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Wearable Bolus / High Volume Injectors

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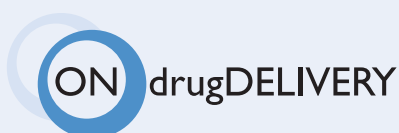
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INTRODUCTION: DEVICE DEVELOPER PERSPECTIVE

A year has passed already since ONdrugDelivery Magazine's first edition devoted wholly to wearable bolus (large volume) injectors. In that year, a great deal has happened but, before we launch into the latest industry news, let us review the need for and state of wearable bolus (large volume) injectors.

Much has been said and written about the growth in the pharmaceutical industry coming principally from biologics as opposed to small molecules. Research by the Judge Business School of Cambridge University predicts that biologics will enjoy a compound annual growth rate of 7.2%, compared with only 2.9% for small molecules (Figure 1).

If we look at the global sales of existing biologics (Figure 2), we see that the majority are for autoimmune and cancer indications, both of which are dominated by monoclonal antibody-based drugs (mAbs) such as Humira, Remicade, Rituxan, Herceptin and Avastin.

Typically, biologics need to be injected and the most common format is a 1 mL syringe, often prefilled and sometimes in an auto-injector. However, many of the biologics under development require large masses to be injected. In addition, some formulation processes such as PEGylation can increase viscosity. The choice is then whether to use high concentration to fit within 1 mL (which can lead to high viscosity and molecule aggregation) or standard concentration and increase volume above 1 mL. Larger syringes do exist but are avoided due to patient discomfort¹ and long injection time.

There are several alternatives to "traditional" syringes and auto-injectors available now or under development. For example:

- Using more than one syringe or auto-injector in series
- High-pressure auto-injectors such as Oval Medical's plastic syringe device, which is claimed to deliver drugs at 2,000 cP.²

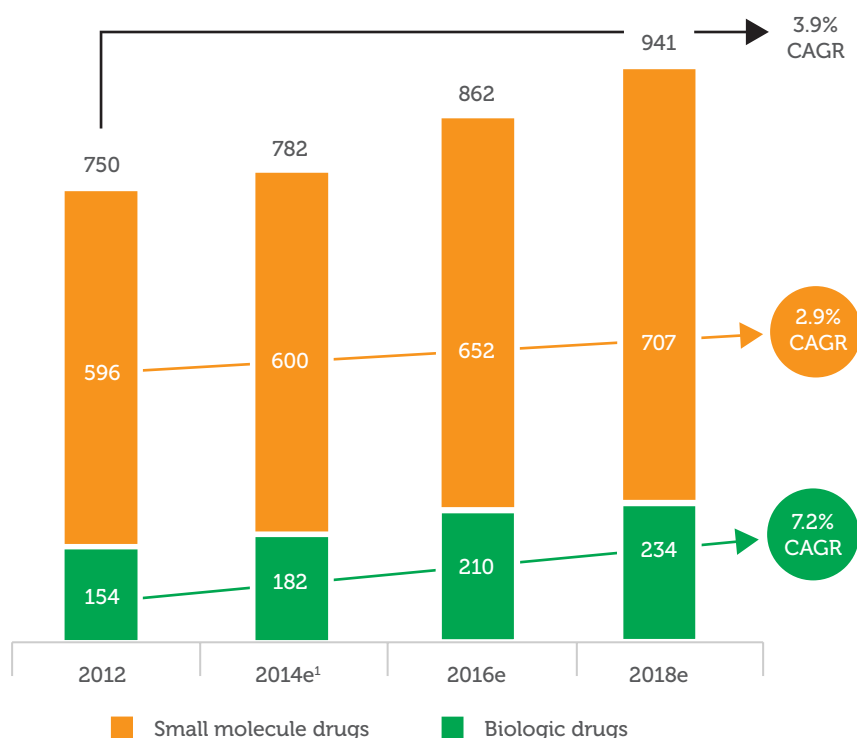


Figure 1: Predicted global pharmaceutical sales volume growth for biologics and small molecules.



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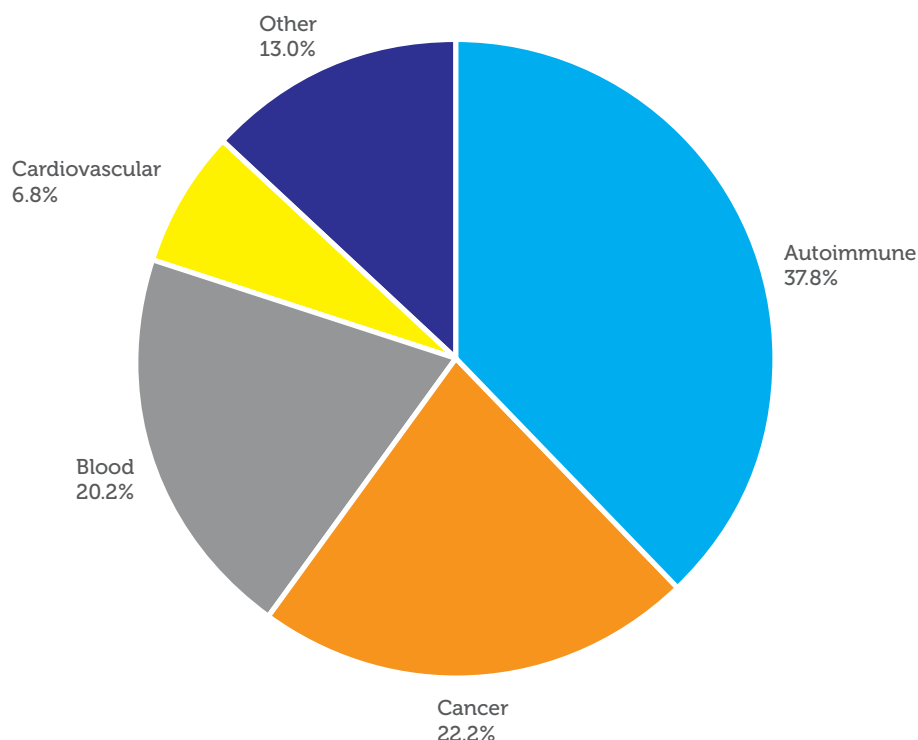


Figure 2: Biologic drug sales by indication [Source: Bloomberg review of top 13 pharma, 2012].

- Needle-free injectors such as Zogenix' DosePro, which is claimed to deliver drugs up to 1,000 cP.³
- Non-spring-powered auto-injectors such as Bepak's gas-powered Syrina which is claimed to deliver drugs at 200 cP.⁴
- Wearable bolus (large volume) injectors, which are described later.

Even if the pharmaceutical requirements discussed above were satisfied, there are two other important drivers for developing a new class of devices:

1. A perception of increasing consumerisation of medical devices, with some patients expecting their medical devices to have the same attractiveness and ease-of-use as their familiar consumer devices. Indeed some patients (and payers) are interested in electronically-enabled and possibly "connected" devices, which could remind and monitor patients and potentially increase adherence (see Unilife's article on page 8, and West's article on page 20).
2. The need from pharmaceutical companies to differentiate their product and add value relative to innovative competitors, and to biosimilars.

From a device developer's perspective there is strong and growing demand for new

injection devices that deliver large-volume and / or high-viscosity drugs.

We could argue that ambulatory infusion pumps already used for insulin and other drugs could meet the demand, but there are important differences between wearable bolus (large volume) injectors and infusion pumps:

- The injection time in an infusion pump is clinically relevant, whereas for bolus injectors it is as short as patient comfort allows. For example, it may be only a minute or two.
- Many infusion pumps were designed for delivering insulin and cannot deliver the high viscosity biologics described above.

Therefore a need exists for a wearable injector which can deliver high-volume

SURMOUNTABLE CHALLENGES

The development challenges to wearable bolus (large volume) injection devices are varied but surmountable. Usability (human factors) is critical, and the regulators recognise this. The US FDA released draft Guidance in March 2012; and a new revision of IEC 62366, "Application of usability engineering to medical devices", was published in February this year. Many patients, caregivers and healthcare professionals are familiar with auto-injectors, but the use scenarios with bolus injectors are unfamiliar and therefore the occurrence of certain usability risks could be increased.

Commonly used primary packs were not intended, designed or manufactured for use in bolus injectors. The materials (often

"The injection time in an infusion pump is clinically relevant, whereas for bolus injectors it is as short as patient comfort allows"

(typically 5 mL but sometimes more) and high-viscosity (many tens of cP) drugs over a few minutes. Such devices are called "bolus injectors" or "large volume delivery devices" or sometimes "patch pumps".

type 1 borosilicate glass or cyclic olefins) might not be appropriate for the drive mechanisms or shock protection in bolus injectors. Additionally, the form factor of the primary pack used in auto-injectors, pen

injectors and some infusion pumps is commonly the 1 mL ‘long’ syringe, or the ‘Lilly type’ 3 mL cartridge, both of which are cylindrical. A bolus injector might desire a flat form because it is attached to the body, so cylindrical primary packs are suboptimal. Pharmaceutical companies tend to be reluctant to use non-standard primary packs due to the large investment in existing infrastructure and knowledge, and the increased risk of any change.

Some devices, like the one from Enable Injections (see this issue, page 24), navigate the primary packaging problem by keeping the drug in a standard vial until immediately before use, at which point the drug is transferred into the bolus injector ready for injection.

In almost all designs, the bolus injector propels the drug formulation from a reservoir into the patient via a thin cannula or needle. These cannulae are subject to pipe-flow physics⁵ and so, if the cannula must be thin for patient acceptability, the injector must provide a high pressure or accept a long injection time.

Any combination of high pressure, long injection time, large delivered volume or high drug viscosity will place force, energy and power requirements on the injector design which are likely to increase size, weight, cost and sometimes technical risks. It is no surprise that device developers have looked beyond the “traditional” spring-powered mechanisms and used novel energy stores. SteadyMed’s expanding battery (see page 34) and Ratio’s expanding hydrogel are two examples.

It is said that, “with great power comes great responsibility”. Indeed, if the injection device is required to provide high pressure, force, energy or power, then there may be challenges to control these during manufacture, storage, use and disposal in a safe way. Sometimes device engineers are pushed down the path of complex mechanical, or electronic, actuators which can have reliability and cost issues.

Some drugs require cold chain transport and storage, which can increase viscosity further (and decrease comfort) if warm-up

times are not adhered to. Other drugs need reconstituting from powder form.

Additionally, the intellectual property space is crowded and so freedom to operate is a key issue.

RECENT NEWS AND DEVELOPMENTS

In the past year, we have seen some interesting developments in this area.

On the standards front, ISO 11608-6 “Needle-based injection systems for medical use – requirements and test methods – Part 6: Bolus Injectors”,⁶ is making its way through the drafting process.

Examples of the requirements to be clarified in the standard are:

- Method and robustness of the attachment to the body (or perhaps clothes)
- Interaction with the needle or cannula
- Whether IV injection is covered
- Testing (such as shock) whilst delivering drug, which is not required for syringes or auto-injectors.

In the area of partnering, deals that have been made public include the master services agreement for Unilife to supply wearable injectors to Sanofi for 15 years.⁷ Another is the development deal between Enable Injections and CSL Behring.⁸

There have been various other newsworthy developments in the field. Roche received regulatory approval in Europe for the Single Injection Device (formerly MyDose) with Herceptin SC. However, it has not been launched on the market at the time of writing. Bepak has announced its Lapas bolus injector, targeted at the low-cost end of the bolus injector market.⁹ Ratio Drug Delivery ceased developing its NuPrivo hydrogel-based bolus injector, and BD has renamed its Microinfusor to Libertas (page 30).

Looking forward, we can expect to see continued strong interest from pharma companies in the large volume device sector, and the race to launch the first true bolus injector is still wide open.

REFERENCES

1. Jorgensen JT et al, “Pain assessment of subcutaneous injections”. *Annals Pharmacother*, 1996, Vol 30, pp 729-732.
2. <http://www.ovalmedical.com/technology-2/>.
3. <http://www.zogenix.com/content/technology/dosepro.htm>.
4. <http://www.bepak.com/Syrina>.
5. See the Hagen-Poiseuille equation.
6. http://www.iso.org/iso/catalogue_detail.htm?csnumber=61173.
7. <http://ir.unilife.com/releasedetail.cfm?ReleaseID=874635>.
8. Furness G, “Interview with Dr Jeannie Joughin of CSL Behring”, *ONdrugDelivery*, 2015, Issue 55, pp 53-55.
9. <http://www.bepak.com/Lapas>.

