascular disease	
Number of patients	1	3	1	

**Certain patients suffered from more than one chronic condition*

Table 1: Chronic disease states of patients (n=17)*.

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(i.e. acceptability of size and weight) were collected from simulated self-injections. During a non-interventional observational study, 23 participants, including patients and HCPs, simulated the use of a large-volume patch injector, performed predefined movement and activity tasks, and reported their experience in terms of device usage, comfort while moving and confidence while wearing the device. The disease states of the patient participants are presented in Table 1. The complete study has been published in "Medical Devices: Evidence and Research"[1] and is presented here in summarised form.

METHOD

Two injections were simulated for each participant using an YpsoDose patch injector prototype device as illustrated in Figure 1. The device is placed on the abdomen or thigh and held in place with a medical-grade adhesive. A single button activates the device after placement on the skin, with a sensor that determines when it is in contact with the skin. The device automatically inserts the needle when activated. It contains an LED-based progress bar and status lights, as well as a red warning light and audible indicator to indicate an error state. The injection progress is visible through a clear window on the device that shows the drug container and movement of the plunger.

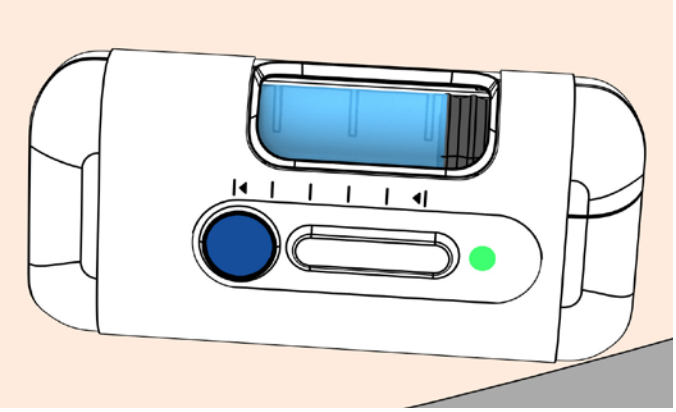

Figure 1: Prototype YpsoDose injection device used in the simulated use study.

"Participants responded favourably to the patch injector prototype, citing an expected advantage in terms of convenience compared with their current standard of care were they to use it to take their medication regularly."

The devices used in the study were fully functional, including the aforementioned lights, sounds and sensors. However, the devices did not contain a needle or liquid filling. The user steps required to simulate an injection with the study devices are shown in Figure 2.

RESULTS

General Impression

Participants responded favourably to the patch injector prototype, citing an expected advantage in terms of convenience compared with their current standard of care were they to use it to take their medication regularly. Multiple participants recognised the value of using a large-volume patch injector to enable them to administer their therapies at home, which would otherwise require them to be in a clinical or hospital setting. This observation was particularly pronounced among oncology patients, who welcomed an alternative to their current complex treatment process and the considerable time commitment it requires in relation to visiting inpatient care and infusion centres.

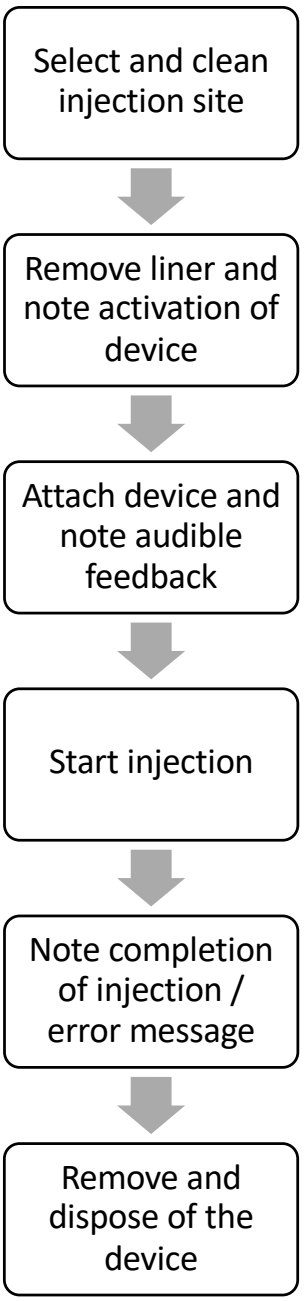

Figure 2: User steps required to perform a simulated injection with the YpsoDose patch injection device.

Usability

Regardless of their body size and shape, participants were able to find sufficient space to place the device and generally found wearing it to be comfortable and secure. In general, only a few user errors and difficulties were observed. During the simulated injections, participants were able to clearly identify that the injection process was proceeding correctly and verify the progress and status of the delivery. All participants were able to determine the state of the patch injector by checking the visual progress indicators (i.e. the visual feedback lights and plunger movement in the drug observation window). Most participants did not have any issue detecting the occurrence of an error state. Participants were able to remove the device without difficulty and knew that it had to be discarded in the sharps bin. The overall success rate of participants completing the simulated injections is illustrated in Figure 3.

Wearability

In general, patient participants were positively surprised by how easily the patch injector could be worn on the body during the simulated injections. The only issues related to wearability that were noted in the study were in cases of excessive body hair and small body size. For patient participants, the comfort and security of the patch injector were tested through multiple movement-based tasks during the simulated injection, with almost universal success across participants. Moreover, participants indicated that the patch injector was easily forgotten whilst performing the tasks.

Wearers quickly reached the point of sensory satiety, notably more so when the device was attached to the abdomen, rather than the thigh. This is a positive attribute, as the device does not seem to call attention to itself, either because of its size or a potential pull from the adhesive whilst moving. Thus, despite perceiving the device to be large, participants reported that the patch injector was comfortable when worn.

The ratings for abdomen and thigh placement in terms of comfort were almost identical, whereas removal was rated to be somewhat easier when the device was worn on the thigh. The participant ratings on perceived security while wearing the device were marginally lower than the comfort ratings, with participants viewing the abdomen as a more secure spot for the patch injector than the thigh.

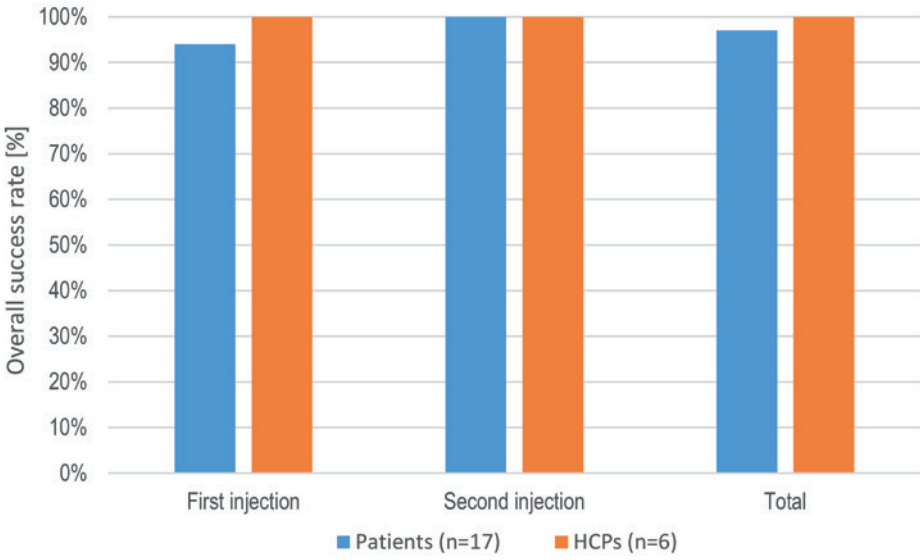

Figure 3: Injection success rates per injection and overall. An injection was rated to be successful if the user was able to successfully complete a complete simulated injection, regardless of usage errors or difficulties.

> "The primary findings were that, although participants generally had a positive first impression of the device and injection technology, they were initially rather sceptical about the size of the device."

SUMMARY & CONCLUSION

This study investigated the usability and wearability of a wearable patch injector, simulated with a prototype YpsoDose device. The primary findings were that, although participants generally had a positive first impression of the device and injection technology, they were initially rather sceptical about the size of the device. In terms of usability, participants were predominantly successful in performing the simulated injections with few user errors or difficulties. The self-reported rating for usability was high. In terms of the wearability, all participants were able to place the device on their bodies, irrespective of body size or habitus, and found the injector comfortable to wear. Participants were able to move around and perform predefined activity tasks with the device attached to them and rated the different wearability aspects positively.

In terms of self-reported usability, HCPs provided lower ratings than patients, although all ratings were high and the differences between the groups were small. Understanding the perspectives of HCPs is particularly important, as they are likely to continue to be involved in their patients' care even with a move from clinic-based intravenous infusions to subcutaneous drug administration using novel large-volume patch devices. This is particularly true in oncology, where the development of subcutaneous formulations has recently attracted significant interest.

The choice of the injection site (abdomen or thigh) had a limited effect on perceived wearability. Patients rated most aspects of perceived wearability the same regardless of the injection site, with the exception of perceived security of attachment, which was rated higher for the abdomen, and ease of removal, which was rated higher for the thigh. These differences may be related to the size of the device, which is designed to hold a 10 mL cartridge.

These results indicate that the YpsoDose large-volume patch injector can be safely and effectively used by the intended broad patient and HCP population.

ABOUT THE COMPANY

Ypsomed's comprehensive drug delivery device platforms consist of autoinjectors

for prefilled syringes in 1 mL and 2.25 mL formats, disposable pens for 3 mL and 1.5 mL cartridges, reusable pen injectors, ready-to-use prefilled wearable patch injectors and injection devices for drugs in dual-chamber cartridges. Unique click-on needles and infusion sets complement the broad self-injection systems product portfolio.

With over 30 years of experience in the development and manufacture of innovative injection systems, 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. Anticipating the future needs of patients, pharmaceutical customers, payers and HCPs, Ypsomed moves beyond manufacturing connected sensors. Ypsomed's smart device solutions strive to transform patients' lives by capturing therapy-relevant parameters, processing them to facilitate self-management of chronic diseases, and integrating these insights with digital therapy management ecosystems.

The company leverages its in-house capabilities in electronics, software and connectivity for the development of new devices and digital product systems. Ypsomed is ISO 13485 certified and all its processes comply with design control and cGMP guidelines with operational QA/QC experts on-site at each location. Ypsomed's US FDA-registered manufacturing facilities are regularly inspected by pharma customers and regulatory agencies to supply devices for global markets, including the US, Europe, Japan, China and India.

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ABOUT THE AUTHOR

Jakob Lange, PhD, is an engineer and materials scientist, with an MSc degree in Chemical Engineering from the Royal Institute of Technology in Stockholm, Sweden, and a PhD in Polymer Science from the Swiss Federal Institute of Technology in Lausanne, Switzerland. He has written and published more than 40 peer-reviewed papers on medical devices, packaging materials and polymers and is a regular contributor to technical and scientific conferences. At Ypsomed, Dr Lange has held various positions within marketing and sales, as well as in R&D project management. Currently he has the role of Senior Director Delivery Systems, overseeing a team managing Ypsomed's autoinjector platforms, as well as the associated customer relationships for development projects and marketed products.

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DRUG DELIVERY DEVICES THROUGHOUT THE DRUG DEVELOPMENT CYCLE

In this article, Ori Ben-David, PhD, Vice-President of Research and Development, Pharmaceutical Solutions, at Eitan Medical, discusses the considerations that must be made over the course of injectable drug development and how the company's Sapphire™ and Sorrel™ platforms offer pharmaceutical companies a full suite of device tools from early discovery through to commercialisation.

THE DRUG DEVELOPMENT PROCESS

As colleagues in the pharmaceutical industry can attest to, there are multiple stages in the drug development cycle, ranging in length and complexity, all of which must be passed successfully prior to commercialisation and market introduction of a new drug product (Figure 1). In the early discovery and development stages, a pharmaceutical company will conduct the necessary research to develop a new chemical or biological entity, initially testing it in preclinical animal studies, followed by three phases of clinical trials to determine the safety, efficacy and therapeutic effects of the medication. Following the successful completion of clinical studies and subsequent clearance by the relevant regulatory authorities, the drug can then be prepared for commercial launch.

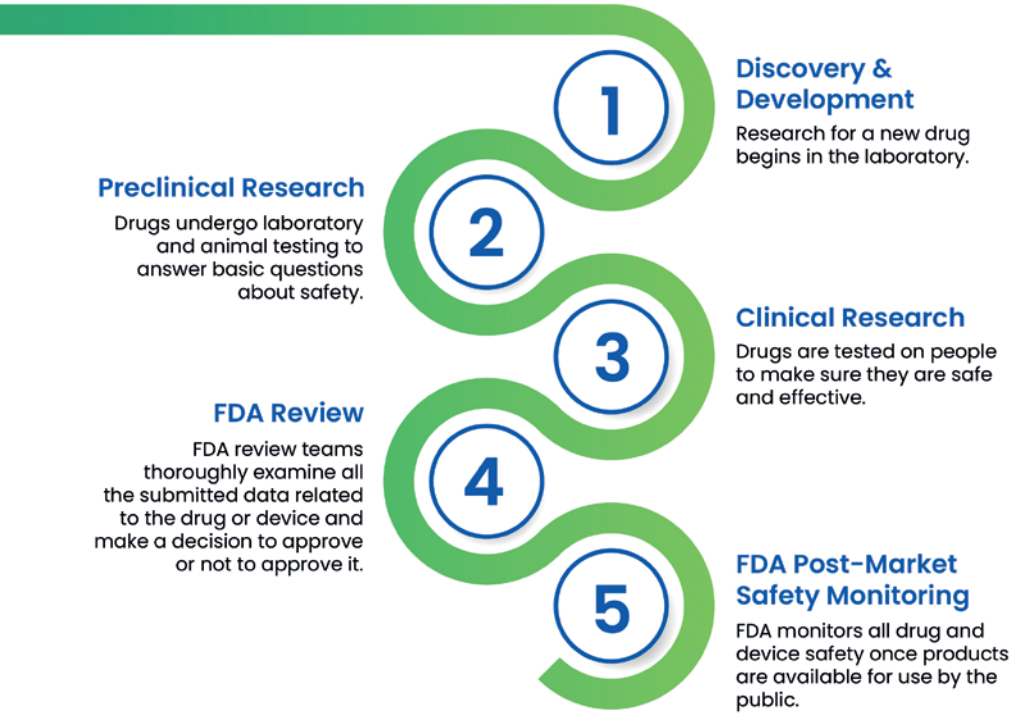

Figure 1: The drug development process as outlined by the US FDA.[1]

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"For injectable medications, an additional consideration must be addressed throughout the development and clinical phases – how should the drug product be administered?"

However, for injectable medications, an additional consideration must be addressed throughout the development and clinical phases – how should the drug product be administered? At each stage of the drug development cycle for an injectable medication, pharma companies must consider which primary container and drug delivery device is most appropriate to store and administer the medication (Figure 2). This is necessary to ensure a smooth drug development process through clinical trials and all the way up to commercialisation, not only introducing to market a therapeutically beneficial medication, but also an overall positive and convenient drug delivery experience for the patient.

Figure 2: A key factor in the development of an injectable therapy is consideration of which primary container and associated drug delivery device will be most appropriate for the drug product. Image courtesy of Ompi, Stevanato Group.

THE EVOLUTION OF PRIMARY CONTAINERS THROUGHOUT DRUG DEVELOPMENT

During the early discovery and clinical trial phases, pharmaceutical companies generally use glass vials as the primary container for their drug product. This vial will not necessarily be the primary container for the final commercial representation but is chosen due to the wide availability of ready-to-use, off-the-shelf vials and the availability of supporting filling lines. Due to their popularity, vials are manufactured in large quantities and therefore have a very low cost per unit compared with cartridges or prefilled syringes (PFSs).

However, using a vial for commercial representation does not come without its challenges. Using a simple syringe to extract drug product from a vial generally requires multiple accessories, including syringes, needles and vial adapters, and is generally only performed by trained healthcare professionals, caregivers or experienced patients. Additionally, in general, because vials are non-collapsible drug reservoirs, the orientation of the vial must be maintained as the drug is drawn out into a drug delivery device.

As an alternative to vials, primary containment manufacturers have recently started bringing more options for cartridges and PFSs to market, which are designed to offer a more patient-centric, easy-to-use solution for drug delivery. However, the move from vials to cartridges and PFSs is a significant investment for pharmaceutical companies, considering all the necessary validation activities required for transitioning from one primary container to another. In many cases, this will also require collaboration with an additional manufacturer and possibly a dedicated development project, which will further add to development costs and increase time to market.