ABOUT THE AUTHOR

Tom Oakley is co-founder and Director of Drug Delivery Device Development at Springboard, a leading medical device development company. His first degree was a Master of Engineering from Cambridge University, and he was later appointed the Choate Fellow in human physiology and pathology at the Harvard School of Public Health. Since 2001, he has focused on creating safety-critical designs for mass production and is named inventor on numerous medical device patents.

Since 2005, Tom has led scientific and engineering teams developing new technology in the areas of injection devices, infusion pumps, inhalers, cryogenic surgery, regenerative medicine and electronic blood lancing. Tom has delivered lectures and workshops on innovation at the Cambridge University Engineering Department, mentored MBA research projects at the Judge Business School, and been a speaker at various international conferences on innovation and medical device development such as Management Forum, SMi, Pure Insight, MEDTEC, and EphMRA.



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SELECTING THE RIGHT WEARABLE INJECTOR TECHNOLOGY AND PARTNER

Unilife prides itself on addressing each and every customer and patient need with its injection device products. In this article, Alan Shortall, Chairman and CEO, Unilife, provides a detailed run-down of how the company's wearable devices portfolio meets the numerous requirements that pharma partners and patients demand of such a device, and explains how this differentiates Unilife's products from others in the space. Mr Shortall also highlights Unilife's partnership with Flextronics, which provides Unilife customers with alternative sources of manufacturing and supply for its wearable injection systems and thus long-term continuity of supply.

Converging market forces are driving the emergence of wearable injection systems as a new frontier in healthcare. The shift to patient self-injection is creating demand for safe, simple and convenient therapies that minimise the frequency of injection and complement normal daily life. The rise of biologics and other patient-centric drugs is guiding pharmaceutical investment towards the use of disposable delivery systems that can be worn on the body during the administration of large dose volumes over minutes, hours or days. The quest for value-based healthcare outcomes is also encouraging prescribers and payers to support the use of smart devices that demonstrate therapy adherence.

As a result of these and other converging trends, a multitude of pharmaceutical and biotechnology companies today recognise the importance of wearable injection systems to enable or enhance the clinical development and commercial success of large portfolios of injectable therapies. Many of these companies have several to a dozen or more approved or pipeline drugs, such as monoclonal antibodies, that are being targeted for use in a wearable injection system. In many cases, each of these drugs is being targeted for use across multiple indications.

The selection of a different wearable injection system on a case-by-case basis for each pipeline molecule has the potential to create significant operational risk and financial inefficiencies for a pharmaceutical company across key business areas including supply chain, regulatory, filing and packaging, and brand management. To address these risks and ensure long-term continuity of supply, many pharmaceutical companies are making it a strategic priority to enter into a long-term relationship with a preferred supplier that has the products, expertise, technical capabilities and partnerships to serve all their requirements over a period of ten to fifteen years or more.

By utilising a single platform-based technology from a preferred supplier, companies can minimise risk, speed time to market, and obtain the desired flexibility to address the specific needs of each target molecule and patient population across their drug portfolio.

To serve the needs of pharmaceutical and biotechnology customers, Unilife has created a broad portfolio of platform-based technologies that can accommodate the specific requirements of any injectable therapy that can benefit from being worn on the patient's body. These platforms (shown in Figure 1) include:



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Figure 1: Unilife's platform of wearable injection devices: (a) The Precision-Therapy™; (b) The Flex-Therapy™; (c) The Imperium™.

- The Precision-Therapy™ platform of wearable injectors, which is best suited to short-duration therapies that require the delivery of large dose volumes over pre-programmed periods such as a few minutes.
- The Flex-Therapy™ platform of wearable injectors that deliver customised rate profiles, which can be used for long-duration therapies requiring large dose volumes or unique delivery profiles.
- The Imperium™ platform of instant patch pumps that are prefilled and pre-assembled with insulin for compact, convenient and intuitive basal-bolus multi-day wear by insulin-dependent people with diabetes.

Each of these platform-based technologies is fully customisable, and can be supplied by the customer in a prefilled and pre-assembled format ready for injection to minimise packaging and steps of use. None of Unilife's wearable injection systems require terminal sterilisation and all can be pre-configured to the optimal delivery-rate and duration-period specifications for each drug within a customer's portfolio

to maximise clinical outcomes and brand management strategies.

For pharmaceutical companies seeking wearable injectors for a portfolio of large dose volume therapies targeted for subcutaneous patient self-injection, Unilife has observed that three key criteria are commonly used during the process of selecting a preferred technology and partner.

1. **Simple to Customise:** How easily can the system be efficiently customised to fit the operational, commercial, regulatory and therapeutic requirements of each target therapy?
2. **Simple to Commercialise:** How seamlessly can it be integrated with approved manufacturing methods and materials, allowing rapid development to get the drug onto the market quickly and minimise supply chain and regulatory risk?
3. **Simple to Use:** How well does it enable an intuitive, effective, comfortable and confident user experience by the target patient population and also potentially provide the necessary data informatics to monitor rates of therapy adherence?

SIMPLE TO CUSTOMISE

Pharmaceutical companies evaluating prospective wearable injector technologies and partners should assess the modular design flexibility of a device platform to ensure it can deliver the right therapy, user experience and brand message for a portfolio of target drugs and indications.

Criteria that may be used to assess the customisability of a wearable system (see Figure 2) include dose volume, drug viscosity, delivery duration, delivery rate, external shape and feel, user notifications, user initiation, product disposal, needle type, data connectivity and mode of patient wear.

Dose Volume

Many pharmaceutical companies recognise the therapeutic and commercial benefits of striking the right balance between dose volume, drug viscosity and injection frequency. A common goal is to select the formulation that requires a less frequent dosing regimen without causing an undesirable user experience.

While Unilife has received enquiries to utilise wearable injectors for drugs with

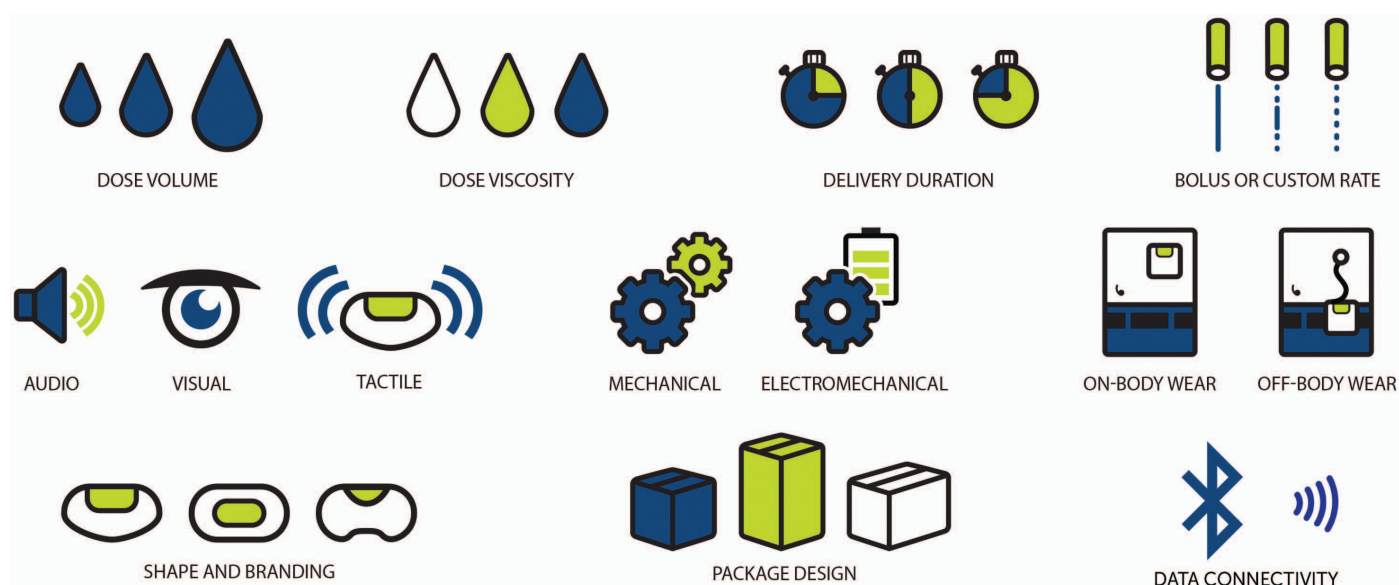


Figure 2: Wearable technology customisation options.



Figure 3: Unilife's wearable injectors provide the flexibility for the external design and functionality of each device to be tailored to match requirements. Options extend far beyond brand labelling or colours to include: single button or dual-button activation; the button force required for activation; button size for population needs; and an ergonomic and distinctive external design.

"Unilife has developed all of its wearable injection systems for integrated data connectivity via systems including Bluetooth LE. Smart phone apps have also been developed that can remind the patient when it's time to take their medication, and to send them regular prompts until they have done so"

target dose volumes from 1-100 mL, the overwhelming majority of customer requirements tend to fall between 2 and 10 mL. A platform of wearable injectors should be able to accommodate the full spectrum of target dose volumes required by a pharmaceutical customer across its portfolio of injectable therapies.

Drug Viscosity

Drug viscosity is a common factor that can influence the decision of a pharmaceutical company as to whether to utilise a hand-held device such as a prefilled syringe or auto-injector, or a wearable injector. As a general rule, the lower the viscosity of the drug the more comfortable and convenient will be its administration by a target patient population.

Typically, it is those molecules which are considered too viscous for a liquid dose of 1 mL or less that are selected for use with wearable injectors. Based upon the requirements of many pharmaceutical companies engaged with Unilife, the standard range of viscosities being targeted for use with wearable injectors is between 1 and 100cP. Unilife's wearable injectors have been proven to accommodate drug viscosities of greater than 100cP.

Delivery Rate and Duration

A wearable injector should be able to be pre-set to deliver a fixed dose of drug accurately at the controlled rate or duration that generates the best clinical outcomes. The selection of rate controlled or the duration controlled for a target therapy will be determined by the specific dose delivery rate profile, or the dose delivery volume requirements.

Unilife works with its customers to adopt the simplest solution for their needs, as well as their target patients, to avoid them having to pay for unnecessary complexity. Wearable injector options that are provided by Unilife include bolus, basal or variable rates over very tightly controlled delivery durations. The option to pre-program the device for an

immediate or delayed start to the injection is also available.

External Design

Drug delivery systems are increasingly being used by pharmaceutical companies to generate brand differentiation against competitors. Furthermore, human factors have become integral to securing the regulatory approval of drug-device combination products, as well as increasing rates of therapy adherence. A platform technology for wearable injectors must therefore not only be simple to use, but also easily customisable with respect to look, feel and functionality.

Unilife's platform of wearable injectors provides pharmaceutical customers with the flexibility to have the external design and functionality of each device tailored to match their requirements in several important ways. Options extend far beyond brand labelling or colours to include: single button or dual-button activation; the button force required for activation; button size for population needs; and an ergonomic and distinctive external design that best fits the grip of the user and enables comfortable wear during the injection period (Figure 3).

Product Disposal

Unilife has developed its platform of wearable injectors with the option of removable electronics to enable the recovery, re-use and recycling of electronic waste. This removable electronics option enables pharmaceutical companies to strike the right balance between patient usability and green disposal and recycling.

Bluetooth LE Connectivity

For many chronic diseases, rates of patient adherence with a therapy regime are sub-optimal. Frequent patient challenges can include forgetting to take their medication at the recommend time, administering the wrong dose, or incorrect use of the device. Unilife has developed all of its wearable injection systems for integrated data con-



Figure 4: Unilife's wearable injection systems require only three simple steps to deliver a therapy.

nectivity via systems including Bluetooth LE. Smart phone apps have also been developed that can remind the patient when it's time to take their medication, and to send them regular prompts until they have done so.

Before use, the data-enabled device can automatically assist the patient in determining that they are using the right drug at the right concentration. During use, the smartphone can also provide active notifications and alerts to ensure patients know the status of the device, with clear indications for end-of-use or error conditions. After use, the smartphone app can ask the patient whether they were satisfied with the injection experience, with all applicable data sent to data hubs for access by authorised healthcare stakeholders. Injection therapy data can also be integrated with other significant markers of therapy effectiveness for enhanced clinical assessments.

Other Customisation Options

Other customisation options available to Unilife's pharmaceutical customers include the gauge and length of needle used either for injection or the automatic insertion of the Flexwear™ comfort catheter, on-body or off-body wear options and packaging design.

SIMPLE TO USE

Unilife is committed to the design, development and customisation of injectable drug delivery systems that are as safe, comfortable and easy to use as possible. As a general rule, intuitive devices with fewer steps of use are most likely to reduce the risk of error, minimise the need and cost for user training, optimise rates of therapy compliance and drive preference rates amongst patients, prescribers and payers. Such device-related benefits can be leveraged by a pharmaceutical company to build

or protect market share and differentiate a drug brand from the competition.

Unilife understands that many pharmaceutical companies are increasingly seeking access to a wearable injector technology that is prefilled, pre-assembled and ready-to-inject, and requires as few as three simple intuitive steps for use by the patient.

Final Supply to User

To overcome the inability of most wearable injector technologies to be terminally sterilised (see below under Sterilisation Method), other systems require the user to insert the drug into the device manually using either a prefilled cartridge or a vial and a syringe.

While some wearable injection technologies necessitate seven, twelve or even more steps of use, Unilife's wearable injection systems require only three simple steps to deliver a therapy. The steps are commonly described as "Peel, Stick and Click" (Figure 4). The presence of user-vetted visual and audio-indicators that are designed to clearly convey the status of the device at all times during use is also strongly favoured by user study participants.

This convenient, ready-to-use format has been found to be strongly accepted and preferred in user studies. It can also help to minimise the need for additional training and associated overheads that a pharmaceutical

"Unilife wearable injectors can be aseptically filled and then pre-assembled in a non-aseptic environment without any special processes ... The successful development of a wearable injector technology that can be prefilled and pre-assembled without terminal sterilisation allows a great deal of flexibility in the supply chain without creating new manufacturing technologies or compromising the biologic or drug"

Delivery systems with multiple parts that place an extra burden on the user are not only less convenient, but they may create additional risks of error, result in sub-optimal rates of therapy adherence and reduce levels of acceptability amongst patients or prescribers. Unilife's platform of wearable injection systems can be prefilled and pre-assembled in their final-packaging by the pharmaceutical manufacturer and then supplied to the end user in a ready-to-inject format.

company may otherwise incur which can impair broader acceptance into the market.

Ergonomics and Patient Wear

Wearable injection systems should be ergonomically designed for convenient, comfortable and confident patient wear over minutes, hours or days. When used to deliver drugs over duration periods longer than a few minutes, wearable injectors should enable the user to wear the device discreetly underneath clothing. Environments where a



Figure 5: Wearable injector technologies should be designed to enable seamless integration into standard filling systems and processes.

wearable injector could conceivably be used by a patient include home, work, cafes, restaurants, gymnasiums and outdoors.

The ability to wear a device in itself is, however, insufficient to help optimise rates of therapy adherence and drive patient preference and acceptance towards a particular drug product. Factors that can influence the level of user acceptance towards a particular therapy can include the degree of ease and comfort associated with the attachment, activation, wearing and removal of the device from the body.

In addition to the size, shape and adhesive of a wearable injector, the angle by which a needle or cannula is inserted into the body during the period of injection can be a particularly important factor for patient comfort.

In line with the growing trend towards personalised medicine, Unilife customers can have the look and feel of each wearable injector tailored to the specific requirements of a drug, its commercial brand strategy, target patient population and indication.

User Interface

An effective user interface for a wearable injector should enable a patient to inspect the drug visually prior to and during administration, facilitate the initiation of an injection with an appropriate force and provide accurate visual, audio or vibratory indicators relating to the status of an injection.

Unilife's wearable injection systems provide a 180-degree viewing window to the medication container during all stages of

use. Likewise, electronic and mechanical systems can provide visual, audio or vibratory indicators to facilitate user confidence and under-clothing awareness. An audio status feature, which can inform the patient of the initiation status and completion of an injection, can be silenced for discreet use. Various light colours, illumination patterns and tone frequencies can also be customised based upon customer and brand requirements and user study outcomes.

Drug Security

A wearable injection system should not only protect the drug during shipment and storage, but prevent potential drug wastage prior to the point at which the user is ready to commence the injection of the dose. Unilife's wearable injection systems feature a robust, tamper-evident external casing, and are suitable for final shipment in sturdy yet easy-to-open packaging. Where applicable in cases such as the delivery of insulin with a patch pump, automatic priming can occur directly upon removal of the device from the packaging.

For Unilife's wearable injector platforms, a proprietary safety interlock mechanism must also be depressed on the body prior to the start of an injection, to prevent premature activation. These safety features help to minimise the risk of drug wastage, and enable clear and confident use during the injection period. When combined with Bluetooth LE connectivity, wearable injection systems may also provide verification to the patient that they are about

to administer the right drug at the right concentration and that it is not counterfeit or expired.

For potentially lethal drugs such as insulin, Unilife also provides a range of additional features and functions that together provide triple-redundant safety during all anticipated scenarios of use including over-delivery protection.

SIMPLE TO COMMERCIALISE

A fundamental goal of any wearable injector business is to ensure that each pharmaceutical customer can easily get its drugs to market with as minimal risk as possible. The incorporation of new materials, new filling processes or novel methods of delivery represent examples of unnecessary risk that can be mitigated through the upfront development of a robust, modular platform that is customer-centric in design and fully scalable.

Unilife's philosophy is that wearable injectors should leverage well understood materials and fit seamlessly into approved manufacturing methods to mitigate the need for a customer to change any of its standard processes and preferred equipment suppliers.

Platform Architecture

To support the rapid commercialisation of several injectable molecules in parallel for a customer, Unilife has developed its wearable injector platform under a modular framework that enables customisation to one component without the need to redesign the other components. Unilife can therefore efficiently customise each product to a range of customer specifications such as dose volume, drug viscosity and duration rate.

Primary Drug Container

Unilife follows an open architecture model in the selection of components and suppliers to provide customers with a level of flexibility that is typically not possible with traditional device suppliers. Rather than having to rely on a device to sell a specific material, each of Unilife's products exists to meet the specific needs of customer, its target drugs and associated patient populations. Most importantly, the primary drug container for Unilife's platform of wearable injectables uses a standard glass cartridge utilising well-characterised materials, including borosilicate type I glass and commonly used elastomers.

Customisable aspects of the primary drug container include the use of silicone

oil, baked silicone or coated elastomers. Unilife can also provide products with a plastic (polymer)-based primary container should the customer desire it.

Sterilisation Method

Many biologics and other injectable drugs are not recommended to go through a terminal sterilisation cycle due to the risk of causing damage to the molecule, as well as cost. Unilife has developed a unique, proprietary system that can be aseptically filled and then pre-assembled in a non-aseptic environment without any special processes.

The primary drug container is only accessed once the injection sequence has been initiated by the user. The successful development of a wearable injector technology that can be prefilled and pre-assembled without terminal sterilisation allows a great deal of flexibility in the supply chain without creating new manufacturing technologies or compromising the biologic or drug.

Supply for Filling

Wearable injector technologies should be designed to enable seamless integration into standard filling systems and processes (Figure 5). Technologies which require a pharmaceutical manufacturer to modify existing processes, purchase extra equipment or invest in new or unconventional filling processes may encounter customer resistance and potentially impact commercialisation timelines for a program. To support regulatory processes and enable modular scale-up during clinical trials and commercial rollout, wearable injector technologies should also be designed to enable filling to occur on multiple scales.

Unilife has developed a robust and modular-based design platform to ensure each product is thoroughly engineered and aligned with established manufacturing processes.

Unilife's wearable injectors can be integrated seamlessly into filling and inspection equipment with simple change parts. Filling and stoppering can be conducted in high-speed syringe filling equipment in aseptic operations. Unilife can provide pharmaceutical customers with an in-depth evaluation of how its devices can be integrated into established syringe filling equipment, and be filled on multiple scales, up to hundreds of units per minute. Unilife's existing relationships with well-known CMOs and filling equipment manufacturers can also be leveraged to support the commercialisation pathway for a customer's target drug products.

Sources of Production

With a proprietary wearable injection system being crucial to the clinical development, regulatory approval and commercial success of a relevant injectable therapy, Unilife recognises the importance of providing its customers with multiple sources for production and supply to help maximise risk mitigation.

Unilife has thus entered into a strategic partnership with Flextronics, one of the world's leading end-to-end supply chain solutions companies. Flextronics has existing relationships with many pharmaceutical and biotechnology companies, and is considered to be the largest medical device OEM in the world. This relationship provides Unilife customers with alternative sources of manufacturing and supply for its wearable injection systems. In addition to providing long-term continuity of supply, the partnership also allows customers to ramp up to higher volumes more quickly.

FINAL CONSIDERATIONS

The selection of a wearable injector platform should not only be based on how simple it is to customise, commercialise and use. As a preferred wearable injector technology will ultimately play a significant role in the

needs in real-time and encourages a close and collaborative relationship between the respective project teams.

Unilife has also developed a company structure and culture that is highly customer-centric. Each wearable injector team established for a customer is composed of engineers, scientists and other experts from the drug delivery industry, with many having experience in class three devices and infusion pumps. Unilife has established arguably the largest team in the wearable injector market, which boasts deep technical knowledge and advanced industry expertise.

Unlike other companies where the business is predominantly based around materials or commodity components, Unilife was created from the ground up as a developer, manufacturer and supplier of sophisticated injectable drug delivery systems. It has a deep understanding of primary container technologies, and how they must be integrated into the effective production and functionality of a drug delivery system. From a customer perspective, this translates into having a partner that has the expertise, processes and capabilities to take full responsibility for all aspects of the device and its integration within the overall drug-device combination product.

"Flextronics has existing relationships with many pharmaceutical and biotechnology companies, and is considered to be the largest medical device OEM in the world. This relationship provides Unilife customers with alternative sources of manufacturing and supply for its wearable injection systems. In addition to providing long-term continuity of supply, the partnership also allows customers to ramp up to higher volumes more quickly."

approval and commercial success of a target therapy, pharmaceutical companies should carefully consider how a device manufacturer can serve their long-term requirements with speed, agility and reliability.

In addition to having world-class, US-based manufacturing facilities and unparalleled innovation credentials, Unilife employs a dedicated team approach to customer programs. This approach enables Unilife to be fully responsive to a customer's

With Unilife also having a broad portfolio of injectable drug delivery systems, it offers the neutrality to help pharmaceutical customers determine whether a particular molecule is best suited for use with a wearable injector, prefilled syringe, auto-injector or a combination of two or more platforms. Unilife is ready to serve pharmaceutical customers under long-term partnerships to enable and enhance the delivery and commercial success of their injectable therapies.



A LARGE-VOLUME SC DELIVERY SYSTEM MUST ADJUST TO DRUG & PATIENT NEEDS ... NOT VICE VERSA

Here, Gerhard Mayer, PhD, Vice-President Business Development North America; Sandra de Haan, Head of Business Development outside North America; and Helmut Thiemer, Head of Technology; all of Sensile Medical, describe the SenseCore micro pump and, in particular, relate aspects of its mechanism to specific advantages when applied in the area of large volume injection devices.

As your new drug moves from the early stages of dose finding and clinical trials through commercialisation, there will be a number of unknowns that the drug developer and their “customers” in marketing may have to deal with:

- What will the drug formulation be in the end? Viscosity? Flow rates?
- What will be the need for dosage accuracy?
- Is the primary packaging clearly defined? Vial or cartridge? Would cartridge development potentially endanger the targeted launch date?
- How and where will drug delivery take place? Are there special requirements dictated by therapy or patient needs?
- When and to what extent will the needs be in clinicals?

Sensile Medical has developed a wearable large volume injector (also known as a patch pump) that can be adjusted to meet the needs of your drug and potential patients – while enabling meaningful product differentiation for the marketing team.

For the drug development and drug delivery specialists at pharmaceutical companies, this article provides broad detail on the options and capabilities provided by Sensile Medical’s large volume injector technology.