Regardless of the ultimate choice for a primary container, pharmaceutical developers will need to test, challenge and validate the drug product's stability and compatibility with the primary container for the full shelf life of the drug.

THE INTEGRATION OF DEVICES THROUGHOUT THE DRUG DEVELOPMENT PROCESS

In parallel to considering the question of primary container, a pharmaceutical company must address the topic of the drug delivery device. There are multiple considerations for choosing a drug delivery device. These differ and evolve as the drug product moves through the early discovery phases, then preclinical and clinical phases, and ultimately prepares for commercial launch. During the initial stages, the availability and configurability of a drug delivery device is key. Researchers need access to solutions for administering drugs and examining the effects of different injection volumes, flow rates and viscosities on the subcutaneous tissue. As drug parameters are not yet determined during these early phases, companies generally prefer to avoid investments in customised devices at this stage.

Accordingly, the early development stages generally benefit from professional, off-the-shelf, software-controlled infusion pumps with a rich feature set. Such devices with a detailed event log and options for connectivity can assist early stages and clinical studies by allowing for automatic recording and documentation of configured parameters and events throughout the infusion. The additional benefits of connected drug delivery devices in terms of recording and monitoring are especially profound during decentralised and hybrid clinical trials, taking the burden and responsibility of self-reporting out of the study subjects' hands, instead moving it to an automated, controlled and reliable method.

As the drug development process continues through the clinical research stage and prepares for Phase III trials and commercial launch, the pharmaceutical manufacturer must shift its focus towards considering the ideal commercial representation of the drug product once it is on the market. Injectable medications are generally launched as combination products, with an inseparable device constituent launched with them to enable drug administration. Accordingly, choosing a commercial drug delivery device and a device partner is not an easy task. Often, dedicated device teams within pharmaceutical companies are tasked with this challenge, acting as liaisons between the drug product and pharmaceutical manufacturer on the one hand, and a drug delivery device manufacturer on the other.

One consideration for choosing a commercial drug delivery device is the intended patient and user population for the device. While in the development and clinical stages, the user of the drug delivery device is generally a researcher or healthcare professional; however, if the device is intended for self-administration, it would require an assessment of the target patient population. Would the average patient be a child or an adult? Does this patient population suffer from vision or dexterity issues relating to their disease, and would those issues affect their ability to operate a device? Are these patients with chronic diseases that can be trained and familiarise themselves with the use of a more complex device over time, or are these patients that require a simple and easy-to-use device as a priority? Do these patients generally have familiarity with drug delivery devices and medical technology, or should it be assumed that this self-administration device would be a new concept for them?

A second leading consideration, tied to the first, is the intended use environment in which the drug product is to be administered. Is this drug product intended to be administered in a homecare environment? Is a healthcare provider or caregiver expected to be present? This, too, will dictate the required user interface, use steps and maximum level of complexity of the drug delivery device. As the move towards home-based care continues to develop following the covid-19 pandemic, devices that can administer medication outside of traditional clinical settings and without requiring additional supervision are seen as the future of drug delivery.

In parallel, a landscape assessment should be conducted to analyse the drug delivery devices associated with competing or similar drug products on the market. In certain cases, for generic or biosimilar drug products, the device experience would need to mimic that of the originator drug, so that patients transitioning from one drug product to its generic or biosimilar version would essentially have the same drug delivery experience. For competing molecules, pharma companies may look for a competitive edge when introducing a drug delivery device to the market, such as a wearable device, a smartphone app that is able to track the injections or a sleek and discrete new device design.

OPTIMISING THE ROAD TO COMMERCIALISATION WITH A DEVICE PARTNER

As the road from discovery to commercialisation of an injectable medication is intertwined with drug delivery devices along the way, selecting a reliable, flexible and versatile device partner is key. Eitan Medical's flagship product is the commercialised Sapphire™ infusion pump (Figure 3). This pump is small in size yet big in performance, offering tailored solutions for a variety of infusion needs, including hospitalisation, ambulatory and home infusion, all in a single pump.

Figure 3: Eitan Medical's flagship Sapphire™ infusion pump.

The Sapphire™ family of infusion solutions is based on patented magnetic flow control and advanced technologies aimed at enhancing patient safety and reducing total cost of ownership. These devices use a colour touchscreen, allowing for a quick setup and intuitive workflows, and support a wide range of flow rates, positioning it as the ideal, flexible off-the-shelf solution for clinical research phases.

Figure 4: Eitan Medical's Sorrel™ wearable drug delivery platform.

eitan medical
care & beyond™

Eitan Medical partners with pharmaceutical & biotech companies

to bring to market tailored, smart drug delivery and infusion solutions across the continuum of care - from the hospital to the home.

"The Sorrel™ platform of wearable drug delivery devices is a true platform solution, conforming to the primary container of our pharma partner's choice, whether vial, cartridge or syringe. Coupled with our patented UV technology for disinfection at point of care, our wearable injectors are pre-filled and pre-loaded for an optimal self-administration drug delivery experience."

Dr. Andrei Yosef, General Manager, Pharmaceutical Solutions at Eitan Medical

Meet the team at upcoming PDA and PODD events, or schedule a visit at our headquarters, by contacting the Sorrel™ business development team: **partnerships@eitanmedical.com**

The Sorrel™ and Avoset™ products are not for sale, pending regulatory approval/clearance. Specifications are subject to change.

"Taken together, this means that Eitan Medical's pharmaceutical partners can use a range of products throughout the drug development process."

Eitan Medical's Sorrel™ wearable drug delivery platform is ideally positioned for large volume injections in the homecare environment (Figure 4). The Sorrel™ device is a subcutaneous wearable injector that is simple to use and easy to scale up with configurations for both prefilled and preloaded cartridges and vials, as well as a device filled at the point of care by a syringe (Figure 5). With the Sorrel™ device, pharmaceutical developers can use the primary container of their choice. The unique electromechanical primary-agnostic pumping mechanism provides the flexibility to allow Sorrel™ devices to accommodate a wide range of vials and cartridges, minimising the risks, cost and time associated with the development of a new delivery system or primary container.

Figure 5: The Sorrel™ can be configured for use with prefilled and preloaded cartridges and vials, as well as filling at point of care with a prefilled syringe.

Taken together, this means that Eitan Medical's pharmaceutical partners can use a range of products throughout the drug development process – the Sapphire™ infusion pump in early discovery stages, a Sorrel™ vial-based wearable injector for clinical phases, and either a Sorrel™ vial-based or cartridge-based wearable injector for commercial use. Doing so can provide both the company and the end user with greater flexibility, control and ease of use. Additionally, innovative new technologies are in development allowing for lyophilised medications to be used within a Sorrel™ wearable injector, potentially introducing the use of convenient-to-use wearable injectors to even more drug products and markets.

Furthermore, the recently introduced Eitan Insights™ digital health platform will provide clinicians and homecare providers with remote treatment data and visibility of Eitan Medical's suite of advanced infusion and drug delivery devices. The system will track patient treatment status, as well as the device's location and status, allowing clinicians to assess events and conduct remote follow-ups on treatment progress. Aggregated patient data and cloud-based processing will allow caregivers to identify treatment patterns and provide data-based adjustments. Eitan Medical is envisaging a future with connected health, flexibility and usability at the forefront, putting patients, physicians and pharma at the heart of drug delivery.

ABOUT THE COMPANY

Eitan Medical is re-imagining drug delivery, with reliable innovations that put patients at the center of care, making drug delivery easier and safer than ever before. Patient safety and care are only the starting point, as Eitan Medical goes beyond, delivering connected, intuitive drug delivery and infusion solutions that are designed to improve patient and clinician quality of life across the continuum of care, including hospital, ambulatory and homecare environments.

For over a decade, Eitan Medical has provided safe, intuitive and flexible solutions that meet evolving drug delivery needs. Eitan Medical's product lines include the Sapphire™ infusion platform, which provides connected infusion therapy systems for hospital and ambulatory settings; the Sorrel™ wearable drug delivery platform, a patient-centric on-body injector for delivery of biologic treatments; and the Avoset™ infusion pump, a connected infusion system for the homecare market.

REFERENCE

1. *"The Drug Development Process". US FDA website, accessed Sep 2021.*

ABOUT THE AUTHOR

Ori Ben-David, PhD, is the Vice-President of Research and Development, Pharmaceutical Solutions, at Eitan Medical, responsible for research and development of the Sorrel™ device platform, where he applies his extensive hands-on expertise in medical device innovation. Prior to joining Eitan, Dr Ben-David served as Manager of Research and Mechanics at Q Core Medical (Netanya, Israel), and Research and Development Director at Bmax (Toulouse, France). He holds a PhD in Energy, and an MSc and BSc in Mechanical Engineering, all from Ben-Gurion University of the Negev (Israel).

MIKRON AUTOMATION: A LEADER IN THE COMPLEX ASSEMBLY OF ON-BODY INJECTORS

In this article, Mikron Automation sets out its expertise in the assembly of on-body injectors, a field requiring exceptional precision and innovative approaches, as well as discussing how Mikron works with its partners from the very earliest stages of device development to help ensure projects are completed efficiently and successfully.

Mikron Automation is a leading partner for scalable and customised assembly systems and has an excellent track record in the pharmaceutical industry, particularly in the complex assembly of drug delivery devices. With more than 3,900 machines designed and installed worldwide (Figure 1), the Swiss assembly machine designer and manufacturer continues to demonstrate its commitment to innovation with its implementation of assembly processes for on-body injectors, which are used in the treatment of diabetes and other chronic diseases. These small injection devices adhere directly to the skin and therefore require Mikron to address several assembly challenges – critically, the handling and manipulation of the highly miniaturised parts that make up the device and the ability to perform simultaneous engineering with customers when the product is still undergoing design changes.

> "Similar to the way autoinjectors underwent lengthy development periods before experiencing their recent boom in demand, on-body injectors are still an emerging technology at present."

Figure 1: A fully automated Mikron assembly line.

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"Particularly innovative and the subject of numerous patents, on-body injectors are very complex in their assembly and require several parts, some of which are no larger than a few tenths of a millimetre."

PUSHING THE LIMITS

Mikron Automation is well-versed in the diabetes market, having produced numerous assembly systems for pen injectors and other connected devices. However, similar to the way autoinjectors underwent lengthy development periods before experiencing their recent boom in demand, on-body injectors are still an emerging technology at present.

"We began receiving the first customer requests for this type of device in 2013–2014," recalls Flavio Pointet, Key Accounts Manager at Mikron Corporation Denver (CO, US). Mikron is well-known in the pharmaceutical market for the precision of its machines, the quality of its systems and its expertise in complex assemblies. This reputation led to the company being approached for the first on-body delivery device projects. Although Mikron's expertise was already well established, embarking on the assembly of a new type of highly innovative device is always a challenge. "It required us to go even further in our capabilities to implement miniature part assembly processes to be able to achieve these previously unattainable high-precision systems", acknowledges Jean-François Bauer, Head of Marketing and Business Development at Mikron Automation.

EXTREME MINIATURISATION

Medical device manufacturers design on-body drug delivery devices to be as small as possible. This technology is pushing the boundaries of miniaturisation so that the patient can benefit from the device without it obtrusively impacting their daily life.

Particularly innovative and the subject of numerous patents, on-body injectors are very complex in their assembly and require several parts, some of which are no larger than a few tenths of a millimetre. For example, some silicone seals have an external diameter of less than 1 mm. In addition to their soft and sticky material, their small size makes all gripping, placement and control operations during the assembly process very challenging. The drug delivery needles used in these devices are also extremely thin, with an external diameter of 0.3 mm. During the assembly process, they have to be bent while ensuring that there will be uninterrupted passage of the fluid in the final product (Figure 2).

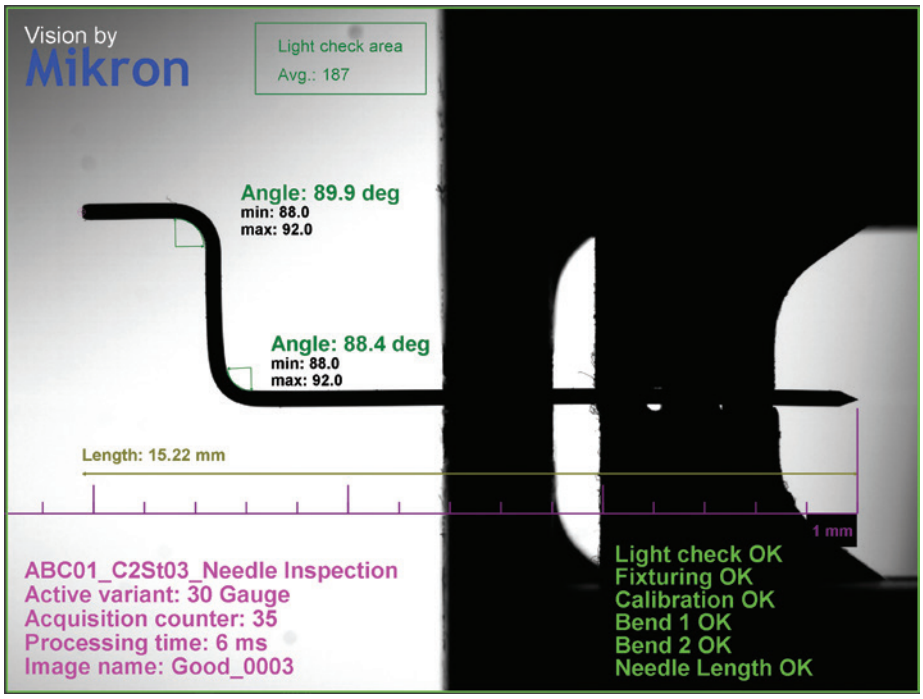

Figure 2: Highly precise control is needed to bend the needle during assembly without blocking the fluid path.

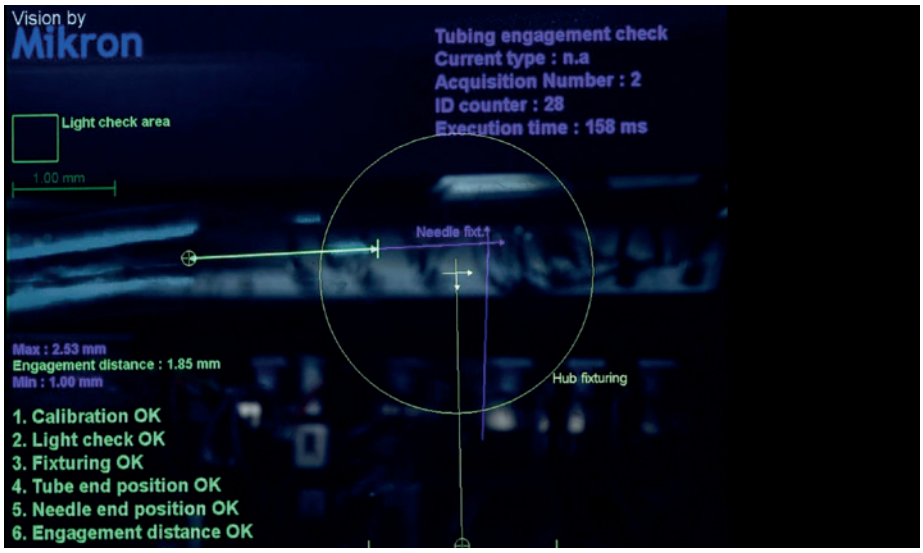

Figure 3: Precise connection between the needle and silicon tube.

The challenge for Mikron Automation was to develop a system that could assemble these various miniature components, some not even visible to the naked eye. "Originally, our automation systems were not deployed to assemble intricate assemblies of this size and precision," notes Mr Pointet. "We had to perform micro-assembly and micro-adjustment operations that we had never done before!"

Therefore, to meet the exceedingly high-precision requirements for the design and adjustment of these systems, the Swiss company's engineers and technicians had to use high-resolution cameras and large screens that allowed them to zoom in on certain areas of intervention during the assembly process and make extremely fine adjustments and specific alignments (Figure 3). In the end, the technology deployed was exceptional in terms of precision and assembly efficiency.