THE HEART OF SENSILE'S LARGE VOLUME INJECTORS

Sensile has developed a novel micro pump concept called SenseCore, which lies at the heart of its large volume injectors.

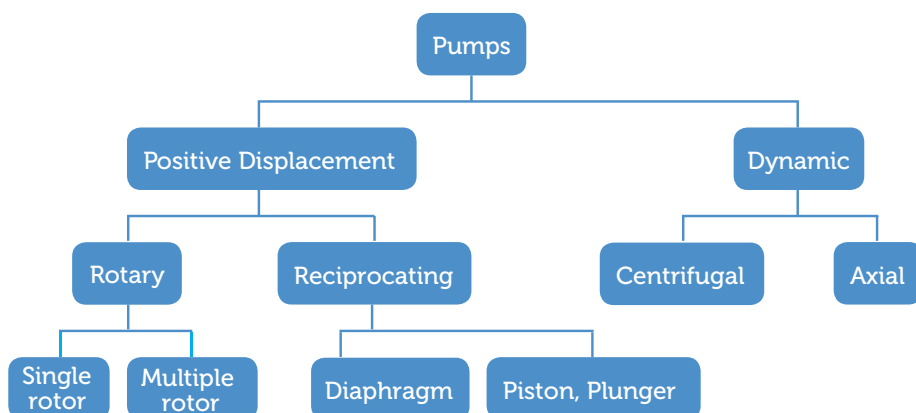


Figure 1: Classification chart for types of pumps. SenseCore is a reciprocating-type positive displacement pump.



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Medical devices based on this concept offer a wide range of advantages and are superior in many aspects over narrowly defined drug delivery systems or even syringe pumps, which may be used in clinical trials.

This article lists some key features and advantages.

CLASSIFICATION / PRINCIPLE

Within the classification scheme of pumps (Figure 1), SenseCore is a reciprocating-type positive displacement pump. Specifically, it is a piston pump (as well known in pharmaceutical filling technology) with a ring shaped piston area.

The rotating piston, together with an injection moulded valve structure, mechanically drives intake and outlet valves and additionally generates the correct pumping stroke derived from the primary rotation.

The design is flexible and can operate bidirectionally by defining the pump direction just by selecting the appropriate sense of rotation of its pump drive.

As is typical of piston pumps, each pumping cycle:

- generates a good suction pressure
- intakes a well-defined volume of drug
- accurately delivers a nominal pump volume at a defined delivery pressure and time.

SCALABILITY

The nominal delivery volume can easily be designed to the required optimum delivery volume per stroke, typically ranging (but not limited to) from less than 1 μ L to 25 μ L per cycle. Taking advantage of the active piston area being a ring, the delivery volume is defined by the ratio of the two diameters of the stepped piston (Figure 2). Even at very small delivery increments, the parts allow for tight tolerances as well as a very robust product.

MATERIALS

The two pump elements – the pump housing and the shaft (piston) – can be chosen from a variety of materials. For the housing, all suitable outer-shell materials can be chosen as long as they allow adherence of the inner soft component, which is injection-moulded into the shell using a two-shot moulding concept.

For the inner soft component (forming the valve structure) typically thermoplastic elastomers (TPE) are used, allowing for low

cost, while also liquid silicone rubber (LSR) is available and can be used.

For the piston the material of choice is injection moulded plastics just by the obvious cost advantages in large scale production.

Alternatively, shafts from stainless steel or ceramic can be used depending on needs.

DRUGS AND DRUG FORMULATIONS

As a piston pump, SenseCore handles liquids as well as gases and liquid gas mixtures. While liquids are delivered exact to the designed volume, just defined by the pump's displacement, with gases, on account of their compressibility, the delivered volumes are only defined if the pressure conditions are taken into consideration.

Still SenseCore does pump gases. With its compression ratio of typically 1:1, it is absolutely self-priming and generates a suction pressured of 0.5 bar at standard atmospheric conditions (MSL).

Sensile works on projects where a SenseCore pump is intentionally delivering gas. By its chosen design and working principle it further does not accumulate air



Figure 2: The delivery volume is defined by the ratio of the diameters of the stepped piston.

DOSAGE ACCURACY

As a positive displacement pump with its incremental delivery, SenseCore offers large improvements when judged via the trumpet curve, which represents the maximum percentage deviation from the expected dose for a given time interval.

Unlike syringe pumps (even being equipped with a high-precision, linear drive) where the elasticity and varying break-loose forces of the plunger first under deliver and then, after some time, overshoot, SenseCore delivers one nominal pump volume per each and every stroke to the patient.

By its design and specific concept, the accuracy achieved with SenseCore, consisting of only two precision plastic parts, holds at $\pm 5\%$ over large scale production.

All parameters influencing the delivery accuracy are injection moulded in one shot into a single part, the piston. As shrinkage influences both of the relevant piston diameters in common mode, the difference remains nearly unchanged,

"A standard vial can be combined with an internal device reservoir, potentially eliminating the need for costly and time-consuming development of a prefilled cartridge"

bubbles but instead passes such microbubbles through.

On the drug viscosity the limiting factor is not the pump itself, but more generically the throttling effects occurring on the suction / intake side, and the counter pressure generated by the downstream side of the fluidics path. Typically this is determined mainly by the gauge of the injection needle. Sensile carefully considers the relevant conditions when defining an application-specific device, by aligning needed flow rate, planned needle size and given drug viscosity to stay safely within the specified performance data for suction and delivery pressure.

generating only a negligible effect on the resulting ring type piston, assuring low delivery-volume changes.

OPTION TO USE STANDARD VIAL AS PRIMARY PACKAGING

As a piston pump, it provides for very good suction capabilities. This combined with the bidirectional capability allows new device concepts that use a standard vial as primary packaging (see Figure 3, overleaf).

A standard vial can be combined with an internal device reservoir, potentially eliminating the need for costly and time-consuming development of a prefilled cartridge.

“Occlusion on the downstream side is monitored using contactless sensors”

MEETING SPECIAL DRUG AND PATIENT NEEDS

Delivery patterns can be programmed to meet potential daily basal profiles, specific drug delivery rates, a high flow constancy performance, or fast bolus delivery. These are easily achieved by running the drive at a different speed and/or combining this with an On-Off pattern. Furthermore, SenseCore technology allows for methods that Sensile has developed to stretch out delivery increment for the sake of flow consistency or to realise extremely low flow rates, for example in neonatal applications.

SAFETY

With the SenseCore, functional principle is inherently safe. This is due to mechanically and actively driven valves, a mechanically defined angular relation between valve elements, and (again mechanically) a fixed relation between valve elements and intake as well as expel stroke.

The valves are defined by mechanical design that ensures at any given time only one valve can be open. In an angular position where the pump is parked (inactive), both valves are closed at the same time. This feature allows for double safety against free flow.

SenseCore technology monitors the pump's angular position, sense of rotation and rotational and axial speed. In addition, occlusion on the downstream side is monitored using contactless sensors. These sensors are part of the reusable subsystem of the device and monitor the relevant elements in the disposable portion.

Figure 3: SenseTrial, a patch pump designed to be used in clinical studies for subcutaneous drug delivery, uses a vial as its primary packaging. This is possible because of SenseCore's good suction and bidirectional capability.



For additional monitoring requirements, magnetic or optical sensors can also be selected.

BASIC DEVICE CONCEPTS

For many applications, semi-disposable product concepts may be preferred. The disposable portion contains all parts in contact with the drug or the patient: the pump, fluidic channels, and patient interfacing elements like the needle and the adhesive. Drug delivery systems of the patch pump variety are often affixed to the patient with an adhesive and with an integrated needle that deploys and retracts automatically.

The reusable portion of the device includes electronics, sensors, drive, rechargeable battery and the simple user interface.

ABOUT SENSILE MEDICAL

Sensile Medical AG is a leader in the area of advanced micro pump technology, developing a broad range of customer-specific delivery and dosing solutions. Its pumps are increasingly being used to enable, for instance, large-volume subcutaneous delivery of modern pharmaceutical and biotech products for self-administration by patients. Due to Sensile's SenseCore technology, the products are highly cost-efficient, accurate, and safe. They are increasingly used in drug delivery, medical and consumer applications. Founded in 2004, Sensile Medical is located in Hagendorf, Switzerland. For further information consult www.sensile-medical.com.



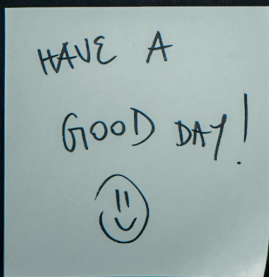
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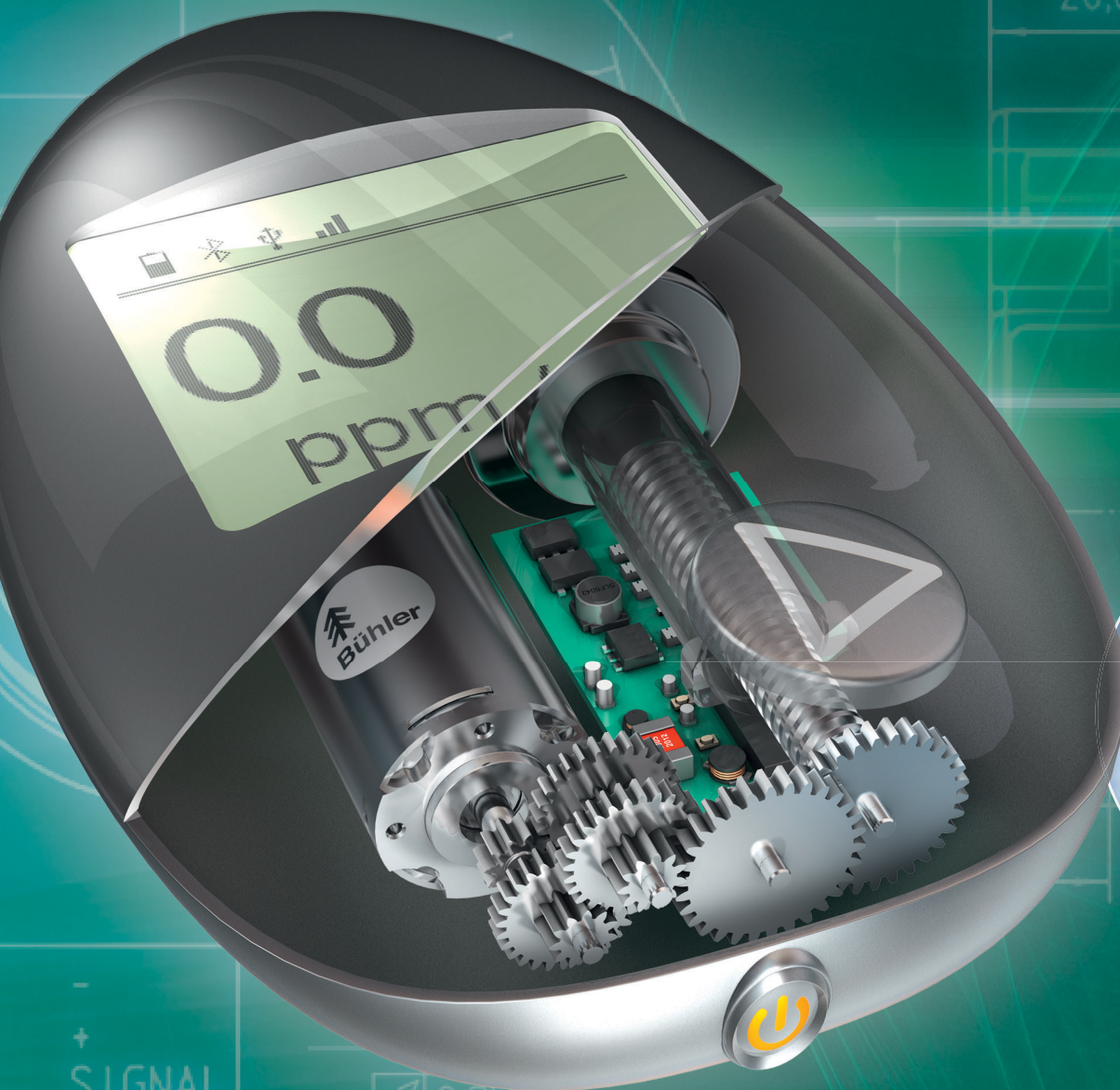


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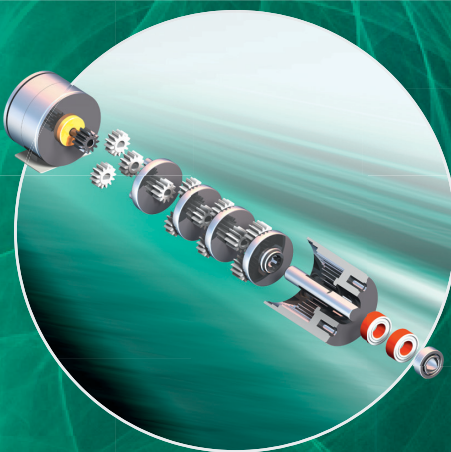
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DRUG PACKAGING SYSTEMS FOR THE DIGITAL HEALTH ERA

In the context of the SmartDose high-volume injection device, in this article, Nicolas Brandes, PhD, Business Development Manager, Daikyo Crystal Zenith, West Pharmaceutical Services, describes how the company is bringing together primary containment materials, the delivery device and a smartphone app from HealthPrize, in order to achieve significant advantages, including optimal patient compliance to chronic therapeutics.