SIMULTANEOUS ENGINEERING WITH THE CUSTOMER

Another challenge for Mikron in the implementation of automation in this field is that it is a rapidly developing market. Few products are currently on the market, and many are still under development. "With this type of device, our support is provided at a very early stage of the project, with products whose development is not yet finalised and that do not yet work in practice", notes Mr Pointet. "For the past five years, clients have been asking us for help well before the clinical testing phase. They have a clear idea, prototypes of parts made in 3D printing, but they are still very far from the final product stage."

For this reason, Mikron has expanded its pre-production services to meet some of these specific needs. To demonstrate its ability to perform certain complex operations and assemblies (Figure 4), Mikron provides proof of principles for certain assembly processes and key operations that can later be integrated into the overall assembly system. Similarly, Mikron will engage with its partners during the product development phase to suggest design improvements.

When performing a design for manufacturing and assembly (DFMA) analysis, Mikron will use its experience to suggest design changes that may improve the assembly process. For some projects, Mikron also provides use of its ISO 13485 certification and qualified Class 7 clean room, in which device-level tests can be carried out. As a result, the customer's device is developed simultaneously with Mikron's assembly system.

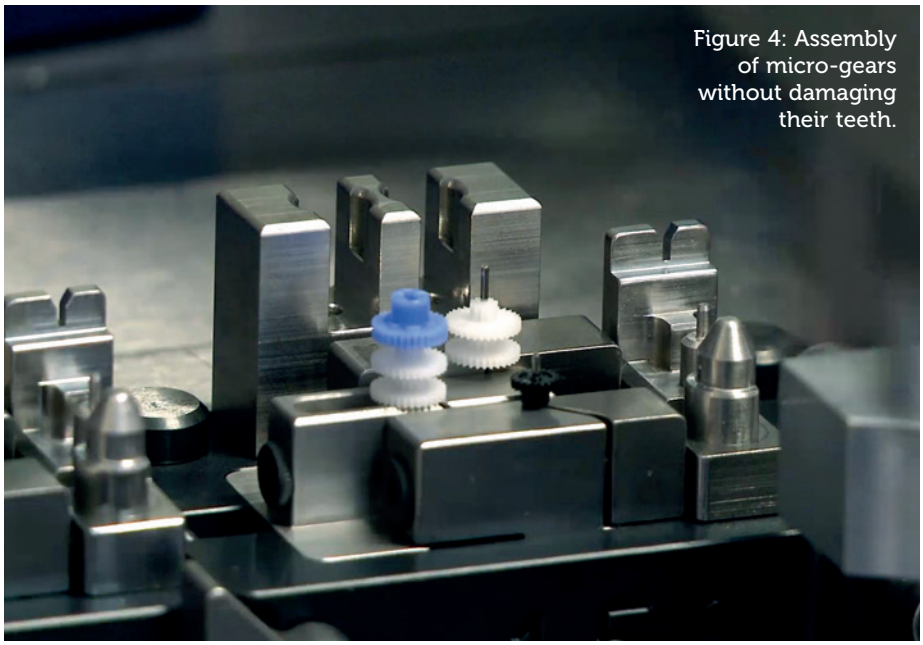

Figure 4: Assembly of micro-gears without damaging their teeth.

A PARTNERSHIP BUILT ON TRUST

For a supplier such as Mikron, being involved in a customer's project at a very early stage means that a relationship based upon trust must be established between the two parties. "For devices like on-body injectors, where we start working with customers at a very early stage of the project, it is essential to establish a real partnership with the customer in regard to the technological challenges involved and the financial investments", says Mr Bauer. "This implies that there is an open communication and a real collaboration between the two partners. Very often, clients are developing new products that have a lot of intellectual property. Confidentiality and trust are essential to the success of the programme."

Mikron Automation has proven to be the partner of choice for assembling on-body injectors, enabling the best risk mitigation for its customers, thanks to the security offered by its process expertise, its corporate culture based on customer success, and its global scale, which enables it to support the challenges of such projects financially (Figure 5).

ABOUT THE COMPANY

Mikron Automation, a division of the Mikron Group, is a leading partner for scalable and customised assembly systems – from the first idea to the highest performance solutions. Distinguished by a commitment to innovation, flexibility, unparalleled customer service and an evolving platform portfolio, Mikron delivers state-of-the-art solutions to the most complex assembly and testing demands.

To date, Mikron Automation has installed more than 3,900 assembly and testing systems worldwide. Its international customers operate in the pharmaceutical, medtech, automotive, electrical/industrial and consumer goods markets. Mikron Automation currently employs around 750 people and is headquartered in Boudry (Switzerland), a region that is regarded as the heart of the Swiss watchmaking industry. It also has sites in Denver (CO, US), Singapore, Shanghai (China) and Kaunas (Lithuania). It is a member of the Mikron Group, a publicly traded company with more than 100 years' experience in precision machinery.

Figure 5: Mikron Automation's headquarters in Boudry, Switzerland.

MicroMED
Precision Drug Delivery Platform

A NEW MEMS ENGINE FOR LARGE-VOLUME SUBCUTANEOUS INJECTORS

Here, Jiunn-Ru Lai, PhD, Associate Professor, Tsung-Chieh Cheng, PhD, Professor, both of Kaohsiung University of Science and Technology, and Brian Li, PhD, Chief Executive Officer of MicroMED, discuss how MicroMED's Primary Actuator technology for driving high-volume, high-viscosity injection devices compares with current spring and motor technologies.

Lately, a significant trend has been noted in the biologics market – the shifting of the preferred administration route from intravenous (IV) towards subcutaneous (SC) injection.[1] Due to the challenge represented by the frequent need for large-volume doses, SC delivery of biologics faces difficulties with solubility and large-volume form factors. This large-volume requirement is also difficult for traditional SC injection techniques due to the pain and tissue responses it causes. As such, there is a clear need for new delivery technologies to assist both patients and caregivers in improving the experience of large-volume injections.

Pharma companies have adopted two major approaches to resolve these large-volume SC injection challenges – manual SC injection formulation and device-assisted injection technology. For example, some blockbuster antibody biologics, including Herceptin® (trastuzumab, Genentech), Rituxan® (rituximab, Genentech) and Darzalex® (daratumumab, Janssen), now have both IV and SC versions (specifically formulated for manual injection).[2] On the other hand, advanced injection devices, such as autoinjector or on-body injectors (OBIs), have demonstrated huge potential to enable SC administration of biologics.

Many advanced injection devices have shown promising performances in both at-home and clinical settings. 2.25 mL autoinjectors are one of the large-volume solutions launched by many traditional 1 mL autoinjector manufacturers.[3] Beyond 2.25 mL formats, even larger volume

Large-Volume Engine Mechanism	Spring	Micro-Motor	Primary Actuator
Initial Impact	✶	✶✶✶	✶✶✶
Maximum Driving Force	✶✶	✶	✶✶✶
Storage Load	✶	✶✶✶	✶✶✶
Stable Injection Flow	✶	✶✶	✶✶✶
Size of Device	✶	✶	✶✶✶
Noise	✶✶	✶	✶✶✶
Connectivity Integration	✶	✶✶✶	✶✶✶
Cost	✶✶✶	✶	✶✶

Table 1: Comparison of the current driving technologies for large-volume injectors. Performance scale: ✶✶✶ Excellent, ✶✶ Good, ✶ Normal.

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Figure 1: 3D model and photo of the MicroMED Primary Actuator.

autoinjectors, including 5 mL and 10 mL,[4,5] are on their way to the market. Meanwhile, in the world of OBIs, the 2 mL Neulasta Onpro for pegfilgrastim (Amgen)[6] and the 3.5 mL Repatha Pushtronex for evolocumab (Amgen)[7] have already received market approval and proven successful on the market. More OBIs, including some with volumes larger than 5 mL,[3] are now on the way.

Springs and motors are commonly used to provide the driving force in large-volume injectors – however, they are not without their flaws compared with more modern technologies (Table 1). For example, a preloaded spring can generate an initial impact force capable of breaking a 1 mL glass prefilled syringe (PFS). This issue can be more serious when dealing with larger volume PFSs, such as 2.25 mL, 5 mL or 10 mL. Another example is the low driving force provided by micro motors, due to the fact that a motor's torque is proportional to the radius of its rotor. Therefore, to generate a large torque force to drive an injection, a micro motor has to increase its rpm (rotational speed), resulting in high frequency noise and significant vibration during use, making it difficult to meet the requirements of advanced large-volume injectors.

MICROMED'S PRIMARY ACTUATOR

Previously, MicroMED presented an innovative micro linear actuator – the Primary Actuator® (Figure 1 and Table 2). The company's goal is to apply this small-footprint, accurate and powerful microelectromechanical system (MEMS) to solve the current unmet needs in large-volume SC drug delivery.[8] This MEMS engine is an enabling driving force solution evolved from the semiconductor industry, offering superior strength and accuracy for injections, a broad range for injection rate and a low cost. These qualities make this technology particularly suitable to address the needs of large-volume, high-viscosity SC biologic injections.

The device is specifically designed to drive the actuation of primary containers such as PFSs or prefilled cartridges with a telescopic push rod mechanism (Figure 2). This miniaturised engine uses a small but powerful MEMS microchip and integrated micro control circuitry to provide the injection force, speed and control required by even the most challenging high-viscosity, large-volume biologics.

A strong partnership between MicroMED and industry partners will enable the MEMS engine technology to be developed into a high quality commercial injector product that meets the true need of today's large-

	PA-001-6W	PA-001-12W	PA-001-24W
Input Voltage	6.0 V	8.0 V	12.0 V
Input Power	6.0 W	12.0 W	24.0 W
Stroke	28mm	40mm	40mm
Maximum Static Force	1000 N	1000 N	1000 N
Ingress Protection	>IP66		
Operating Noise	<25dB		
Operating Temperature	0°C – 60°C (32°F – 140°F)		
Pin Length	5.3mm	20	20
Materials Telescopic Push Rods Actuator Housing Input Pins	Stainless Steel Polycarbonate Copper		
Dimension Body Rod	12 x 12 x 10.8 mm 9.5 (D) x 14.8 (L) mm	15 x 15 x 15.8 mm 8.5 (D) x 36 (L) mm	23 x 23 x 16.3 mm 13 (D) x 16.3 (L) mm
Free Sample Available	No	No	Yes

Table 2: Standard product specifications for the Primary Actuator. Customisation of the device is available upon request.

volume biologic injectables. The following sections showcase the performance of the Primary Actuator in case studies where it was integrated into injector prototypes with the following form factors (Figure 3):

- A 1.0 mL autoinjector
- A 2.25 mL autoinjector
- A 5.0 mL large-volume autoinjector
- A 10 mL large-volume OBI.

PRIMARY ACTUATOR IN LARGE-VOLUME AUTOINJECTOR

Force Performance

To begin with, both the static and dynamic force-to-time responses for the Primary Actuator were calibrated. First, the real-time static force output of the actuator was measured using a load cell force sensor (Figure 4). The peak driving force was over 500 N at a time of around 4 seconds. While higher forces were also tested (up to 1,000 N), the 500N force measured already surpasses most of the currently used driving technologies (springs and motors) by more than 10 times.

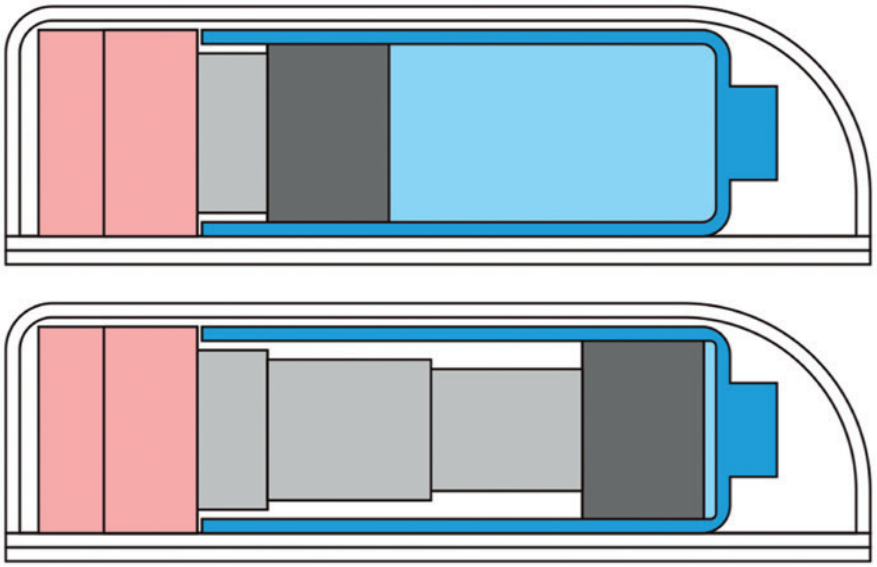

Figure 2: Telescopic rod actuation of the MicroMED Primary Actuator.

Second, the dynamic force output (Figure 5) of the Primary Actuator was measured in real time while driving a 5.0 mL PFS with a 26G needle and 8.5 cP testing fluid to simulate actual administration conditions. The force smoothly ramped up from zero until reaching a steady-state operating force of 50–60 N. When the plunger reached the end of the primary container (at around 20 seconds), the force increased linearly, showing a characteristic feature of the dynamic force performance of the Primary Actuator.

Figure 3: Prototype 2.25 mL autoinjector, 5.0 mL autoinjector and 10 mL large-volume OBI.

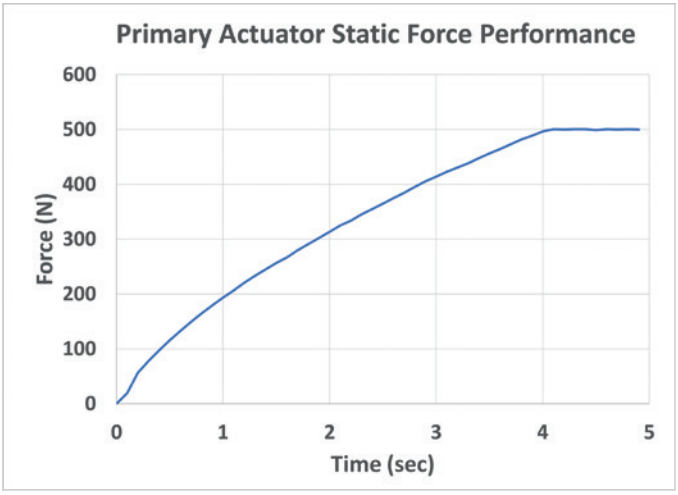

Figure 4: Real-time static force output of the Primary Actuator.

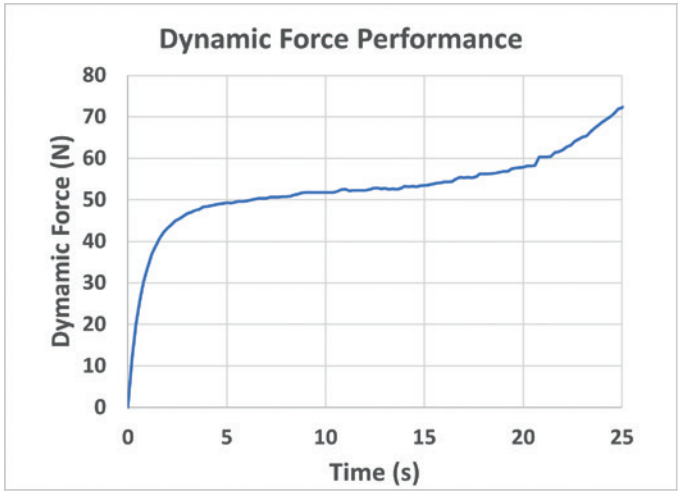

Figure 5: Dynamic force response of the Primary Actuator driving a 5 mL PFS.

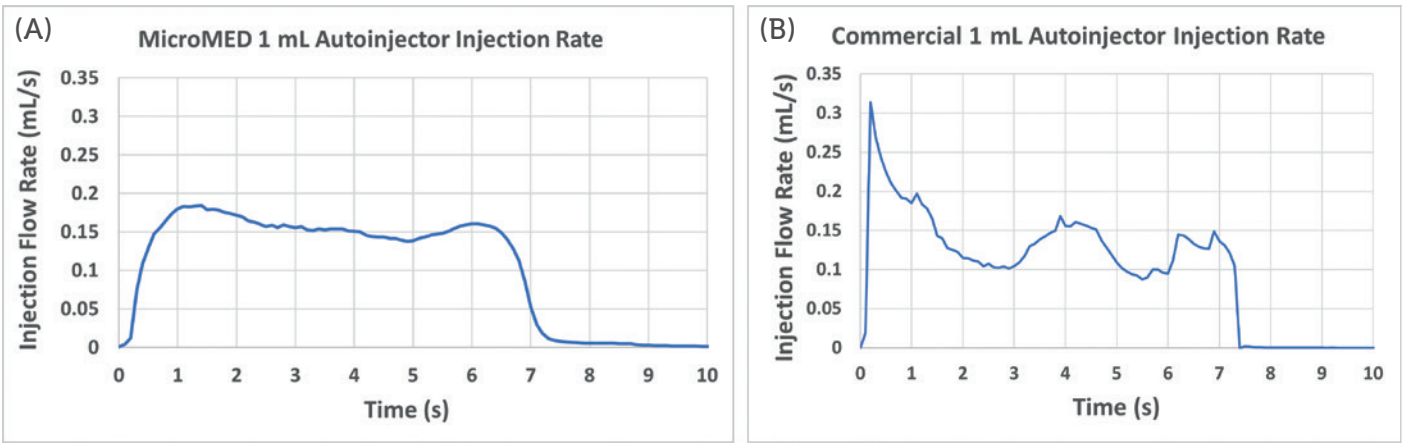

Figure 6: Injection rate performance of (a) the Primary Actuator and (b) the off-the-shelf autoinjector driving a 1 mL PFS.

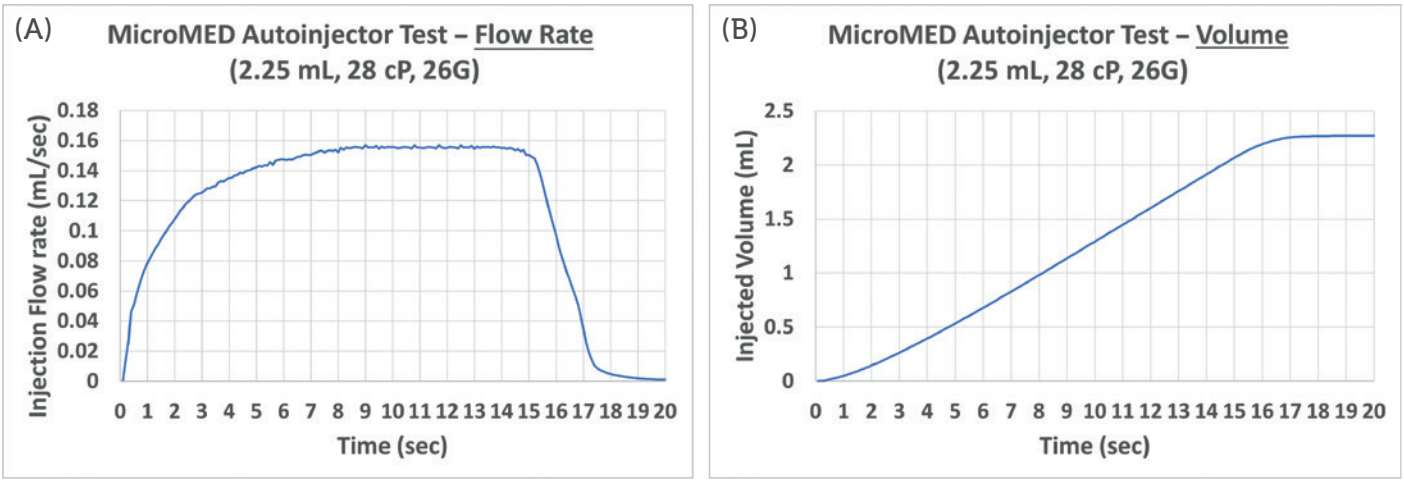

Figure 7: (a) Injection rate and (b) injected volume performance of a Primary Actuator-driven 2.25 mL autoinjector.

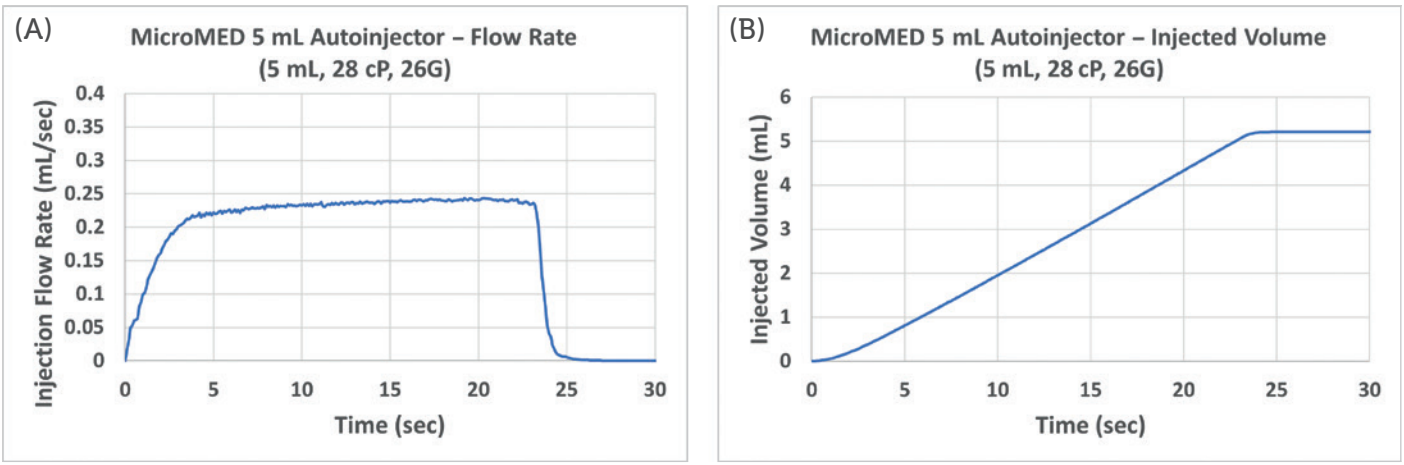

Figure 8: (a) Injection rate and (b) injected volume performance of a Primary Actuator-driven 5 mL autoinjector.

Flow Control Performance

The injection flow control for the Primary Actuator was assessed in real time as the driver for three different autoinjectors:

- A 1 mL PFS with 26G needle and 1 cP testing fluid (Figure 6)
- A 2.25mL PFS with 26G needle and 28 cP testing fluid (Figure 7)
- A 5 mL PFS with 26G needle and 28 cP fluid (Figure 8).

Since the rubber plungers used in many primary containers are known for suffering from stiction issues, this real-time injection-rate performance provides a detailed insight into how smoothly the Primary Actuator was able to overcome this challenge. When the resulting data from this test was compared with an off-the-shelf 1 mL autoinjector (Figure 6B), two obvious differences were observed:

- The Primary Actuator provides a gentle flow increase at the beginning of injection, whereas the commercial autoinjector shows an instant initial spike in flow rate

- The Primary Actuator demonstrated a smoother and more stable flow control after reaching a steady-state flow compared with the off-the-shelf autoinjector, which had an up-and-down variance in flow rate during use.

As previously discussed, spring-driven autoinjectors are known for their high initial impact force when the spring is first released. This problem becomes much more serious in large-volume autoinjectors, such as 2.25 mL, 5 mL or even greater volumes. Therefore, current large-volume autoinjectors with volumes greater than 5 mL cannot use PFSs as their primary container and require pharma companies to use non-standard alternatives, such as prefilled cartridges or custom plastic containers, which regularly results in the US FDA and other regulatory authorities requiring additional tests and reviews, increasing the risk and time-to-market involved in product development. Additionally, line springs – those normally used in autoinjectors – are also known for their varying driving force across the overall injection process and problems related to the plunger sticking, which occur quite often due to misalignment of force in combination with the plunger stiction issue.

Next, MicroMED's Primary Actuator was demonstrated to be capable of actuating a 2.25 mL PFS with 28 cP simulated fluid through a 26G needle with a total injection time of about 17 seconds. The flow-rate-to-time performance data were collected using a commercial high-accuracy flow sensor (Figure 7a). It went smoothly from zero to steady-state without an instant initial spike and ceased when the plunger hit the end of the container, showing good end-of-the-injection flow behaviour.

These data were then converted into an injected volume-to-time graph (Figure 7b). This injected volume curve shows a flat and smooth increase, representing an excellent drug injection performance. These results show that Primary Actuator driven autoinjector products offer a much lower risk of causing pain to the patient, due to the stable flow control, and breaking the glass container, due to the lack of initial impact commonly seen in spring-actuated autoinjectors.

Figure 8 depicts the MEMS engine's performance driving a 5 mL PFS autoinjector with a 26G needle and containing 28 cP fluid. Similar to the 1 mL and 2.25 mL autoinjectors, there was no initial spike of force and a steady-state

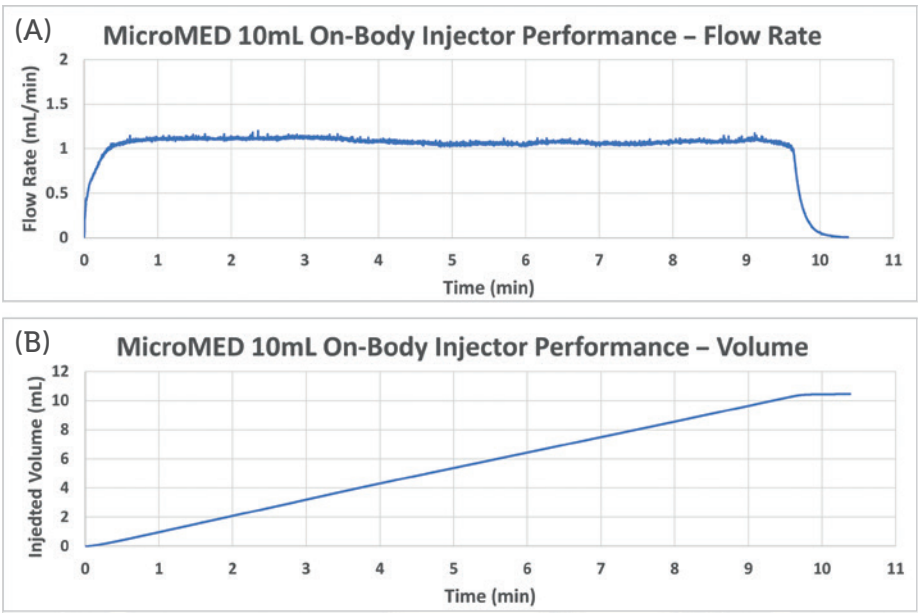

Figure 9: (a) Injection rate and (b) injected volume performance of a Primary Actuator-driven 10 mL OBI.

"The Primary Actuator is an innovative, small-footprint, low-cost solution for the delivery of large-volume, high-viscosity biologics."

stable flow was established. This represents a key signature of the Primary Actuator's innovative technology. Additionally, the Primary Actuator achieved an injection time of around 23 seconds for the 5 mL injection.

PRIMARY ACTUATOR IN LARGE-VOLUME OBI

A prototype 10 mL OBI with 28 cP drug simulated fluid and a 26G needle cannula was developed using MicroMED's Primary Actuator to demonstrate a smooth and stable injection control with a target injection time of 10 minutes. Figure 9 shows the results of this test, as measured by a commercial flow sensor. The flow rate (Figure 9a) was smooth and stable throughout the whole injection process and the converted injection volume (Figure 9b) shows a linear increase, demonstrating extraordinary injection speed control for the MEMS-enabled OBI system.

The total capacity needed from the battery was about 17 mAH and the electrical power needed was 0.4 W, meaning a small commercial lithium ion primary battery would be able to power the micro actuator. This enables designers to simplify the design and lower the overall drug delivery device footprint. Overall, these tests demonstrate that MicroMED's Primary Actuator is superior to many current injection driving technologies, such as springs and motors (Table 1).

CONCLUSION

The Primary Actuator is an innovative, small-footprint, low-cost solution for the delivery of large-volume, high-viscosity biologics. Unlike springs, the MEMS engine has a gentle push in the beginning, followed by a smooth and stable injection flow control toward the end of the injection. This technology represents a next-generation-device-enabling technology with the potential to solve major challenges in current large-volume SC injector product development.

Enabling device designers to use standard PFSs even at high volumes and viscosities can lead to significant savings in development time and resources for pharma companies. The Primary Actuator has demonstrated its capability as a smart solution for drug delivery that will benefit all stakeholders in the SC injection market. A successful partnership between strategic collaborators and MicroMED will enable this engine technology to be developed into a high quality commercial injector product meeting the real needs of today's large-volume biologic injectables.

ABOUT THE COMPANY

MicroMED is a MEMS microchip design house specialising in the development of microinjection devices targeting unmet needs in the most challenging drug delivery applications. MicroMED has established a proprietary high-precision MEMS drug delivery engine system, capable of delivering broad flow rate from 1 nL/min to 10 mL/min (eight orders of magnitude) with driving force up to 2,000 atm (29,000 psi) of pressure. MicroMED welcomes all types of business connections/relations in the PDA drug delivery value chain (pharma, biotech, medical injector developer and insurance payer) with the goals below (but not limited to):

- Purchasing of the current micro-engine products
- Co-development of advanced injector products
- Licensing of the micro-engine proprietaries/intellectual properties.

MicroMED has established a strong and experienced supply chain for the development of injection devices from raw material suppliers, semiconductor foundries and component providers to contract manufacturers in both the US and Taiwan. These valuable partners have required regulatory certifications and years of experience in supporting medical device design and manufacturing. MicroMED applies its quality management system, providing the necessary structure and controls to help its value-chain supplier team develop products that meet defined safety and performance requirements for high-value drug delivery customers.

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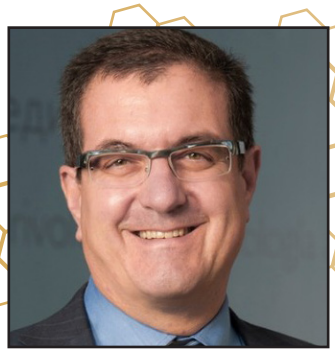

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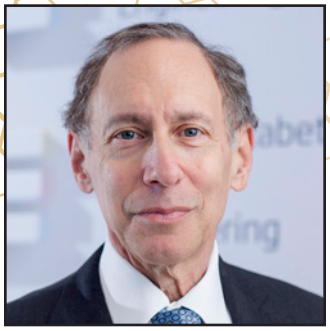

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THE EVOLUTION OF WEARABLES – REPRESENTING THE VOICE OF THE ENTIRE ECOSYSTEM

In this article, Lauren Orme, Director, Regulatory Policy and Intelligence, Victoria Morgan, Director, Segment Marketing, Global Biologics, and Shari Krusniak, Director, Strategic Marketing, Contract Manufacturing and Integrated Solutions, all of West Pharmaceutical Services consider the current landscape for on-body delivery systems and discuss how West is responding to the demands of various stakeholders.

As with so many aspects of drug delivery post-pandemic, there have been tangible improvements in the evolution of on-body delivery systems (OBDSs). Today, OBDS platforms can deliver higher volumes of medicines subcutaneously that have traditionally required an infusion to be administered intravenously at a clinic under the supervision of a healthcare professional (HCP).

Shifting the focus of treatment away from clinical settings means that patients can benefit from greater choice and control over the management of their disease, but also has wider implications for payers and HCPs in terms of adherence, symptom management and, of course, cost. However, as the evolution of OBDSs continues, regulators have begun to weigh in on the agenda – the updates to the ISO 11608 series of standards, as well as ongoing developments in the guidance issued by regulatory authorities, mean there is a great deal for pharma companies to consider in their OBDS development paths.

> "It is hardly surprising that there is growing interest in this novel and ever-evolving delivery route across the pharmaceutical ecosystem, from pharma companies to payers to patients."

A MARKET RICH WITH OPPORTUNITIES AND SOME CHALLENGES

The global wearable injectors market is projected to reach US$11.6 billion (£9.6 billion) by 2026 at a compound annual growth rate (CAGR) of 9.9%.[1] As such, it is hardly surprising that there is growing interest in this novel and ever-evolving delivery route across the pharmaceutical ecosystem, from pharma companies to payers to patients.