Keeping up with new drugs in development and new technologies to support them requires a novel approach for drug delivery. At West Pharmaceutical Services, we believe in the importance of connecting delivery systems with tools that can improve the user experience and drive adherence. Through our partnership with HealthPrize, a leader in patient engagement and medication adherence solutions, we are able to combine the strengths of the Daikyo Crystal Zenith® polymer cartridge available in the SmartDose® Electronic Wearable Injector with the power of a smartphone app. In doing so we have created a patient-friendly injector for pharmaceutical manufacturers – allowing for system configurations that not long ago seemed part of the distant future.

But this is just the beginning of the potential that exists for drug delivery, which patients – not to mention health insurance payers – have eagerly awaited. They are demanding more autonomy from the physician's office in managing their own self-care at home whenever possible. However, as the use of biologic therapies is on the rise, patients tasked with injecting large quantity doses are challenged with delivering a consistent dose every time. This is especially true for patients with chronic conditions such as diabetes, haemophilia, rheumatoid arthritis and multiple sclerosis.

By focusing on value-added offerings, along with the right primary packaging for injectable biotech drugs early in the drug development process, pharmaceutical companies can now set their product apart with unique packaging and delivery systems that may help aid patient compliance, and ultimately, outcomes.

Putting all three together – the right containment materials, delivery systems, and apps that record doses and reward patients in order to reinforce medication adherence – creates a powerful next-generation system that can help solve some of the more significant issues that new healthcare models pose.

CRYSTAL ZENITH: NEW BIOLOGICS MAY REQUIRE NEW PRIMARY PACKAGING POLYMERS

Some biologic drug products do not react well with glass, requiring drug manufacturers to look at other options for containment and delivery. For example, modern biologic formulations sensitive to silicone oil or tungsten may require alternative packaging. Silicone oil, used as a lubricant in glass containers to obtain plunger gliding functionality, has been strongly connected to protein aggregation as well as the presence of subvisible particles in the suspension.

Other undesirable effects in combination with glass primary packaging include potential breakage, delamination, or heavy metal release, low dimension control and lack of design flexibility.

Challenges with glass as well as a sharpened focus on safety – now that chronic disease patients are treating themselves more frequently at home – drives pharmaceutical companies' demand for increased quality from drug containment and delivery system manufacturers. While glass remains the standard for injectable drug containment for the prefilled syringe market, the material's higher dimensional variability in manufacturing could be a concern when evaluating



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Figure 1: The West SmartDose® electronic wearable injector, designed for patient convenience, incorporates a Daikyo Crystal Zenith® cartridge and can deliver a dose of up to 3.5mL, which may allow for viscous biologics that are sensitive to glass, metal ions and/or silicone oil to be administered over longer periods of time.

the functionality of the syringe or cartridge in conjunction with the delivery system.

These high-quality polymers maintain the quality of sensitive biologics through enhanced cleanliness and decreased interaction with the drug product. Primary containers made from materials such as the Daikyo Crystal Zenith polymer (Figure 1) can help contain higher dose volumes or provide delivery options for viscous drug products. Cartridges and syringes moulded from Daikyo Crystal Zenith polymer are free of silicone oil and tungsten, and exhibit break resistance as well as consistent and predictable gliding forces. The rubber components that are used in the CZ® systems are laminated with Flurotec®, which functions as an effective barrier against extractables and provides lubrication at the same time.

SMARTDOSE INJECTOR: DESIGNED HOME USE

Some patients either do not want to inject themselves with medications in pre-filled syringes, or their conditions make it difficult. Furthermore, some drugs – including the aforementioned cutting-edge biologics – might require large volumes of viscous solutions, making a single-dose option either difficult or impossible.

While there are numerous auto-injector devices on the market, pharmaceutical companies need innovative and responsive packaging partners that can keep up with the requirements these biologics create. Some glass-sensitive biologics must be housed in polymers

because of potential breakage or protein aggregation with glass. Others are more suited to injectors that can control the delivery of large doses over time when the drug is too much for a single injection. An example is West's SmartDose® electronic wearable injector system (Figure 2), incorporating a polymer-based drug container (made from Crystal Zenith resin) and designed to enhance the experience of patients required to self-inject a larger volume biologic drug at home.

Choosing the correct packaging and delivery system can not only make medica-

tion adherence easier on the patients, but it can also encourage brand preference among patients and practitioners. By making the right choices early on in the development process, packaging and pharmaceutical manufacturing can mitigate risk and deliver a high-quality product to patients.

HEALTHPRIZE APP: MEDICATION ADHERENCE SUPPORT IN YOUR POCKET

Digital health, mHealth and the wearables revolution are all current catchphrases that describe the movement to enhance traditional clinical care with patient-owned mobile devices. On the simplest level, apps associated with drug delivery systems can drive adherence by sending reminders to the patient and provide a means to log when and how much of a drug they administered.

On a more advanced level, a wearable injector paired with an app offers opportunities to educate the patient on the medication and its administration; automatically track when and where a dose was administered, and how much was used; and even offer feedback to the physician as well as data analytics over time.

Research indicates that a patient's medication adherence is directly linked to favourable treatment outcomes for a variety of chronic therapies, including multiple sclerosis and diabetes. Yet patient compliance with chronic medication therapies is remarkably low – the World Health Organization



Figure 2: West's SmartDose® electronic wearable injector provides a solution for the challenge of delivering a large-volume dose of a drug product. Easily tailored to specific pharmaceutical customer needs, West's SmartDose technology, which incorporates Daikyo Crystal Zenith® prefillable cartridges, is designed for the delivery of viscous biologic drugs.



Figure 3: HealthPrize's medication adherence and patient engagement platform is intended to be integrated with West's injectable drug delivery systems, including the SmartDose® electronic wearable injector and injectors for drugs and various biologics.

estimates it at 50% internationally. Non-compliance leads to poor clinical outcomes, lost revenue for pharmaceutical companies worldwide and increased costs for many healthcare financial stakeholders, including the patients themselves.

New formulations such as some once-a-month biologic injections take some burden off of patients administering medications in self-care. But as the time between doses grows, it becomes easier to forget to take it. The problem to solve, then, becomes one of reminding – and even rewarding – patients for medication compliance. Technology offers a potential new solution to this ongoing problem, as smartphone and tablet app developers attempt to create software that helps chronic disease patients stick to their medication regimens.

As a company invested in next-generation care, West has joined forces with HealthPrize to develop apps in conjunction with self-injection drug delivery (Figure 3). It is our way of getting involved with the connected health movement for the sake of patient engagement: A way of adding value for patients living with disease and who sometimes need a little help improving their health, and to offer our pharmaceutical partners a range of choices. The heart of the HealthPrize system is motivation through rewards – giving the patient a gift card after achieving medication-adherence milestones set by the pharmaceu-

tical company or healthcare provider.

Product development in the pharmaceutical industry takes time in order to ensure that we are adhering to the highest quality standards. That is neither good nor bad; it just is reality. By partnering with an established, connected-health company that has built a healthcare gamification app we hope to be able to help more patients by making it available to our pharmaceutical partners.

At first, patients will be able to scan barcodes manually or otherwise enter data about their medication compliance into the smartphone/tablet app or on an internet browser from a computer if they don't have a wireless device. It is imperative for us and our partners to make the app as intuitive as possible. This way the app itself doesn't become a barrier to medication compliance. In the future, pending applicable regulatory requirements, we would like to make app usage even more automated, streamlined and interactive. We would accomplish this by enabling our drug delivery system to signal the smartphone numerous data points about each dose administration.

For example, a self-injection patient's app might automatically, in real time, confirm that a particular dose was used, the syringe safety was released, all the medication was injected, and other details. The app is designed to offer the patient feedback and validation, ultimately reinforcing the efficacy of the treatment path.

CONCLUSION: PUTTING THE PIECES TOGETHER

Each element of these novel drug delivery models – the Daikyo Crystal Zenith polymers, the SmartDose electronic wearable injector system, and the HealthPrize app – are powerful next-generation tools by themselves.

Taken together, they put pharmaceutical companies in a position to create cutting-edge systems that not only benefit patients by helping avoid the consequences of skipping their medications but help the drug manufacturer ensure that the products delivered to market are used to their full potential.

The combination of these three drug delivery components also can yield data points previously unavailable to drug companies for analysis. By performing data analytics on usage patterns, more can be learned about these medications and the way they are used by patients in their homes, with an eye toward ultimately help improving therapies and creating better, more comfortable lives for patients living with chronic diseases.

SmartDose® is a registered trademark of Medimop Medical Projects Ltd., a subsidiary of West Pharmaceutical Services, Inc. West seeks partners for its SmartDose electronic wearable injector technology platform. This platform is intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical/biotechnology company.

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ABOUT THE AUTHOR

Nicolas Brandes is responsible for business development and all project and product management activities related to Daikyo Crystal Zenith products in Europe, working hand-in-hand with West's strategic partner Daikyo Seiko in Japan. Dr Brandes received his PhD in Biology from the University of Wuerzburg, Germany in 2010, after performing his research studies at the University of Michigan, US.

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**Health
Prize**



West seeks partners for its SmartDose electronic wearable injector technology platform. This platform is intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical/biotechnology company. The SmartDose system, HealthPrize platform integration is for conceptual purposes only.

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GETTING TO KNOW ENABLE INJECTIONS

Enable Injections was founded in February 2010 in Cincinnati, OH, US, and develops and manufactures devices for patient self-administration of high volume / high viscosity drugs. The Enable Injector, which has just successfully completed its first-in-humans clinical trial, is a body-worn device that provides a comfortable injection experience allowing the patient administer their own medication and to continue with normal daily activities. It is designed to utilise any standard container closure system, including a syringe, vial or cartridge.

Since ONdrugDelivery Magazine first came into contact with Enable Injections, we keep on hearing how the

company is all about its people. From one perspective, by "people" they mean they are always focused on the patients who will use their devices. However, "people" also very much means those who helped conceive and set-up the company and those who are working there to develop and bring the Enable device to market.

The importance of people is a strong theme with Enable, and so we thought we should get to know some of them! Here follow five mini-interviews with key Enable members. We asked each of them the same five questions, and their answers give interesting insights, from varied perspectives, into what really makes Enable Injections tick.

enable
injections

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Matthew Huddleston

Vice-President Product Development & Program Management, Enable Injections

Q Please could you tell us a little about yourself? – your background and business interests, and your current connection with Enable?

A From an education standpoint, I have a Bachelors in Mechanical Engineering and a Masters in Biomedical Engineering. I've been in medical device development and manufacturing for my entire career. Prior to Enable, I worked for a contract design and manufacturing company where I worked on various medical devices across multiple therapeutic areas. I have previous auto-injector experience, multi-axis machine experience, coronary bypass clips and delivery instruments, and laparoscopic accessories – so a wide range of device experience.