This projected growth can be attributed to several factors, not least of which is the sustained effort to shift treatment from clinical to at-home settings, a factor that was accelerated by the practical difficulties triggered by the pandemic. Indeed, the global home healthcare market is expected to expand at a CAGR of 7.9% from 2022 to 2030 as patient behaviours that pivoted during the pandemic become habitual.[2] Other drivers include the rising prevalence of chronic diseases and advancements in technology that have enabled OBDSs to deliver larger volumes of drugs subcutaneously over longer time periods and in non-clinical settings.

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Non-communicable diseases (NCDs) are the leading cause of mortality and ill health globally and account for seven out of ten deaths worldwide,[3] with a sustainable development goal (SDG) target to reduce premature mortality from NCDs by a third by 2030, relative to 2015 levels. West believes that the market readiness of OBDS platforms that can deliver higher volumes of more viscous biologics is a key step forward in achieving this SDG target.

ADDRESSING KEY PATIENT NEEDS

Established in 2012, patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs and priorities are captured and meaningfully incorporated into drug development and evaluation. As experts in what it is like to live with their condition, patients are uniquely positioned to inform the understanding of the therapeutic context during the development of a drug product.[4]

For example, insights from the series of reports into lung and breast cancer from PFDD entitled "The Voice of Patient" highlighted the real challenges patients with these conditions face.[5,6] Cancer and its treatments impact all aspects of patients' lives, with participants in both studies describing limitations in physical activity due to fatigue or pain, as well as the burden of frequent doctor or hospital visits. Indeed, fatigue or lack of energy was highlighted as a key pressure point throughout these patients' treatment regimens, with one participant describing not being able to walk without feeling "like I was lifting up weights".

> "There is a great deal of evidence to suggest that supporting disease self-management offers several benefits to patients, including an increase in overall wellbeing, improved mental health, better clinical outcomes and smarter, more cost-effective use of health services."

There is a great deal of evidence to suggest that supporting disease self-management offers several benefits to patients, including an increase in overall wellbeing, improved mental health, better clinical outcomes and smarter, more cost-effective use of health services.[7] In this context, it is clear that OBDS platforms can play a critical role in delivering a successful self-management approach.

ADDRESSING KEY PHARMA NEEDS

This evolving patient preference landscape inevitably drives how pharma needs to deliver medicines. While patient safety and regimen efficacy are prerequisites for any therapy, adherence and the patient experience have always been high on the list of pharma priorities – ones that OBDS platforms can certainly play a key role in delivering.

From an experiential perspective, all the objections raised about travelling to a clinic or hospital are nullified, along with many of the other common reasons for non-adherence. Advances in therapeutic proteins are also enabling better treatment regimens for patients with cancer, cardiovascular or other chronic conditions, such as Crohn's disease or rheumatory arthritis – in particular by decreasing the required dosing frequency, which contributes to improved patient adherence. This means that the scope for OBDS platforms is also growing as the historic challenges of delivering higher volume, more viscous drugs is increasingly overcome.

ADDRESSING KEY PAYER NEEDS

For payers, OBDS platforms represent a significant potential for change. Currently, these stakeholders are facing several challenges, whether in the form of increasing healthcare costs or the growing level of complexity in personalised healthcare provisions. As payers have already acknowledged, increased patient engagement results in better outcomes, with the net effect often being a lower overall cost of care.

Greater patient engagement, in many cases, comes from patient-driven care in a home environment. OBDS platforms could therefore provide part of the game-changing, disruptive influence payers need as the need for treatment for chronic diseases grows, relieving the strain on healthcare centres by reducing their need for staffing, patient capacity and expensive equipment. Add to that the fact that transitioning from infusion therapies in hospitals,

	Injector	Pump
Dose Delivery Profile	Delivery is comprised of administration of a fixed dose of drug product from a prefilled container in a predetermined time	Delivery is comprised of administration of a fixed dose of drug product from a prefilled container in a predetermined time
Determination of Time and Rate of Delivery	Rate and time of delivery is based on patient tolerability and/or convenience	Rate and time of delivery is based on clinical relevance (e.g. medication efficacy)
FDA-Recognised Consensus Standards	ISO 11608 Series (Part 1–6)*	ISO-26825, Second Edition 2020-10 ISO-7886-2, Second Edition 2020-04 AAMI TIR38:2019 ISO 9626, Second Edition 2016-08-01 ISO 23908, First Edition 2011-06-11
Applicable Regulations	21 CFR 880.5860 – Piston Syringe	21 CFR 880.5725 – Infusion Pump

**Note: Current consensus standards are not defined for product code QLF. The ISO 11608 series is expected to be the approved by the FDA for product code QLF.*

Table 1: Key differences between injectors and pumps.

A Logical Choice for Biologics

Biologics and biosimilars hold tremendous promise to address unmet medical need, but manufacturing these products is fraught with complexity and risk. Having trusted partners with expertise in containment and delivery systems is essential for any company working to bring advanced therapies to the market.

West Is a Trusted Manufacturing Partner

For more than 100 years, West has provided packaging, transportation, storage and manufacturing solutions to pharmaceutical and biopharmaceutical partners all over the world. The success of these partnerships has resulted in the use of more than 112 million West components and/or devices each day, including wearable devices and self-administered injectables. In fact, eight out of 10 biggest-selling biologics rely on West packaging.

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West's SmartDose® drug delivery platform is not independently cleared or approved by any Regulatory Body for general healthcare professional or patient use, nor is it available for general commercial purchase. Its distribution and use are subject to applicable regulatory requirements for clinical investigation, and for marketing authorization, as used in combination with a specific drug or biological product. Each component of a combination product is subject to the requirements established by the Regulatory Body for that component (drug, biologic or device). The regulatory process can be more complicated for combination products including an evaluation of the product characteristics, delivery system and its functionality, as well as the potential for undesirable interactions between the drug or biologic and the delivery system. As a result, we note that the SmartDose® drug delivery platform's compatibility with any particular drug or biologic must be confirmed, and its ability to achieve the desired patient benefits must also be confirmed, on a case-by-case basis in a manner sufficient to meet Regulatory Body requirements.

clinics or infusion centres to at-home care could result in a cost saving of up to 70% for both patients and healthcare payers,[1] and there are many compelling reasons for payers to welcome OBDSs as an important part of the modern healthcare delivery mix.

ADDRESSING KEY REGULATORY NEEDS

Of course, any gains for patients or payers must be realised within the changing regulatory framework. The original ISO 11608-1:2014 has recently been updated for the first time since 2014 and is now in its fourth iteration, providing several new technical updates and a new chapter dedicated to requirements for OBDSs. The ISO 11608 series includes requirements for design verification of the needle-based injection system's conformance with its design specification to a highconfidence level.

Because OBDSs can now deliver larger volumes of a drug product, a key consideration is whether the dose-delivery profile classifies the device as an injector or a pump. Answering this question is key to applying the correct product classification and standards during development, meaning that determining whether a device is a pump or injector should be decided as early as possible in the development process.

Using available information from the US FDA and ISO,[8,9] the key consideration to determine if an OBDS qualifies as an injector or a pump is whether the dose-delivery profile is tied directly to the clinical efficacy of the product. If the drug sponsor confirms that the delivery rate has a significant impact on the clinical efficacy via its clinical study, the OBDS will be classified as an infusion pump, otherwise, it will be classified as an injector. The key differences between injectors and pumps are summarised in Table 1.

THE WEST RESPONSE

As therapies become more complex and self-administration increasingly becomes the new norm, pharma companies are responding by demanding devices that are both more intuitive and capable of delivering more complicated medicines. This all comes against a backdrop of an evolving regulatory landscape.

OBDS platforms offer a range of tangible benefits throughout the ecosystem.

> "With increased market opportunity comes greater oversight, and the evolving regulatory landscape requires pharma and biotech companies to partner with an expert device developer that can help them navigate the development path successfully."

For patients, disruption to daily life is limited, with a growing body of evidence that clinical outcomes are improved via the patient-driven care route.[7] For payers, there is the potential of a very real cost saving. For HCPs, there are reduced treatment times and workloads. And for pharma companies, there is now an opportunity to develop more complex therapies, with higher-volume capacities than previously possible.

Figure 1: The SmartDose 10 OBDS is an adaptive technology for large-dose volumes.

With increased market opportunity comes greater oversight, and the evolving regulatory landscape requires pharma and biotech companies to partner with an expert device developer that can help them navigate the development path successfully. West combines its full-service portfolio of expertise, including device development, containment systems, regulatory support, analytical testing, combination product manufacturing and fill-finish solutions, to enable partners to develop OBDSs faster, more safely and with less risk, all while ensuring that the end product is reliable and usable (Figure 1).

West leverages over 90 years' experience in developing, testing, manufacturing and commercialising containment systems and devices to support development teams in navigating the challenges and mitigate the risks encountered on the path to commercialisation. From preclinical support to post-market launch, West's full-service portfolio, complemented by a range of drug delivery devices, enables pharma and biotech partners to maximise the benefits only an integrated provider can deliver.

ABOUT THE COMPANY

West Pharmaceutical Services is a leading provider of innovative, high-quality injectable solutions and services. As a trusted partner to established and emerging drug developers, West helps ensure the safe, effective containment and delivery of life-saving and life-enhancing medicines for patients. With approximately 10,000 team members across 50 sites worldwide, West helps support its customers by delivering over 45 billion components and devices each year.

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Lauren Orme is Director of Regulatory Policy and Intelligence at West Pharmaceutical Services. Ms Orme has over 15 years of experience in the pharmaceutical packaging, medical device and analytical testing services industries. Currently, Ms Orme leads a regulatory team that oversees the monitoring of global regulatory requirements, changes in the regulatory landscape and the implementation of related strategies.

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DEVELOPING AN ON-BODY PLATFORM FOR EFFECTIVE POST-OPERATIVE PAIN MANAGEMENT

In this article, Paolo Golfetto, Drug Delivery Systems Business Development Director at Stevanato Group, and Sheldon Moberg, Senior Vice-President of Drug Delivery at Bexson Biomedical, discuss an urgent requirement to meet an unmet patient need.

Medical operations are generally initiated to save lives, repair trauma or improve quality of life. But there is no escaping the fact that medical procedures also carry inherent risk to patients, with the potential to trigger undesirable outcomes.

Post-operative pain is a case in point. In the immediate aftermath of surgery, patients commonly experience acute pain for days – and sometimes weeks – as bones, tissues and muscles repair the damage that stems directly from surgical procedures, as well as the initial triggering trauma.

Data from multiple hospital sites across the UK shows that, within 24 hours of surgery, around half of patients report moderate levels of pain, while around a fifth experience severe pain.[1] For patients in these circumstances, opioids have become a common source of prescribed relief. Over time, however, their benefits have been counterbalanced by a growing body of evidence around the potential for harm. Opioids, after all, are highly addictive, and long-term use increases the risk of developing tolerance, leading patients to high-dose dependency and substantial risk of overdose and death. Pain signalling often gets worse over time with opioid therapies. As such, even with appropriate medical care and sincere attempts to taper opioid use, many patients graduate to long-term addiction and chronic drug abuse.

In the US, this situation has been described as a national crisis, with the National Institute on Drug Abuse reporting that opioid abuse affects more than two million Americans, and an average of 90 deaths from opioid overdose every day.[2] Statistics such as these have led to greater attention being paid to opioid alternatives in pain management. One such example is ketamine, which has been shown at low doses to have analgesic effects through its properties as a non-competitive N-methyl-D-aspartate receptor antagonist.[3] In contrast to opioids, treating acute pain directly with ketamine stimulates a secondary action that appears to ratchet down chronic pain signalling over time.

> "The partnership was established to create a discreet wearable device that can safely and conveniently allow patients to manage acute pain."

As a controlled drug, the use of ketamine is carefully managed in medical settings by healthcare professionals, and administration is typically via on-site infusion at a clinic or hospital. While this ensures appropriate steady-state plasma levels can be achieved, the associated procedural burden and cost prevents patients managing their own pain relief from the comfort of their own home.

A MEETING OF MINDS TO MEET A SPECIFIC NEED

In 2020, Stevanato Group and Bexson Biomedical announced a collaboration designed to address these limitations and further unlock ketamine's potential as a patient-managed pain-relief treatment.

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Figure 1: The first form factor used for initial usability studies (for illustration purposes only).

The partnership was established to create a discreet wearable device that can safely and conveniently allow patients to manage acute pain. It was founded on the combined promise of Bexson's proprietary subcutaneous ketamine formulation, BB106, and Stevanato Group's broad, integrated capabilities in drug delivery, drawing specifically on the potential for the company's existing wearable device platform to be modified for the delivery of a pain-management therapy.

Constituting a disposable pod and handheld controller, this existing platform was originally developed as an alternative to pen injectors for diabetes patients, providing a comfortable, intuitive route for administering multiple subcutaneous drug therapies. On this basis, with appropriate customisation it could evolve to become a convenient and secure device for self-administration of Bexson's proprietary ketamine formulation.

However, it was clear from the outset that a wide range of important considerations would have to be accommodated to realise the shared ambitions of both parties successfully. These considerations included explicit requirements relating to the medicine's delivery, device manufacture and patient use. Resolving these issues in a timely fashion would be essential to limit the overall development cycle, reduce time-to-market, manage risk and contain costs.

The resulting flagship product is designed to support patients experiencing post-operative pain with a wearable device capable of administering ketamine-related pain-relief for up to five days after a procedure (Figure 1). A low-dose, continuous infusion of the therapy would establish an appropriate analgesic effect by addressing the short half-life of ketamine through the pump delivery profile. In addition, patients would have access to bolus doses for pain flares, with time-limited lockouts to avoid excessive dosing.

Given ketamine's status as a controlled drug, a key consideration was to find a balance between the available volume of ketamine, dosing control parameters and design elements capable of ensuring patient safety. This meant that the device would need to accept a preloaded drug cartridge, while offering precise dosing delivery increments and consistent flow rate. At the same time, the drug-containment mechanism would need to be both tamper proof and tamper evident, to protect against potential instances of misuse.

The Collaborative Evolution of an Existing Technology Platform to Address Post-Operative Pain Challenges

The nature of the partnership between Stevanato Group and Bexson Biomedical was a critical factor in ensuring these various challenges could be successfully and efficiently resolved. While some partnerships simply describe a mutual agreement between aligned stakeholders, in the case of this project, both parties contributed proactively and equally to an integrated, open collaboration. By elevating the relationship from a transactional supplier-client level to a more involved partnership, Stevanato Group and Bexson Biomedical laid positive foundations from which tangible operational gains could be realised.

For example, at the early stages of the project, Stevanato Group worked closely with Bexson Biomedical, providing space and time to develop an extensively detailed, nuanced understanding of the patient's experience and their needs. With deeper knowledge of the device requirements and the potential points of friction that could exist within user scenarios and manufacturing environments, Stevanato Group was afforded a significantly stronger opportunity to achieve its right-first-time delivery targets, avoiding costly complications and delays. For Bexson Biomedical, the collaboration produced a better appreciation of device capabilities and allowed the group to tailor the BB106 ketamine formulation towards a cost-effective and convenient device.

Ultimately, the result of this constructive, highly engaged collaboration will be an application-specific on-body device that integrates Bexson Biomedical's BB106 ketamine therapy based on its proprietary SEVALENT™ technology into a secure, patient-friendly drug delivery system. While it builds on many of the fundamental elements from pre-existing wearable technologies for diabetes care, a high degree of customisation ensures the specific and precise dosing requirements set out by Bexson Biomedical for its first ketamine use case are met.

As with the legacy platform, the device is based on a disposable injection unit, referred to as a pod, which is linked to a reusable electromechanical controlling unit with integrated circuitry. These elements are connected using a patented magnetic coupling system that drives the injection mechanism. The controller features a simplified user interface that incorporates activation buttons for basal and bolus dosing as well as lights and audible signalling to inform users of the start of the injection, error modes or incomplete doses. Regimens can be factory preprogrammed to adjust the dosing profile according to the patient application, and the logged user data can be transferred for use within broader healthcare support programmes.

Figure 2: The Nexa® platform features excellent mechanical resistance, offering superior compatibility with drug products and delivery devices.

Each pod is preloaded with a BB106 prefilled Nexa® 3 mL ISO cartridge from Stevanato Group's broad, integrated container offerings. While ketamine does not present particular challenges with regard to viscosity or stability, precise dosing is vital in controlled release of such a pain-relief drug. This demands that the quality and geometry of the cartridge is flawlessly consistent. Stevanato Group's rich heritage in glass expertise and market-leading position in cartridge manufacturing combine to produce the Nexa® product (Figure 2). This cartridge satisfies the stringent requirements necessary to support repeated accurate dosing with enhanced levels of mechanical resistance to withstand external forces. This system also offers the capacity to eliminate air from the drug-filled cartridges, which is a key consideration in dosing accuracy as bubbles of unpredictable size can potentially disrupt the fluid pathway and affect dosing precision.

At the time of administration, activation via the controller leads the pod to undergo an automatic priming function before the needle is deployed. This enables basal delivery and a limited number of patient-activated bolus deliveries based on user need. With sustainability in mind, the pod is free from electronic components, with both Stevanato Group and Bexson Biomedical committed to exploring the use of alternative materials that will further reduce the system's impact on global warming potential targets.

A PAIN-FREE PARTNERSHIP DELIVERING PAIN RELIEF FOR PATIENTS

From the beginning of the partnership, Stevanato Group's role as a device and manufacturing partner with integrated capabilities meant that it was able to contribute meaningfully at every stage of development, establishing a model that can scale with demand. This meant taking both direct responsibility for aspects such as container closure system characterisation, component manufacture and device sub-assembly, while also providing indirect support by advising on a suitable contract design and manufacturing organisation for the final assembly, fill and packaging phase.

The selection of a 3 mL cartridge was deliberate. This sizing allows for a small on-body device that enhances the patient experience and maximises compliance, while supporting a modular delivery system for Bexson Biomedical's SEVALENT™ technology. Bexson Biomedical's pharmacologic breakthrough enables liquid formulations of many small molecules at substantially higher concentration than typical intravenous presentations, while also optimising pH and osmolality to match subcutaneous tissue. The partners' strategic collaboration will maximise the potential offered by combining a modular delivery device with new subcutaneous formulation technology capable of innovating or repurposing existing drugs and new chemical entities for delivery to this sensitive tissue.

The success of this collaborative approach between Stevanato Group and Bexson Biomedical has led to the partnership entering a newly expanded phase beyond the treatment of chronic and acute pain disorders. This phase is defined by the development of Stevanato Group's on-body drug delivery system to accommodate additional small-molecule therapeutics from Bexson Biomedical targeted at a wide range of health conditions, including opioid overdose, benzodiazepine withdrawal, treatment-resistant depression and post-traumatic stress disorder.

> "The device is highly modular and could accommodate many other small-molecule formulations."

Figure 3: Stevanato Group's integrated offering, including analytical and testing services, can help derisk pharma companies' processes and accelerate time-to-market by ensuring right-first-time decisions.

The device is highly modular and could accommodate many other small-molecule formulations. At the same time, Bexson Biomedical is tailoring its formulations so that a therapeutic dose can be delivered with this type of device in mind – a 3 mL cartridge in a wearable subcutaneous infusion device. The companies' respective technologies complement each other.

Having one partner that can manage an entire project – from container closure system to assembly technology, up to mass production – is key to bringing a device to market faster and more easily. Stevanato Group provides a range of flexible, scalable capabilities to handle device projects, whether they are delivered with Stevanato Group intellectual property or as a contract manufacturer. The company's services range from designing, producing, testing and controlling a glass container's integrity to the integration of such drug containment systems with device technologies for parenteral drug delivery. It offers precision injection moulding and tooling, and product development services, including automation equipment, to ensure Stevanato Group is well positioned to optimise performance of the entire system (Figure 3).

The partners aim to deliver controlled, consistent dosing through a subcutaneous on-body drug delivery system that can be tuned to the needs of healthcare professionals in clinic and home health settings. Beyond convenience and healthcare savings, parenteral delivery can avoid gastrointestinal tract discomfort and the comparatively poor bioavailability associated with some orally administered drugs. Looking to the future, it is envisioned that further customisation of the device platform may support the dynamic delivery of a broad range of other small molecules.

From the outset, this collaboration raised the question of whether an existing wearable technology could form the basis of an entirely new device with specific, non-typical therapeutic requirements. Through the creation of an innovative new on-body device, Stevanato Group and Bexson Biomedical have not only shown this to be possible, they have also shown how approaching such a challenge with a collective, collaborative mindset can accelerate innovation, extend horizons and support the continued development of new medical treatments addressing unmet needs.

ABOUT THE COMPANIES

Established in 1949, **Stevanato Group** is the world's largest privately owned designer and producer of glass parenteral packaging for the pharmaceutical industry. From its outset, the group has developed its own glass converting technology to ensure the highest standards of quality throughout the production process. It comprises a wide set of capabilities dedicated to serving the biopharmaceutical and diagnostic industries: from glass primary packaging with its historical brand Ompi, to high-precision plastic moulding equipment, to engineering machines and lines related to glass converting, visual inspection, assembly and packaging. The group also benefits from the SG Lab that provides technical and analytical services to study container-drug interactions and guarantee drug integrity.

Bexson Biomedical is a research-stage company developing BB106, a ketamine therapy for pain management and mental health disorders. According to recent market research, pain following surgery is a US$35.5 billion (£30.4 billion) market and a leading cause of opioid abuse and addiction. Bexson Biomedical is also applying its proprietary delivery platform to several psychedelic and non-psychedelic compounds.

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ABOUT THE AUTHORS

Paolo Golfetto is the Drug Delivery Systems Business Development Director at Stevanato Group. He leads the development and execution of the business strategy in the drug delivery system field, supports the external technical communication of the global product platforms and manages project acquisition and transfer to the internal development structures, securing the integration of the different capabilities of the group. Before taking this position, Mr Golfetto was the Primary Packaging Development and Customer Care Director, leading new glass packaging introduction and technical support to the group's biopharmaceutical clients. Mr Golfetto is a Parenteral Drug Association (PDA) member and lecturer.

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ACCELERATING DEVELOPMENT OF SUBCUTANEOUS DELIVERY OF LARGE-VOLUME BIOLOGICS

In this article, Tom Mayer, Business Unit Manager at Sonceboz, discusses how the company's vial-based on-body injector – the LVI-V – can expedite the launch of large-volume subcutaneous delivery of biologics by leveraging existing primary container technology, thereby helping to reduce associated risks and total cost of ownership.

The pharma industry needs a cost-effective plan of action that makes the subcutaneous (SC) delivery of large-volume biologics possible in the near future. Sonceboz believes its LVI-V is the gateway to that future.

> "The value proposition for OBIs is clear: the ability to deliver larger doses of injectable drugs via the SC route."

The LVI-V is an on-body injector (OBI) that connects to vials, meaning that, in its standard configuration, it can deliver a high bandwidth of volumes, ranging from 1–20 mL (Figure 1). It has a programmable electromechanical pump system capable of delivering drugs at various speeds across a wide range of viscosities while providing accurate and consistent drug delivery. Furthermore, its sensors provide feedback to the user to ensure that the intended dose is delivered. It is part of a platform of products that Sonceboz is developing to seamlessly integrate into current infrastructure, providing pharma companies with new, adaptable tools for complete lifecycle management.

Figure 1: The large-volume injector.

THE CASE FOR VIAL-BASED ON-BODY INJECTORS NOW

The value proposition for OBIs is clear: the ability to deliver larger doses of injectable drugs via the SC route. OBIs (sometimes called wearable injectors, patch pumps or bolus injectors) are being designed to store volumes typically greater than 3 mL.[1] As there is a limit to the time a patient can hold an injection device in place during administration, pen injectors and

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Figure 2: The Sonceboz wearable injector platform offers different delivery volumes, programmable pump delivery profiles and container options.

prefilled syringes are not ideal for drugs that require volumes larger than 3 mL (and therefore require delivery over a longer duration).[2]

Device companies have introduced many different technologies into the injector space over the last 10 years. However, an independent observer may have noticed the limited number of launches for OBI devices. The OBIs currently available on the market can only hold small volumes in the 3–5 mL range. It may seem that the technology, especially for injection volumes greater than 5 mL, lacks maturity and is still in the developmental phase.

Indeed, progress has been stalled by the fact that many designers of OBIs promote the design of custom primary drug containers, which they suggest would improve the ease of use for patients — a feature that is high on the list of requirements for OBIs.[1] The primary container is a crucial component of an OBI because it is the main point of contact between the drug and the device;[2] as such, both the device and the custom primary container must be validated after development to ensure drug integrity and stability throughout the intended shelf life of the drug product.

The primary container (which may contain stoppers, closures, plungers and/or lubricants, such as silicone oil) comes in direct contact with the drug, potentially leading to interactions between the container materials and the complex molecular structure of long-chain biologics, which may then reduce the efficacy of these biologics. Extensive risk analyses and stability tests are required before regulatory approval.[2] In most cases, fully validated internal – or even external – fill-and-finish solutions do not yet exist.

Thus, the development of custom large-volume containers is ongoing and will likely take a while to be ready. Meanwhile, pharma companies seek a solution that will not derail a product filing and launch timelines. Too much focus on custom primary containers is a potential distraction; instead, pharma and biotech companies can leverage existing and proven primary container technology, freeing up resources to focus on other aspects of drug development, while at the same time reducing overall project risks.

> "Too much focus on custom primary containers is a potential distraction; instead, pharma and biotech companies can leverage existing and proven primary container technology."

LEVERAGING EXISTING PRIMARY CONTAINER TECHNOLOGY

Sonceboz is developing a solution that will seamlessly integrate into the pharma industry's current infrastructure. Its electromechanical OBI platform makes it possible to connect to various existing primary drug containers of capacities up to 20 mL, or even higher, such as vials or cartridges — without changing the overall system architecture of the OBI.

To allow maximum flexibility, the large-volume delivery platform comes in different variants (Figure 2), including:

- The vial-connecting injector (LVI-V)
- The prefilled and preassembled injector (LVI-P)
- The prefilled injector that is assembled by the user at the point of use (LVI-U)
- The dual-cartridge injector (DCI)
- The auto-reconstitution injector (ARI).

In the case of Sonceboz's dual-cartridge injector, the same architecture can connect and independently inject from two existing primary containers, either simultaneously or sequentially. Its auto-reconstitution injector will automatically reconstitute lyophilised drug products stored in existing primary containers. Various handheld injectors can reconstitute lyophilised drugs, but it is an unusual feature for OBIs.[1]

The company's most advanced OBI is the vial-connecting injector, LVI-V. Most pharma companies and contract manufacturing organisations have vial-filling capabilities. Vials are easier to adopt from a drug stability and compatibility perspective, since 90–95% of liquid drug formulations already rely on vials as the primary container.

In contrast to electromechanical systems, strictly mechanical systems require a substantial redesign to both the device and the drive system whenever there is a change to the format or size of the primary container. However, because the format or size of the primary container can evolve throughout a product's lifecycle, it is easier to use an electromechanical device with a pump system independent of the drug container, as such a device would only require software adaptations.

Cost effectiveness is the first advantage of an electromechanical OBI platform that can connect to various existing primary drug containers. The smaller patient populations for biologics mean that cost effectiveness is already a top priority for manufacturers to fill these small quantities.[2] Considering that custom primary containers require custom fill-and-finish services,[2] manufacturers would also have to factor in the cost of these services as part of a total cost of ownership (TCO) evaluation.

Furthermore, an electromechanical pump helps to reduce dead volume because the system uses a vacuum to maximise the volume of drug delivered per container to the patient. Sonceboz stringently follows design-for-manufacture and design-to-cost principles, ensuring Swiss quality at competitive prices from a TCO perspective. The company believes that highly integrated platform design leads to better cost efficiency.

Accelerating time to market is the second advantage of these systems. By offering different delivery volumes, programmable pump delivery profiles and container options, pharma companies can easily leverage Sonceboz's platform across multiple drug products, as well as across a single product's lifecycle – from clinical trials (where final dosing often has yet to be determined) to commercial distribution – thereby taking a level of risk out of development.

Patent protection is another advantage. As the pace of competition increases for biologics, originator products are losing market share to biosimilars. Developers of originator intravenous (IV) drugs can adopt an IV-to-SC drug repositioning to maintain patent protection.

IMPROVING DRUG ACCESS BY DECENTRALISING CARE

There is an ongoing need for a simple device that creates new possibilities for administering drug therapies and puts an end to the requirement for patients to visit large healthcare centres. Those new possibilities could include the home, the family doctor's office or the injection clinic.

Healthcare professionals who are active in treating inflammatory bowel disease and patients with this chronic disease exchanged their experiences with SC delivery of treatment in a recent virtual community meeting, revealing that its benefits include self-administration by the patient and shorter application time with fewer infusion-related adverse events – consequently lowering healthcare costs. For patients, being able to administer their treatments at home leads to an improvement in their quality of life and reduced need to travel to a healthcare institution – consequently reducing costs for the patient.[3]

> "The key to successfully implementing self-administration of biologics via large-volume OBIs is avoiding potential user errors during drug and device handling."

Figure 3: The large-volume injector on a patient's body.

> "Patients must be comfortable using the device, physically and socially."

Hospitals carry the connotation of serious illness.[4] Typically, patients prefer SC over IV administration, according to a systematic literature review of studies including patients with chronic immune system disorders. The same study concluded that patients preferring SC administration tended also to prefer at-home treatment because it offers the convenience and comfort of being at home and avoids having to attend hospital.[5]

The key to successfully implementing self-administration of biologics via large-volume OBIs is avoiding potential user errors during drug and device handling. Sonceboz makes device use straightforward: after connecting the drug container to the device via an adapter, the user places the device on the skin (Figure 3) and activates it by touching a single button, as they would an autoinjector. The device will take care of placing the injection cannula and initiating the injection with embedded sensors that monitor these processes.

Users will have full mobility during the injection. The device's orientation while users move around will not affect the treatment delivery because the drug is first transferred from the vial (a non-collapsible container) to a collapsible container (the internal reservoir). While this adds an assembly step, the design ensures that the pump can access the drug regardless of the device's or patient's spatial orientations. This is important to ensure that the intended dose is safely administered. Sonceboz's data suggest compatibility of the GentleTouch™ pump design with large-molecule drugs; both the molecule integrity and activity remain intact. Furthermore, the design is completely free of silicone oil. Some biologic molecules are not compatible with silicone oil, which is often used to lubricate gliding systems in mechanical pumps.

Of course, usability improves with feedback. The Sonceboz OBI platform comes with built-in connectivity using Bluetooth Low Energy and near-field communication (NFC) technology, enabling digital health applications. In addition to transferring data to the patient's healthcare professional, the device can provide feedback, such as confirmation of when the injection is completed.

Consistency is also vital to building confidence in successfully implementing self-administration of biologics via large-volume OBIs. An electromechanical system allows precise injection rate control across the total container volume. Regulators require that the intended dose indicated on the drug label is delivered regardless of the patient or variation in the injection conditions. The designer knows the device's fluid path and mechanical powerpack and can revise the dimensions accordingly. Sonceboz's electromechanical drive system enables load monitoring and helps achieve flow accuracy of about ±2%.

Finally, patients must be comfortable using the device, physically (in terms of comfort with the needle insertion) and socially (in terms of comfort administering a treatment in public). This is helped by the fact that SC injections are less invasive than intravenous infusions. To prevent needlestick injuries, the dynamic needle-insertion system (DNIS) uses a solid needle in combination with a soft cannula made from polytetrafluoroethylene (PTFE). The DNIS releases the needle and then retracts, leaving behind only the soft cannula for optimal patient comfort. The device is palm sized and small enough to be disguised under clothing. Because Sonceboz uses high-quality motors and leverages its high-volume automotive production for assembly, the device emits only a low level of noise.

PREPARING FOR A SUSTAINABILITY-MINDFUL FUTURE

Sonceboz applies, whenever possible, the four "R"s (reduce, reuse, replace, recycle) during the entire lifecycle of its OBI device, especially during design and manufacturing (Figure 4):

- **Reduce** the carbon footprint as much as possible
- **Reuse** the same material as much as possible for several components
- **Replace** and scrap non-conforming components by checking every single part throughout the assembly process
- **Recycle** by creating an efficient collection network and sorting components from used devices.

Just because something is "recyclable", it does not ensure it will be recycled. Sonceboz is actively investigating the end-of-life stage of its OBIs and determining any possible second life for used materials. While sustainability is an effort to reduce the impact on the environment, patient safety cannot be compromised; reusing parts from disposable devices is therefore challenging due to the validation process. Recycling components into other medical devices might not be feasible, but transforming parts into other tools, such as first-aid kits, may be an interesting alternative.