My current position at Enable is Vice-President of Product Development & Program Management, leading all of the efforts relating to product development. So I have a team of development engineers,

as well test engineers and technicians, and human factors specialists. And I would definitely like to focus on the team and not necessarily me, because everyone has made a specific contribution.

Q What attracted you to the company and made you think "yes, I want to be involved"?

A Mike Hoooven was on the board of my previous company and so that's how I got to know Mike. I left my previous company to consult on my own for a couple of years and at that time, around 2010 or 2011, Mike contacted me and asked if I would like to engage with him in a start-up that would do subcutaneous injections of biologics. I knew Mike had a terrific track record with

nology. Looking back, the current technology is much different than the technology we founded the company on. The original technology was not well received by the industry and there were times early on that I thought this thing is not going to work out.

In fact learning that lesson, that the technology you start with is almost certainly not going to be the thing that you end up with, was one of the biggest, key things that I learnt early on. That was a painful transition, a painful letting go period. But Mike reassured us that it was the right way forward and he explained that we don't just invest in technology, we invest in people and it is the people that will make the technology. That was a learning experience for me and at that stage I knew, hey, I'm with the right people here.

"We don't just invest in technology, we invest in people and it is the people that will make the technology."

the work he had done with other companies, and that is largely what attracted me – his previous record of success.

In terms of the technology concept, I thought that was a good fit because of my previous experience in auto-injection tech-

Q Thinking about the Enable Injections device itself, what sets it apart in your view?

A Its elegance and efficiency. All of the other wearable injection platforms being developed are a combination of a

custom rigid container closure coupled with a drive mechanism. There are a few important distinctions in that statement. First, these container closures (typically glass cartridges) have one purpose, to hold the drug. They weren't meant to be worn on the body. In addition, they're custom to the injection platform. This means the drug company that, in most cases, originally developed the drug in a vial, must take on the additional time, cost and risk of revalidating the drug in this new custom container. Second, the drive mechanism must be adapted to the container. Depending on the technology, these drive mechanism can be very complicated with motors, sensors and other electronics that end up being very large to wear (with relatively low payload volumes) and complicated for the user to operate.

In contrast, the Enable Injections platform is a simple mechanical system. The container closure is the power source. So you've taken two complicated elements and combined them into one. Its elegance comes from its simplicity. The platform allows the pharma company to keep their drug in the original container closure reducing their risk and time to market. A particularly compelling efficiency can be seen when you go to larger payload volumes. While other companies are developing platforms up to 5 mL, their technology becomes unwearable in larger volumes. With the Enable device, when you go from 10 mL to 20 mL, you don't double

the size of the device. The change in size is minimal. In fact, I'm willing to compare Enable's 50 mL device to someone else's 5 mL device. I'm betting their sizes are not much different.

Q Regarding the emerging field of wearable injections, what is your take on this industry sector – how is it doing and where is it headed in terms of impact on medicine and healthcare?

A The really exciting thing, and this is going back to what attracted me to Enable too, is that as an individual you get into this field because you have a desire to help people. Often, when you work in medical devices it's hard to make that connection. But here, at Enable, you can always see the direct connection, the direct value.

We were focused on human factors from almost day one, and from the beginning we were able to go out and ask people, "How will this change your life?" When they realise that this would mean they wouldn't have to go out to the hospital anymore, they wouldn't have to visit the clinic for their medication; seeing the effect of that and the effect it is going to have on the healthcare system is what it's really about.

I'm an engineer. I don't really understand the economics in detail. But I can recognise the value and that is what I see – someone is not going to have to get in their car and to go to the hospital. They are going to be able to perform this therapy at home, not

be embarrassed, not have to change their lifestyle. You just put this thing on, pull your shirt down, and go about your business. I've read the market reports and they are saying that this is a potential \$8 billion business. I've read all that but I appreciate more when patients can say, "I don't have to be tethered to a line anymore!" That's what I get excited about.

Q Finally, if I say to you "Enable Injections", tell me the three words that spring to your mind first?

A Okay, I'm going to cheat a bit here and give you the three words I hear the most about Enable! I keep my family and my friends pretty involved, I talk about this on social media, so here is what I hear people say about the Enable device.

The thing I hear most often is COOL. When I explain what it does, how it can change lives, people say, "How cool is this!"

The second is SMALL. People who have looked at it on the website always mention how small it is when they actually hold it in their hands. It is a lot smaller than their expectation of its size from seeing images of it online.

The third is OPPORTUNITY. Everyone recognises the opportunity we have to change people's lives with our technology. Me personally, I'm thankful for the opportunity to be part of Enable Injections and to know and work with a great group of people who will ultimately make this successful.



Richard J D'Augustine
Founding Board Member, Enable Medical,
Ethicon EndoSurgery and AtriCure

Q Please could you tell us a little about yourself? – your background and business interests, and your current connection with Enable?

A My career has been relatively long, well over 30 years, and always connected with life sciences. I started with Johnson & Johnson back in the 1970s, with Ethicon. After a number of positions I was selected to manage the acquisition of a device partner in Cincinnati, Ohio. We had

to set it up as a new business unit within Ethicon. This was how I met Mike Hooven; about a year in I was interviewing him for a product development director position within Ethicon. He was kind of young. The person he was going to be reporting to didn't want to hire him! So we waited, but a few months later we were expanding and I brought Mike back in and hired him into Ethicon. We'll talk about Mike more later.

So I stayed in Ethicon, went back to their New Jersey HQ for some time and was in business development there, responsible for putting together the strategy for what Ethicon should do in the then new market of what we then tended to call laparoscopy, now called minimal invasive surgery. I presented the strategy to the board, the board liked it, they brought in McKinsey & Co, who said it should be a separate company and so I moved back to Cincinnati and became one of the founding board mem-

bers of Ethicon EndoSurgery. So I've been involved with the whole Ethicon-Cincinnati connection since the beginning, from picking the site where we built the building.

I left a couple of years later after licensing in several products and getting the thing going and I had the taste for developing a new technology that was starting a new industry. I then went to work for SenMed Medical Ventures for five years and then became CEO of a drug delivery company, UMD. After UMD, I went to work for CincyTech, which is a local seed investor, a public/private partnership.

I was at CincyTech and was also one of the founding members, with Mike, of his first company, Enable Medical, as well as AtriCure. I've known and worked with Mike for quite a long time. After Mike decided to become less active at AtriCure, he was doing some consulting at CincyTech and that's how we got talking to the people

at Cincinnati Children's Hospital Medical Center. I was Executive in Residence at CincyTech, Mike was consulting, and Cincinnati Children's had a painless injection technology. We decided to start a company around it. Mike was working on several other new technologies as well but once this injection technology started to take over we began to really focus.

CincyTech invested in Enable back then. I left CincyTech a little while later and now I'm an independent consultant focusing in the lifesciences. I do a lot of work with

says he did some work and, "Here, I can do it and the device is about the size of a quarter." And that was the idea for the painless injection device. Then we got started, put a little money together, he went to some of his core people that were involved with him at AtriCure as investors. Since I was working for CincyTech I couldn't invest personally at this time, though I would have obviously!

Of course his invention, his idea, was different from any of the other ideas that anyone had come up with. Typical Mike again – he doesn't want solutions, he likes

system in multiple ways – to the patient, to the healthcare provider, the payer, the drug company itself.

It's so well thought out, so well designed, solves a lot of problems – I'm personally genuinely really excited about it.

Q Regarding the emerging field of wearable injections, what is your take on this industry sector – how is it doing and where is it headed in terms of impact on medicine and healthcare?

A Enable didn't start with this giant market opportunity, although that developed pretty quickly. Biologics already account for half of the top ten drugs by sales, and it's only going to get stronger. And so helping to solve this delivery problem is a huge opportunity.

Like I said, I've been around for a while. This wearable injectors market, at this stage, reminds me of the early days of minimally invasive surgery. There were some people getting involved, things were happening, things were changing, some big players were starting to get interested. Sure a bunch of companies were doing laparoscopic procedures for a long time but they were little metal reusable devices. And then suddenly somebody did a successful cholecystectomy and then "BOOM". And I think we're almost at that stage with wearable injectors. I think we're about to enter that stage when ... well as soon as one these products hits the market the whole thing is going to explode. Honestly, I think that once it does start there will be a feeding frenzy amongst the big players. They'll say, "We have to have something like that!" which is exactly what happened in the early days of minimally invasive surgery.

It's a game changer. I truly believe that. There aren't a lot of them in the device world – angioplasty, stents, for example – but they are there, and I think this is going to be one of them.

Q Finally, if I say to you "Enable Injections", tell me the three words that spring to your mind first?

A The first one is maybe obvious but it's INNOVATIVE. The second is CONFIDENCE. The third is LEADERSHIP. Leadership in terms of Mike Hooven's inspirational leadership, and the board he has gathered together. If you look at this little company, it has truly world class people on the board. I also say leadership because I believe Enable is going to be a market leader.

The drug manufacturers don't have to do anything different – they can put it in the same standard vial"

universities, early-stage technologies, little companies, I serve on a couple of boards. I am on the Enable Injections board and I am an investor as well.

Q What attracted you to the company and made you think "yes, I want to be involved"?

A Mike Hooven is a unique individual. I've worked with tonnes and tonnes of really clever engineers and inventors and he really does just stand out, he's just a head-and-shoulders above. He's a truly inspirational leader and if you get to know him you quickly begin to see he has an effect on people. My attraction to Enable injections was therefore obviously Mike. And also the product. We were talking with people from Children's hospital as they were, and still are, a strong supporter of CincyTech. I happened to be on the board of a scoliosis device company that came out of Children's Hospital and the inventor of that device was a surgeon who was a creative guy. Years earlier he'd come up with this idea for a painless injector. So he'd had this idea, it made a lot of sense, but the problem was that they brought in an engineer and the reduction to practice was about the size of a coffee cup.

I can tell you that Mike sat there and looked at it and just said that's not going to ever work, look, we ought to do it like this. Within 20 minutes he had started drawing designs on the blackboard. I said, "Can you actually do this?" And this is typical Mike: he said: "Leave it with me, let me go home and play around with it." And sure enough a couple of days later he comes back and

to be given a problem and he goes away and he comes up with the solution, and that's exactly what happened here.

When I left Cincytech, Mike asked me to join the Enable Injections board, together with others we'd known for some time including Norm Weldon, Don Harrison and Karen Robards.

Mike really brings the team together. Besides being a great inventor, he uses his board better than almost any other start-up company CEO I've ever seen, and I've been involved with many. He doesn't think he knows all of the answers, and when he needs help he asks for it, and he brings people in. He has a way of integrating input from others – pretty sophisticated people in other fields.

Q Thinking about the Enable Injections device itself, what sets it apart in your view?

A The device is elegant, simple, it's versatile and, crucially, it's user focused, which I think is critical. I wouldn't say that pharma and biotech companies are not user focused, but their focus is on the therapeutic. Enable did a lot of research into what the user needed, what the patient needed, what was going to help the patient. Even the button is designed so that if the injection gets painful, or for whatever reason, you can stop it for a while.

The device is smaller than I think most if not all of the others. The drug manufacturers don't have to do anything different – they can put it in the same standard vial. It answers so many of the right questions. It should be a positive for the healthcare



Michael D Hooven

Founder & CEO of Enable Injections

Q Please could you tell us a little about yourself? – your background and business interests, and your current connection with Enable?

A I was born in Michigan, grew up in Boston, worked in Miami and Los Angeles. My first job was for a medical device company by the name of Cordis, which at that time was being run by Norman Weldon. I have known Norm ever since then, he has been my mentor and helped me start up all of my companies. I've been medical devices for 31 years, started in neurosurgical engineering with Cordis, moved on to manage sensor, and then lead, and then pacemaker development for Siemens Pacesetter in Los Angeles. I then came to Cincinnati to help Ethicon start their Endo-Surgery business. I was responsible for all internal product development and my team and I recruited and hired over 200 engineers from all over the country. And the great thing about that is that when I started working for them I told them I was going to start my own company in about five years, and then after six years I started my company on very good terms and was able to hire quite a few people out of Ethicon for my first company, Enable Medical, and for my second company, AtriCure.