Additionally, since the OBI will enable home treatment, thereby reducing patient travel, it will dramatically reduce the environmental impact while minimising the exposure patients will have to hospital-acquired infections.

DESIGN AND LEADING THE WAY INTO THE FUTURE

Sonceboz has considered many, if not all, aspects of its OBI design, from cost effectiveness to scalability and usability to patient comfort and safety. The design complies with the standards in ISO 11608-6, "Needle-based injection systems for medical use – Requirements and test methods – Part 6: On-body delivery systems." Sonceboz is now partnering with pharma companies to prepare its devices for clinical use. It anticipates that the next generation of devices will be prefilled and preloaded once the development of custom drug containers has been tested to the full extent according to

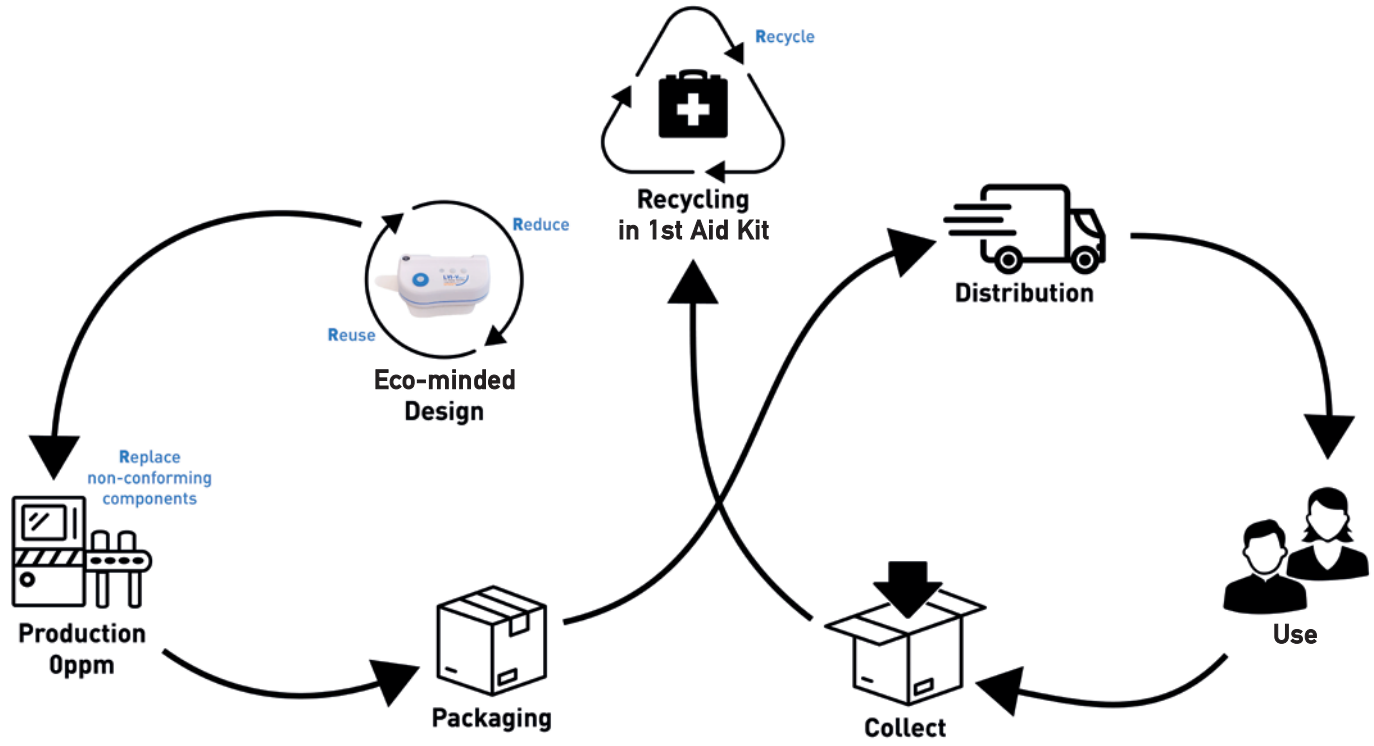

Figure 4: Sonceboz applies, whenever possible, the four "R"s (reduce, reuse, replace, recycle) during the entire lifecycle of its OBI device, especially during design and manufacturing.

ISO standards. Until then, the LVI-V can lead the way to accelerate drug development, extend patent protection and facilitate at-home drug administration in a cost-effective and sustainability-mindful fashion.

ABOUT THE COMPANY

Sonceboz's core competencies consist of design, development and production of mechatronic drive systems. Since 1936, the company's focus has been on innovation and best-in-class quality and service. Sonceboz is ISO 13485 certified and active in wearable drug delivery, medical devices and the laboratory industry. Customised technology modules, including motor drives, electronics, pumps and needle insertion systems, are available for medical device manufacturers. Sonceboz's activity in medical devices is based on long experience in the automotive sector, where top quality, reliability and cost effectiveness is key.

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ABOUT THE AUTHOR

Thomas Mayer is responsible for business development at Sonceboz Medical. Prior to joining Sonceboz in 2016, he held various management positions at Boston Scientific's Cardiac Rhythm Management division. His first interactions with the pharmaceutical industry came early during his apprenticeship at Uhlmann Pac-Systeme in Laupheim, Germany. Mr Mayer holds an advanced degree in Medtech and Pharma Management from EPFL Lausanne (Switzerland) and a diploma degree in Medical Engineering from Furtwangen University (Germany) as well as an MBA with honours from FOM University in Munich (Germany).

KEY CONSIDERATIONS WHEN SPECIFYING A MOTION SYSTEM FOR WEARABLE INJECTORS

The reliable performance of a wearable drug delivery device is understandably paramount, so optimising the motion solution that drives it is crucial. In this article, Dave Beckstoffer, Business Development Manager at Portescap, discusses how best to achieve this and ensure the best match between the motion solution and the characteristics of the specified drug or drug range.

For any medication that is intended for administration over a prolonged period, a wearable delivery system is an advantageous option, both in terms of convenience and comfort for the patient, and in reducing the burden on healthcare professionals. Crucial to the design of a wearable drug delivery device is the motion system, comprising the motor, gearbox and mechanical components that drive the drug delivery pump.

The development of the motion system requires an engineering approach specific to the drug or drug range in question. To optimise this process, as well as accelerate time to market and maximise cost efficiency, it is important for the drug delivery device original equipment manufacturer (OEM) to engage with the motion system designer at the earliest opportunity (Figure 1).

Through early integration with the project, the motion system can be designed according to the characteristics of the drug that will be administered, taking into account its optimum delivery requirements,

> "The development of the motion system requires an engineering approach specific to the drug or drug range in question."

as well as the practical needs of the patient who will have to live with the device. This evaluation should take place as the first stage of the motion solution selection and pump development.

MOTION SOLUTION SPECIFICATION FOLLOWS DRUG DELIVERY REQUIREMENTS

A fundamental step in motion solution design is to clarify the time span of drug delivery. A broad consideration at this stage is whether the delivery device is disposable or reusable. As well as considerations of

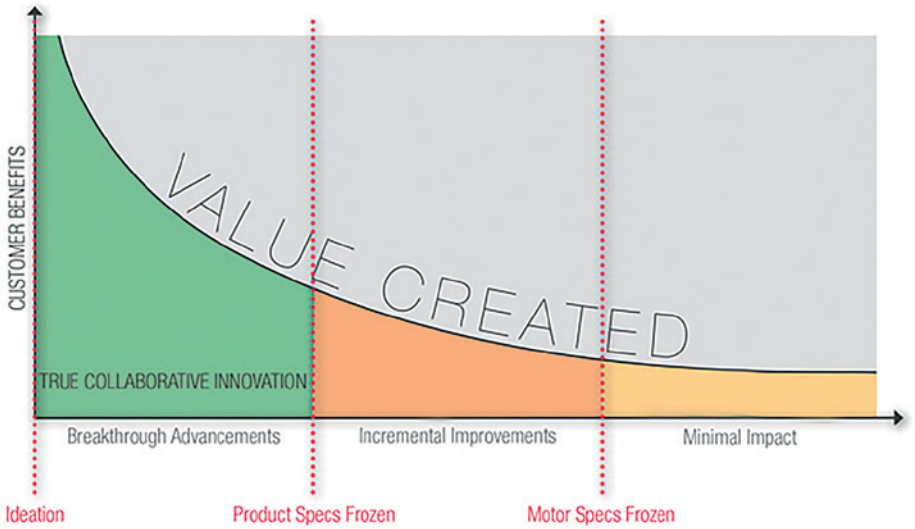

Figure 1: Engaging with a motion solution partner early in the development process can minimise the overall development time.

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patient comfort, the selection of a reusable or disposable device often comes down to economy. Motion systems selected for reusable devices will need to be more durable than their disposable counterparts. This naturally means that they are more costly.

Typically, it is more economical for drugs administered over a short time span – for example, a single dose over 24 hours – to use a disposable patch pump. Where the drug will be administered regularly over a period of months, or even years, then the total costs will be minimised by specifying a reusable pump. Reusable delivery systems may also be specified to administer more valuable drugs, where the importance of reliable performance is greater.

Another determining factor in how the motion system is specified is the process of a delivery cycle. This process can be divided into stages, from power up of the system, to engagement with the cartridge, through to the actual delivery. While each stage must be factored into a motion solution's design, the overall time span of the full delivery cycle has the greatest focus.

The cycle may involve administering the drug over a series of intervals (20 seconds on and a pause of 40 seconds, for example) or simply consist of a single, uninterrupted delivery. Whatever the cycle requirements, it will impact specification of the motion solution's speed, torque and feedback control capabilities. Similarly, understanding drug viscosity for the application dictates the force required to depress the plunger, and therefore the required torque output of the motor and gearbox.

For the system designer, it is also important to understand the interconnection between the life requirement of the pump and the motion solution that will drive it. Reliability is critical for patient care and, while durability and lifetime must be guaranteed, clarifying such requirements with the delivery system OEM enables the motion system designer to target the most appropriate design characteristics at the most appropriate price point. For example, a wearable delivery

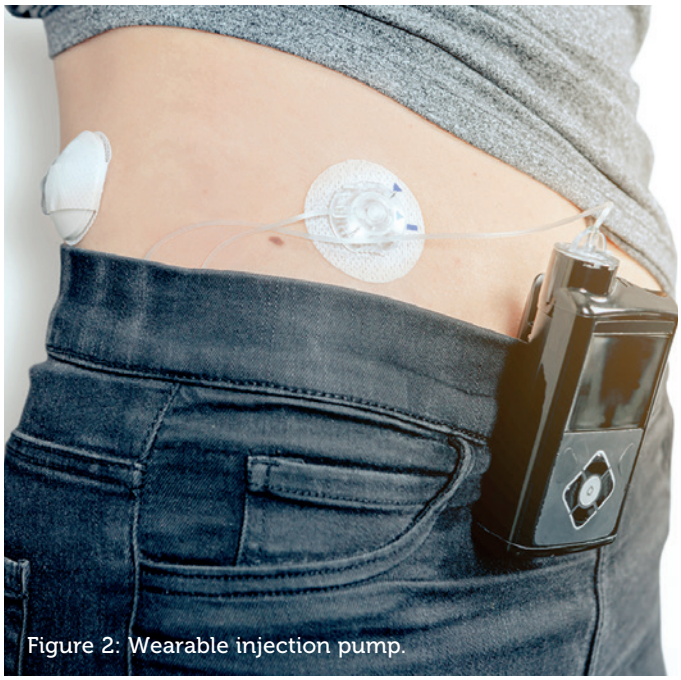


Figure 2: Wearable injection pump.

device (Figure 2) might have an intended lifetime use of five years but, depending the anticipated frequency of use and number of cycles required, the motor might only need to last for 1,000 hours of pump activation on-time.

Motion system design also has to consider efficiency, which is key to minimising the battery size and weight for the wearer. The motion solution engineering team can help to optimise the specification by advising on the most efficient duty cycles. For example, if the pharmaceutical manufacturer requires drug delivery across a five-hour period, efficiency will be optimised if the delivery mechanism operates in pulses, compared with continual operation at a lower speed.

Figure 3: Spur gearhead exploded view.

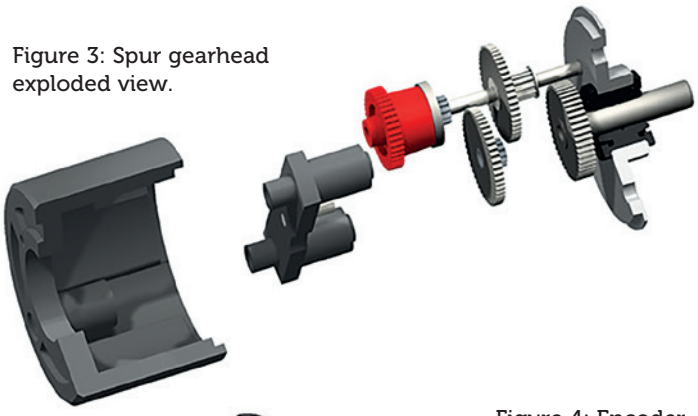
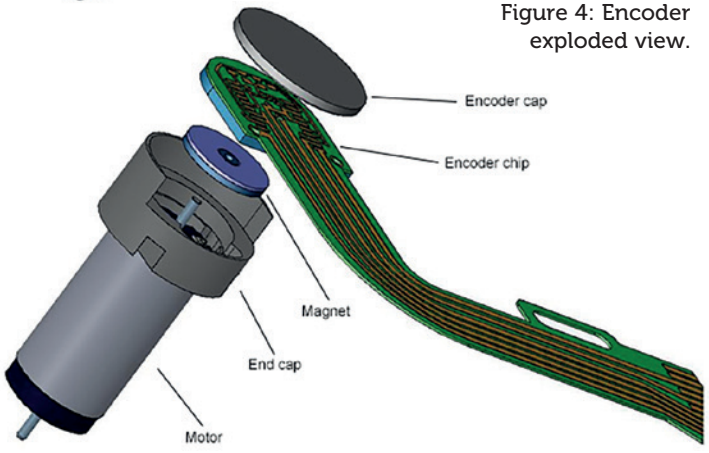


Figure 4: Encoder exploded view.



MOTION TECHNOLOGY FOR WEARABLE SYSTEMS

To fulfil the requirements of wearable drug delivery systems, brush direct current (DC) motors are typically the optimal choice. Most importantly, a brush DC motor provides high power density and can fulfil the speed and torque requirements for virtually all drug types. They are compact and lightweight, enabling integration within a small footprint, which, as the motor design is energy efficient, helps to minimise battery size while maximising charge life. A coreless design (also known as "ironless") increases efficiency still further by removing the potential of iron losses, which have a detrimental impact on energy use, thermal regulation and performance.

As a result of a brush DC motor's simple design, relative to other motor types, it is both reliable as a drive mechanism for wearable drug delivery systems and straightforward to control. Its speed is typically controlled by pulse width modulation (PWM), which regulates the voltage delivered to the motor by the OEM's control device, while its torque is typically generated in a linear relation to speed. To control the torque and speed relation to suit the demands of the time cycle and drug viscosity, the brush DC motor is typically paired with a spur gearhead (Figure 3). This design is efficient and can achieve the gear reduction required to suit a range of viscosities. Importantly for the patient, the design also enables quiet operation, with fewer moving parts compared with a planetary design.

The accuracy of speed and torque control that can be achieved with a brush DC motor and spur gearhead is ideal for wearable drug delivery solutions, even for pulse duty cycles. An encoder (Figure 4) can provide feedback as required to ensure accuracy and, dependent on the need for redundancy, the motion designer can also advise the OEM on safeguards that protect against current spikes.

The extent of control required is a balance between performance and cost, which is another advantage of brush motor technology. Alternatively, a brushless DC motor (BLDC) might be necessary when dealing with the very high torque requirements that are needed to deal with the highest viscosities, or when very high gear ratios are needed for the most precise control. However, these requirements are rare. The higher cost of a BLDC motor, combined with the additional cost needed for brushless electronic commutation, means that this technology is generally not cost effective for a wearable drug delivery device.