Enable Injections is my third company, based here in Ohio. The great thing about being in Ohio is that I have established a good reputation in terms of being able to recruit and retain really good people and in terms of being able to build successful companies that develop, manufacture and release highly successful products into the market place. Based on that, we have a lot of support from the State and from institutions within the State. We think that Enable Injections is positioned really well as one of the premier medical device companies in Ohio and we believe, soon, also in the US.

Q What attracted you to the idea of creating the company and made you think "yes, I want to do this"?

A I was consulting at CincyTech and Bob Coy, the then CEO, put me in touch with the people at the Cincinnati Childrens Hospital. It's a terrific organisation.

They had a project they had been working on for almost ten years but they really hadn't been able to get a lot of traction. They'd spent a fair amount of money and even done some clinical trials. A very innovative doctor there had invented a technology for painless children's vaccines.

That really started me on the path to Enable Injections and I started working with

ring the drug from the standard container closure (standard vial) into the device, this allows the patient to wear a device where the container within the device is also the delivery system. So we're not forcing the patient to wear a container closure that really wasn't designed for drug delivery or to be worn. This then allows the Enable Injections device to be significantly smaller, lighter and lower

"Our transfer system actually warms the drug during the transfer process so that the patient can use the device immediately the standard vial containing their drug is taken out of the refrigerator. This, we hear from users, is a compelling benefit"

people at Childrens Hospital, we put together a very small founding round of funding, and developed an initial technology based on the painless device for children's vaccinations. As has happened in every single one of my start-up companies the technology that we began the company with and raised initial funding for turned out to be different from the technology we actually moved ahead with. We changed the technology to a high volume body worn injector, but we were able to utilise virtually all of the experience and ten years of clinical work that had been done at Childrens Hospital on what causes injection pain and ways to make injections essentially painless. We think this served as a terrific foundation to move into the new technology area.

Q Thinking about the Enable Injections device itself, what sets it apart in your view?

A A crucial thing that sets Enable apart from anyone else is that we allow the pharma companies to utilise absolutely standard container closure. That results in a number of significant advantages.

First, any change to a container closure requires that the pharma company test the drug with that container closure for a period of two years or more. We have experience with working with pharma companies who discovered after 18 months that their biologic was not compatible with a new container closure material. So first and foremost what Enable allows the pharma company to do is to eliminate all of the cost, all of the risk and all of the time associated with packaging their drug in a new container closure.

Secondly, because the Enable system has a very simple and intuitive way of transfer-

profile and it enables us to have devices that the patient can wear that can deliver considerably higher volumes than anyone else.

The third area where we are unique is that our transfer system actually warms the drug during the transfer process so that the patient can use the device immediately the standard vial containing their drug is taken out of the refrigerator. This, we hear from users, is a compelling benefit.

Fourthly, we have the only system that allows for fully automated reconstitution of lyophilised drugs. The user simply inserts the diluent and the powder vial containers into the system and everything else is completely automated so we completely remove the user from the mixing process.

Q Regarding the emerging field of wearable injections, what is your take on this industry sector – how is it doing and where is it headed in terms of impact on medicine and healthcare?

A I believe this is going to be one of the biggest and fastest growing areas in all of medical devices. There are a number of reasons for this. In the next ten years there are going to be over \$250 billion sales of biologic drugs, \$50 billion of those are going to be new drugs, drugs that currently don't exist.

What we are hearing from our pharmaceutical partners is that the only alternatives they have for delivering these drugs are either multiple injections or intravenous injection. What the high volume body worn injector is going to do is first of all allow the patient to do their injection at home, so there is a tremendous patient benefit. Secondly it is going to remove a significant amount of cost from the healthcare system. If you only

think of all of the businesses that are currently set up to deliver intravenous drugs, with we believe that a large number of new biologics can be delivered with our device as opposed to intravenously you have a huge reduction in overall healthcare costs. Pharmaceutical companies are giving these devices away to customers for the most part whereas the cost of an intravenous infusion can be many thousands of dollars.

The payers are driving this as well. They are saying: here I have the choice of reimburs-

ing one drug where the patient simply takes the device at home, puts it on their body presses a button and then throws it away when they have finished, and all I'm paying for is the drug. This is *versus* having the patient spend hours getting to a clinic and paying healthcare professionals to administer that drug intravenously. I think they are going to pay for the wearable product where they don't have to pay all these extra costs, where the patient healthcare benefit is higher and where the compliance is greater.

Q Finally, if I say to you "Enable Injections", tell me the three words that spring to your mind first?

A Number one is the PEOPLE. That means the people in Enable, and the people the product is going to benefit. Then there is the PRODUCT. And there is our PRODUCTION EXPERTISE in devices. I think you put all three of those things together and we stand head-and-shoulders above everybody else.



Dr Jeannie Joughin

Vice-President Corporate Development,
Enable Injections

Q Please could you tell us a little about yourself? – your background and business interests, and your current connection with Enable?

A I have been in the pharmaceutical industry for over 20 years and most recently I was with CSL Behring, for over ten years. I've worked in clinical research, sales and marketing and business development during my time within pharmaceuticals, and my most recent role within CSL Behring was Vice-President of Business Development. I came to know Enable Injections when at CSL we were looking for a technology to deliver our products via subcutaneous infusion. We evaluated several platforms and we licensed the Enable Injector for two therapeutic areas.

I made the decision in 2014 that I would be moving on from CSL Behring, and I joined Enable Injections just three months ago. So my current connection with Enable is that I am the company's Vice-President of Corporate Development.

Q What attracted you to the company and made you think "yes, I want to be involved"?

A The culture at Enable Injections attracted me. Meeting Mike Hooven and the team, while I was at CSL, working through how their technology could be applied to various CSL products, I found Enable to be incredibly responsive to different issues. They were dynamic in coming up

with solutions and product changes that were required for CSL Behring's therapeutic areas. That innovative and responsive culture really spoke to me. I really like that environment and I could see how their device would be able to be applied to many

made available, they could see how this would dramatically change the lives of their children. From small children to older children, they said it would provide a lot more freedom and they would have the convenience to get on and do what children normally do. Potentially

"I found Enable to be incredibly responsive to different issues. They were dynamic in coming up with solutions and product changes that were required for CSL Behring's therapeutic areas. That innovative and responsive culture really spoke to me. I personally like that environment"

other therapeutic areas. I personally wanted to be able to help bring that device to patients requiring chronic subcutaneous infusion in other therapeutic areas.

Q Thinking about the Enable Injections device itself, what sets it apart in your view?

A A key difference is the technology – because it does not have the primary container closure embedded in the device, it can be a lot smaller and have a smaller footprint. The device that we have is this yo-yo, "Oreo" sort of small, round, friendly looking object. So that when patients see it they get a smile on their face. It's not a scary device. It doesn't look "mechanical", it doesn't have flashing lights and sirens, so people – including children, but people of all ages and abilities – relate to it really well. That's where it stands apart the other devices.

In a couple of focus groups in two different therapeutic areas, there were some really memorable patient responses to the injector. People are willing to pick it up. There's no needle visible. They say it looks "really cool", "not scary" – these were the sorts of comments we got. Parents said that if this could be

attending college was an example. Whereas as the idea of attending college was difficult for some young adults because they didn't want people to know that they had this disease, the discreet nature of the Enable device reassured them that they could go there and get on with their lives and no-one would need to know they had a chronic illness.

Q Regarding the emerging field of wearable injections, what is your take on this industry sector – how is it doing and where is it headed in terms of impact on medicine and healthcare?

A We're poised to see a release of these injectors into several therapeutic areas. There is an unmet need to deliver higher volume or higher viscosity products subcutaneously – products that already exist. There's an unmet need from companies looking at what are currently IV-only formulations that they want to develop to be subcutaneous. Usually, if you want to deliver subcutaneously you have to deliver higher volumes. To avoid having to spend years going through reformulation processes to concentrate the product and reduce volume, pharmaceutical companies would have the ability to bring products to market and the

patient earlier with the Enable device. That's one perspective. Another perspective is that wearable injectors will mean that people won't be so inconvenienced because they won't have to go into hospital to have infusions. That should be a really big driver –

patients wanting to manage their own healthcare in the home, and being more responsible for the delivery of their own healthcare. Having these devices in the future will just allow them the flexibility to do that. So you see there is a push and a pull.



Robert W Coy, Jr
President and CEO, CincyTech

Q Please could you tell us a little about yourself? – your background and business interests, and your current connection with Enable?

A I've been in the seed stage investment business since 1983, investing in technology and bioscience companies. Across my career I've been involved in start-ups in the state of Delaware, Pennsylvania, the St Louis metropolitan area and now Cincinnati. I've been with CincyTech now for ten years. We focus primarily in the software sector and the bioscience sectors. For us biosciences include pharma, medical devices, biotech, diagnostics and health-tech. We focus on opportunities that are in our metropolitan area and we've invested in 58 companies since we formed our fund in 2007. Out of our funds we've invested \$26 million in those companies. And another \$480 million has been invested in them by institutional venture funds, high-net-worth individuals and others, under the same terms. We work very closely with two research institutions – Cincinnati Children's Hospital Medical Center, and the University of Cincinnati. Most of our healthcare deal flow comes out of those two institutions. We've invested in eight companies that are based on technology that was developed at Cincinnati Children's, and Enable is one of those companies, and one of the most exciting.

I moved to Cincinnati in 2005 and met Mike Hooven in 2006. When Mike stepped down from his executive role at his previous company, AtriCure – around 2009 – we retained him at CincyTech and asked him to go to the Children's Hospital and the University to interact with research faculties and find a disruptive technology that could be commercialised through a start-up. He met an orthopaedic surgeon named Dr Eric Wall who had invented the initial concept for a painless injection system. Mike evaluated

it and saw potential, formed the company, Enable Injections, licensed the technology, and CincyTech was the first investor. It's interesting because it shows how you can pull technology out of research institutions. You find someone like Mike, who's a brilliant innovator and entrepreneur. You marry him or her up with a brilliant researcher who has no entrepreneurial expertise, and together they make something great.

Q What attracted you to the company and made you think “yes, I want to be involved”?

A We weren't fully aware in the beginning of how large the market could be for this technology and Mike over time evolved the concept significantly. Initially Enable Injections was going to be a less painful way for injecting drugs and Mike evolved it then in a way that we really didn't anticipate at the time, which is often the case with start-ups. He saw a huge market opportunity in, and need for, more cost effective, less painful, more convenient ways to deliver highly viscous biologic drugs.

Many of these drugs need to be delivered on an out-patient basis either intravenously or through a port, or using electronic delivery systems that are awkward and not comfortable. I think what Mike has developed is a really elegant delivery system that will enable the drug to be delivered more conveniently and comfortably to the patient, and at consid-

“It's light,small, it's elegant and not cumbersome, it can easily be concealed under a patient's shirt, and they can continue about their business while the drug is being delivered”

erably less expense to the healthcare system. My personal view is that pharma companies today realise that the method of delivery of these kinds of drugs can be a real differentiator, and can give them a competitive advantage in the marketplace.

Q Thinking about the Enable Injections device itself, what sets it apart in your view?

Q Finally, if I say to you “Enable Injections”, tell me the three words that spring to your mind first?

A PATIENT-CENTRIC, INNOVATIVE, and COLLABORATIVE!

A One of the things that I really like about the Enable system is that it doesn't require an electronic pump. It's very light, small, it's elegant and not cumbersome, it can easily be concealed under a patient's shirt, and the patient can continue to go about their business while the drug is being delivered. You don't have to go to a hospital to be hooked up to a pump machine. It's a more convenient method of delivery. Enable has conducted a lot of human factors studies on patients and the feedback from them, people who are currently having these drugs delivered via conventional methods, is phenomenal. They love the Enable system, for all of these reasons.

Q Regarding the emerging field of wearable injections, what is your take on this industry sector – how is it doing and where is it headed in terms of impact on medicine and healthcare?

A Many pharma and biotech companies today recognise that a better method of delivery is necessary so they have efforts underway to address this. My understanding is that this is being driven in part by the FDA, which is looking at the method of delivery, and the degree of pain and discomfort it involves, as one of the criteria for drug approval. For these reasons, pharma companies now view the systems that deliver their drugs as core to their business. It's no longer just about the

drug and whether or not it works. Especially these viscous biologic drugs that cannot be delivered via a traditional syringe but require other systems.

Q Finally, if I say to you “Enable Injections”, tell me the three words that spring to your mind first?