SPECIFIC DESIGN NEEDS

General customisation for wearable injection systems means reducing the voltage requirement down to 3V to take into account their low-power and high-efficiency needs. However, specific customisation for each project is nearly always required for the motor and gear combination relative to the torque range. Some delivery devices are designed to administer one particular drug, meaning that the motion solution needs to be optimised for a specific set of characteristics. Alternatively, an OEM might develop a wearable delivery device that can handle a range of drug types and suit a variety of pharmaceutical manufacturers. In this case, the motion solution needs flexibility to cover the force and cycle time requirements of various drug specifications, particularly regarding viscosity. As such, expertise in motion solution development is a key part of achieving a balance that accommodates both the lowest and highest viscosity ranges, while also maintaining the optimum efficiency of the average.

Whether the motion solution is developed for a single drug or designed to deal with many, the specialised design integration of the motor (Figure 5), gearbox and encoder demonstrates the advantage of designing an integrated motion solution sub-assembly, rather than treating each component individually. This approach will optimise performance specific to the drug or drug range requirements, with all components developed in synchrony towards a unified objective. It also reduces the dependence on internal design expertise to integrate separate components, as well as reducing the resources needed for manufacturing and assembly processes.

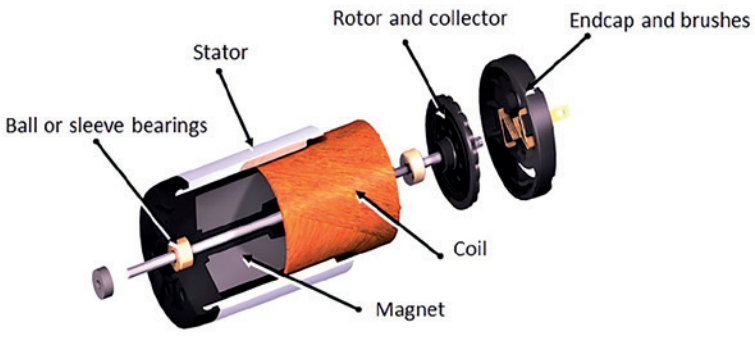


Figure 5: Brush DC motor exploded view.

> "Motion solution development for wearable injection devices depends on the specification of the drug and the patient delivery needs."

When engaging with a motion solution partner, it is advantageous to do so as soon as possible in the development process in order to minimise the overall development time. As the motion solution specification criteria are extensive, the sooner the designer is involved, the more efficient the design revision process is. This approach provides greater awareness, sooner, over any limitations or compromises, and it can also uncover unforeseen advantages to improve or speed up the design. While a period of two years from concept to design confirmation is typical, working in partnership from the outset with experienced engineers can speed up this process.

This approach increasingly applies to disposable pumps as well as reusable designs. Disposable devices are starting to move away from commoditised components to a designed motion solution because it can be more cost effective in the long term. As an increasing number of drugs are administered by wearable systems, including higher-cost medications, sub-optimal delivery as a result of low-cost motors and gearboxes can negatively impact patient outcomes, as well as product value.

Motion solution development for wearable injection devices depends on the specification of the drug and the patient delivery needs. The drive mechanism is integral to the effectiveness of delivery for the patient and, for this reason, a partner in development will help the OEM arrive at the best solution. With the right partnership, it can also help the OEM get there faster.

ABOUT THE COMPANY

Portescap offers a broad range of miniature and specialty motor products, including coreless brush DC, brushless DC, stepper can stack, gearheads, digital linear actuators and disc magnet technologies. Its products have served diverse motion control needs in a wide spectrum of applications including medical, life science, instrumentation, automation, aerospace and commercial for more than 70 years. Portescap has manufacturing centres in the US and India, and uses a global product development network with research and development centres in the US, China, India and Switzerland.

ABOUT THE AUTHOR

Dave Beckstoffer is a Business Development Manager in the medical team at Portescap, with over 31 years of experience in the motion control industry. He brings a customer-focused mindset to every application, understanding the tie between the end product features and the motion system design. Mr Beckstoffer is leading the development of drive mechanisms tailored for the specific requirements of infusion systems, marrying motor, gearing and feedback technologies with multiple drug delivery methodologies to achieve the optimum design for each device.

USING MAGNETIC SENSORS FOR METERING DRUG VOLUME IN WEARABLE INJECTORS

In this article, Tim Resker, Global Business Development Manager at Coto Technology, discusses the application of tunnelling magnetoresistive sensing technology to on-body injectors, including the vital function of accurately measuring the delivered dose, as well as other functions, such as powering on the device.

The ongoing development of new drug therapies, Internet of Things technologies and an increasing preference for self-care among patients are driving a marked increase in the use of wearable, on-body drug delivery systems. However, along with that rise in popularity have come new challenges for medical device design engineers. For instance, one fundamental requirement of a wearable drug delivery device is the accurate measurement of the volume of drug to be injected into the patient. The answer to this device design problem depends on the mechanism used to create pressure during the injection process. Two common mechanisms for "pumping" the drug inside an on-body injector device are:

1. An impeller-driven pump
2. A motor-driven plunger.

Let us look more closely at these two mechanisms and observe how a tiny solid-state magnetic sensor integrated circuit (IC) based on tunnelling magnetoresistive (TMR) technology (Box 1) can address the requirements of accuracy, cost, size and extremely low power consumption. It is then possible to determine what kind of engineering knowledge is necessary for implementation.

The first mechanism to examine is the impeller-driven pump. The impeller is driven by a tiny motor and generates pressure to inject the drug. The volume of drug injected by this mechanism can be calculated using the number of rotations of the impeller. To count rotations, a very small magnet can be placed on the shaft of the impeller and a very small, low-power but highly sensitive magnetic sensor can be used to detect the number of rotations of the magnet, thus providing the desired metering data (Figure 1).

> "TMR magnetic sensors provide the size, low power consumption and sensitivity required to sense small, low-cost magnets, and are available in various sensing frequencies to ensure accurate capture of shaft rotations."

TMR magnetic sensors provide the size (1.45 mm^2), low power consumption (1.9 µA for a 500 Hz sensor) and sensitivity (10 Gauss) required to sense small, low-cost magnets, and are available in various sensing frequencies to ensure accurate capture of shaft rotations. For example, RedRock® TMR magnetic sensors are commercially used in volume metering

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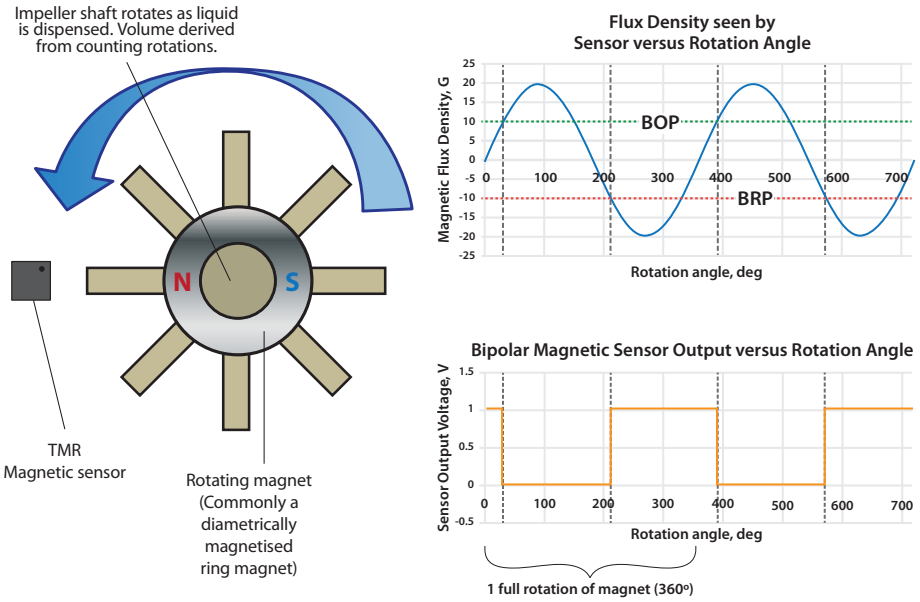

Figure 1: By detecting and counting the number of magnet rotations, the TMR sensor enables accurate measurement of drug injected by a device.

applications that have similar requirements around cost, size and accuracy, such as water utility meters and soap dispensers.

The second conventionally used mechanism for pumping a drug is a motor-driven plunger. Here, metering is achieved by sensing the travel distance of the plunger. Again, small, low-power, highly sensitive TMR magnetic sensors can be used to accurately measure that distance of travel. This is accomplished by placing a magnet on the plunger so that the TMR sensor can detect the change in magnetic flux density as the magnet moves and correlate that to distance travelled.

For this function, TMR sensors have an analogue voltage output that changes ratiometrically to the magnetic field change. The high sensitivity of TMR sensors provides high-resolution distance measurement down to a scale of 1 mm. While most analogue sensors require a higher sensing frequency and generally have a slightly higher power consumption than their digital output counterparts for a given frequency, overall power consumption can be reduced by TMR sensors that have a magnetic field strength threshold that activates the analogue output. This means that the power consumption can be extremely low until the plunger and magnet are pushed back

BOX 1: TUNNELLING MAGNETORESISTANCE

A tunnelling magnetoresistance sensor is comprised of a magnetic tunnelling junction (MTJ) element and complementary metal oxide semiconductor circuitry. An MTJ element is a multilayer, thin-film stack composed of a sandwiched structure of a free layer, a spacer layer and a pinned layer (Figure 2). The spacer layer (made of dielectric oxide material) separates the ferromagnetic free layer and pinned layer from one another. The electrons moving within the free layer and pinned layer planes are unable to cross the spacer layer to the opposite side. However, if magnetic flux is applied to the MTJ, the magnetism direction of both ferromagnetic layers can be switched between anti-parallel and parallel orientation. In the parallel magnetism orientation, electrons can make a quantum leap to tunnel through the spacer layer, whereupon a tunnelling current will be observed across the MTJ structure and the relative resistance of the MTJ will be changed between high resistance and low resistance.

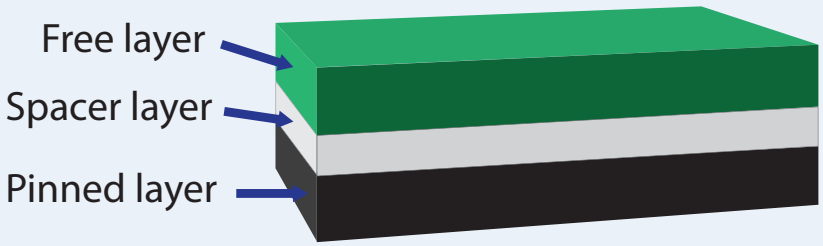

Figure 2: MTJ structure.

The difference of relative resistance is the "TMR ratio" (Figure 3). The TMR ratio can reach approximately 40% at room temperature, and it is comparatively larger than other magnetoresitive technologies. This feature, which is an implementation of quantum physics, makes the ingenious TMR sensor possible, with higher sensitivity, lower power consumption and more stable characteristics.

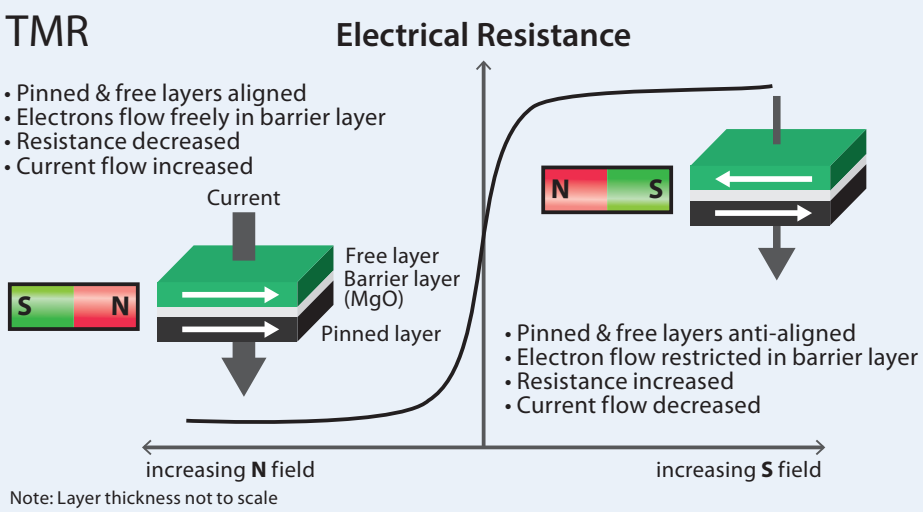

Figure 3: Tunnelling magnetoresistance mechanism and TMR ratio formula.

"Although TMR is an ideal solution to the challenges of wearable device design, integrating a TMR magnetic sensor and magnet into the wearable drug injector design requires specialist engineering knowledge."

as the injector is initially filled with the drug, at which point the analogue sensing is activated to measure the plunger movement forward to inject the drug (Figure 4).

In addition to enabling accurate metering of the delivered drug volume, TMR magnetic sensors can be useful for other functions, such as powering on wearable medical devices. In this case, the TMR sensor detects the presence of a magnet located in the product packaging or in a component of the device, such as the applicator. Proximity sensing is another common use case for TMR sensors and applies to any situation where the proximity of a mechanical component relative to another component needs to be sensed in a reliable, low-cost manner with very little power consumption. For powering on and other proximity sensing use cases, a very low sensing frequency can be used, resulting in an average current consumption of less than 1 nA.

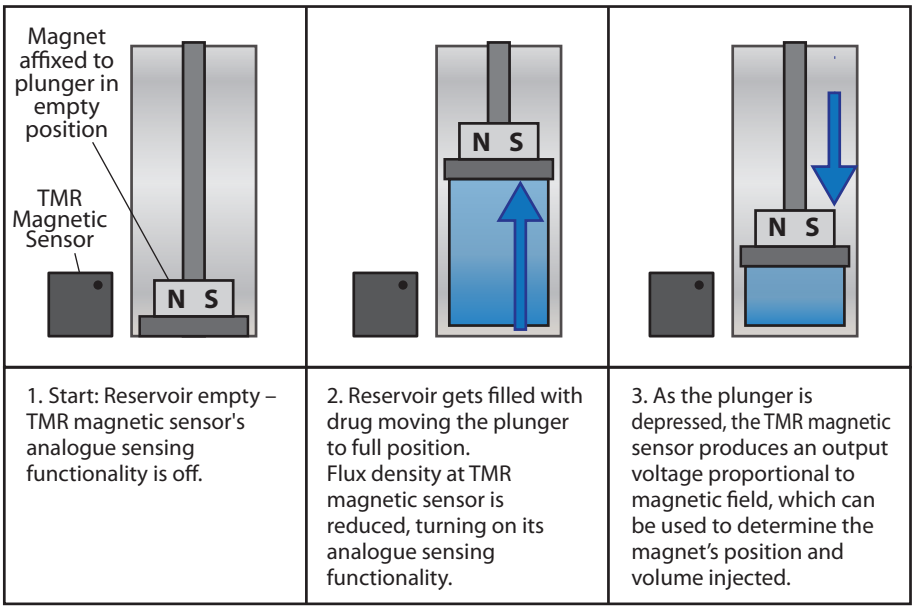

Figure 4: The TMR sensor can detect the change in magnetic flux density as the magnet moves and correlate that to distance. For this function, TMR sensors have an analogue voltage output that changes ratiometrically to the magnetic field change. The high sensitivity of the TMR sensors provides high-resolution distance measurement down to a scale of 1 mm.

Although TMR is an ideal solution to the challenges of wearable device design, integrating a TMR magnetic sensor and magnet into the wearable drug injector design requires specialist engineering knowledge. Some medical design engineers shy away from using a new technology due to fears of extensive prototyping, testing and validation, which can make a project longer and costlier. However, Coto Technology offers engineering support for this exact purpose – vastly simplifying the process and ultimately speeding up time to market. Coupled with and enhanced by experienced medical design assistance and simulation capabilities, Coto's RedRock® TMR sensor "comes with" the specialised knowledge of the sensors, magnetics and simulation tools that are able to provide design verification.

ABOUT THE COMPANY

Established in 1917, Coto Technology is a worldwide market leader in the design and manufacture of advanced, reliable switching and magnetic sensing solutions for the medical, automotive, data acquisition, instrumentation, process control, telecommunications, automatic test equipment and security markets. RedRock® is a registered brand of Coto Technology's Sensor Product line.

ABOUT THE AUTHOR

Tim Resker, Global Business Development Manager for Coto Technology, works closely with solution providers in industrial, consumer, medical and commercial industries to address their magnetic sensing needs. Mr Resker has also worked for Analog Devices (MA, US) and other embedded technology suppliers in product marketing and business development roles.

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