A I'd say COMFORT, CONVENIENCE and COST-EFFECTIVENESS!



Helping all people
live healthy lives

LEVERAGING PATIENT-CENTERED DESIGN TO DELIVER LARGE VOLUME DRUGS

In this article, Maggie Tsai, Marketing Product Manager, BD Medical – Pharmaceutical Systems, describes using a patient-centred design approach to deliver larger volume drugs in a space where current delivery devices are being challenged.

THE NEED FOR CUTTING-EDGE DRUG DELIVERY

Many market factors are driving the need for advancements in drug delivery devices. Pharmaceutical companies are developing more innovative injectable therapies. The injectable drugs market is set to grow at a 14% compounded annual growth rate to reach US\$43.3 billion (£28 billion) in 2017.¹ In the injectable drug delivery market, self-injection devices such as auto-injectors are the fastest growing segment.¹ Many new drugs must be delivered in higher volumes and at higher viscosities than has traditionally been the case, challenging the limits of current delivery devices. At the same time, there is an effort to reduce overall healthcare costs by moving patient care out of the hospital / clinic into the home setting. As a result, drug delivery devices must be patient friendly and intuitive to use in order to drive acceptance and adherence to these innovative drugs.

IMPORTANCE OF FINDING THE RIGHT DEVICE PARTNER

Collaborating with a device partner with the experience and technical compe-

tence to help guide pharmaceutical companies through the device development process could maximise product success in the market. Factors such as human factors engineering, integrated design and development, preclinical and clinical capabilities, and regulatory expertise and support could play an important role. Such factors and criteria could minimise downside risks, reduce time to market, and drive commercial success.

OPTIMISING PATIENT OUTCOMES THROUGH DEVICE DESIGN

With the migration of patient care to a nonclinical setting, the patient is now responsible for his/her therapy. Because the patient may not be as skilled as a health care provider or caregiver, the design of the device needs to be intuitive and patient friendly. Other complications of larger volume delivery include longer injection times and the need to wear the device during this period. Partnering with a device company that has expertise in human factors engineering could help drive product acceptance and preference. Large volume device designs that may enhance usability and total patient experience include button



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"Knowledge from prefilled syringe development (silicone oil level, product contact materials, and extractables and leachables for example) can help in the design of wearable injectors"

force optimisation, feedback indicators and safety features. Understanding the impact and incorporating these features into the product design could enhance patient compliance and improve outcomes.

INTEGRATED DESIGN AND DEVELOPMENT

Many of the biologic drugs in development are sensitive and may require a primary container that reduces the risk of surface interactions and meets the technical requirements of the drug. Factors such as biocompatibility, gliding forces and container closure integrity could impact the performance of the system. According to Diane Doughty, PhD, Scientist II at Medimmune, “Knowledge from prefilled syringe development (silicone oil level, product contact materials, and extractables and leachables, for example) can help in the design of wearable injectors.”² A device partner who has the technical expertise and knowledge of the interactions between the drug, primary container and delivery device for higher volume subcutaneous injections could minimise risk during the development process and optimise robustness of the system.

CLINICAL & REGULATORY EXPERTISE

In order to enable a successful commercialisation, a device partner should have the proper toxicology, clinical and regulatory expertise with global experience. Collaborating with a device company who has the resources and expertise for clinical data collection as well as the capabilities to conduct clinical trials could help navigate through these uncharted territories. Such resources include protocol and clinical method development, investigator and/or patient recruitment, and statistical analysis.

A device partner could also manage downside risk by offering regulatory consultation and support for registration of combination products. The increasing scrutiny within the regulatory environment increases the need for strong partnerships and functional experts on the device and pharmaceutical company side. Since specific guidance has not been fully developed yet for wearable, large volume delivery devices, a device partner who has a breadth of experience in regulatory submission and maintenance could

help effectively advise recommendations, which would support commercial success of the product.

BD'S BROAD AND INNOVATIVE PORTFOLIO

BD Medical – Pharmaceutical Systems offers a broad portfolio of innovative drug delivery systems to meet the current and evolving needs of the pharmaceutical industry. BD's wide range of products includes glass and plastic prefillable syringes (Figure 1), safety and shielding systems (Figure 2), self-injection devices (Figure 3), and needle technology. “BD is leveraging its unparalleled experience to offer innovative solutions for the pharmaceutical industry to meet the emerging needs of large volume and high viscosity drugs,” commented company Worldwide President Peter Nolan. “Such solutions include primary container technologies (for example, BD Neopak™ 2.25 mL glass prefillable staked syringes), 2.25 mL safety and shielding systems, and self-injection systems with potential to deliver up to 15 mL (for example, BD Libertas™ Patch Injector).”

BD LIBERTAS™ PATCH INJECTOR

The BD Libertas™ Patch Injector, as shown in Figure 4 (overleaf), has been designed from deep insights on patient attitudes, beliefs and perceptions about devices and with BD's human factors, ergonomic design and clinical capabilities.³

The product is a single-use, prefillable disposable, injection system for hands-free use during drug delivery and applicable to multiple therapies. Target delivery ranges cover drugs with volumes up to 5 mL (with additional preliminary assessment on volumes up to 15 mL) and high viscosities up to 50 Cp.

KEY CHARACTERISTICS OF LIBERTAS™ INCLUDE:

- Ready to be used by patient (i.e. no patient assembly)
- Prefillable syringe technology developed for biotech drugs
- Needle advantages like hidden needle before and after injection and passive needle retraction
- Feedback indicators, including a large window that can allow easier visual drug inspection and monitoring of injection progression (Figure 5, next page).



Figure 1: BD prefillable syringes.



Figure 2: BD Safety shielding systems.



Figure 3: BD's self-injection portfolio.



Figure 4: The Libertas™ Patch Injector.

BD Libertas™ Patch Injector was designed and optimised through an iterative design approach that puts the patient at the center and uses patient feedback (see Figure 6).

More than 1,000 patients of various demographics and experience levels have been interviewed over the product development process.⁴ The feedback provided inputs to enhance product features and design of the BD Libertas™ Patch Injector, including the elimination of an assembly step for the patient, a separate status indicator window, and an intuitive activation button shape perpendicular to the skin.

“The BD Libertas™ Patch Injector is a patient-friendly device. The design simplifies the patient injection experience and gives the patient comfort and confidence to ensure compliance,” says Peter Quinn, Patch Injector Platform Leader.

BD'S STRATEGIC VALUE-ADDED SUPPORT

With in-house preclinical and clinical capabilities, BD is leading the collection of data to understand the physiological limits of large-volume and high-viscosity drug delivery, and establishing *in vivo* technical feasibility for large-volume and high-viscosity delivery while optimising the function of prototypes. In addition, BD partners with its pharmaceutical customers during the development process to guide development and optimisation for their unique formulations and delivery requirements. As a result, BD is able to understand boundary conditions for delivery feasibility better and develop critical insights for system performance success.

On the regulatory front, BD is actively involved in forums where guidance and standards for large-volume delivery devices is being developed. BD's deep understanding of emerging regulatory challenges across



Figure 5: Viewing window for drug inspection and monitoring of injection progression.

the globe, and its breadth of experience in regulatory submission and maintenance, could help pharmaceutical customers navigate through registration requirements and guidance documents.

SUMMARY

Large-volume, wearable injectors are an emerging class of delivery technologies that enable convenient delivery in alternative healthcare settings. There is a need for pharmaceutical companies to offer solutions that enable delivery of larger volume and high-viscosity drugs while encouraging patient confidence through an intuitive and easy-to-use device. To drive a successful product launch, it is important to find a device partner that has the experience and technical competence to guide pharmaceutical companies through the device development process.

A device partner should leverage and apply patient and therapeutic insights to inform product design, have the technical expertise to ensure integration and performance of the drug delivery system and support the development process through clinical studies and regulatory guidance.

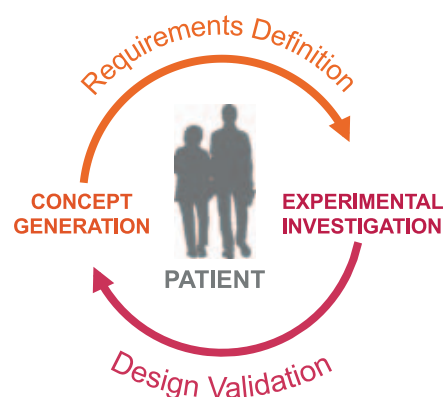


Figure 6: Patient-centered design approach.

REFERENCES

1. Marketandmarkets.com, “Injectable Drug Delivery Market by Formulations [Liposomes, Microspheres, & Nanoparticles], Devices [Disposables & Reusable, Fillable & Prefilled, Pen, Needle Free & Auto Injectors] & Therapeutics [Diabetes & Oncology] - Global Forecasts to 2017”. April 2013.
2. “Wearable Injectors for Large Volume Subcutaneous”. Prefilled Syringes Summit, San Diego, CA. June 23-25, 2015.
3. Injection Device Discrete Study (n=237), BD. October 2011
4. Various Human Factors, Market Research and Advisory Board Studies (n=1,155), BD. Feb 2005 – Feb 2015.

ABOUT BD

BD is a leading medical technology company that partners with customers and stakeholders to address many of the world's most pressing and evolving health needs. Our innovative solutions are focused on improving medication management and patient safety; supporting infection prevention practices; equipping surgical and interventional procedures; improving drug delivery; aiding anaesthesiology and respiratory care; advancing cellular research and applications; enhancing the diagnosis of infectious diseases and cancers; and supporting the management of diabetes. We are more than 45,000 associates in 50 countries who strive to fulfil our purpose of “Helping all people live healthy lives” by advancing the quality, accessibility, safety and affordability of healthcare. In 2015, BD welcomed CareFusion and its products into the BD family of solutions. For more information on BD, please visit www.bd.com.

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Pen
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Safety and
Shielding
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Pen Needles

Your drug is an innovation with significant potential to impact patients' lives.

Competition is intensifying. The regulatory process is getting more complex. Selecting the right device that has been optimized for the patient is fundamental. Integrating device design through industrialization with global freedom to operate is essential.

These are just several critical factors impacting your risk and time-to-market.

Selecting a self-injection partner is a big decision with a lot at stake – for your drug, your company, patients, healthcare professionals. And you.

You need a partner who delivers on what matters to maximize your potential.

Contact a BD expert today
at 1-800-255-3310 or BDPS_marketing@bd.com
Learn more at: www.bd.com/self-injection



Who do you trust with your innovation?

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COMPANY PROFILE: STEADYMED THERAPEUTICS



SteadyMed Therapeutics, Inc, is a specialty pharmaceutical company. SteadyMed leverages its PatchPump® platform to develop its own therapeutic portfolio and partners to optimise the delivery of high volume (greater than 2 mL), high-value, small-molecule or biologic drugs.

Our family of PatchPumps can be customised to deliver liquid drugs, including biologics, with a wide range of volumes and viscosities, in a consistent and controllable manner.

OUR VISION

SteadyMed aspires to redefine the parenteral therapeutics experience for patients dependent upon large doses of intravenous and subcutaneous medications: extending the limits of parenteral therapeutics to restore freedom, joy and dignity to patients' lives.

BREAKTHROUGH TECHNOLOGY

Through its proprietary ECell technology and primary container, the PatchPump® is the only customisable, prefilled, and pre-programmed disposable parenteral delivery platform for large volume and viscous formulations. PatchPump® is the most size-efficient and scalable delivery product for injectable drugs because: one single ECell design acts as both the power source and the driving mechanism for the whole range of drug volumes and viscosities; the volume of the drug container is easily changed without fundamental changes to the technology.

THE "HEART" OF PATCHPUMP®

The ECell® is the compact and self-powered driving mechanism that is used to activate and operate the PatchPump® while maintaining size efficiency, and patient comfort.



The ECell:

- is a unique, small, self-powered expanding battery
- irreversibly expands upon discharge
- is fully disposable
- is electronically controlled enabling accurate and specific drug dosing
- expands under high pressures enabling delivery of viscous drugs
- is IP protected and fully owned by SteadyMed Therapeutics.

PRODUCT ADVANTAGES

A Few Ways PatchPump® Works for You

Our PatchPumps are being developed to deliver liquid drugs, including biologics, in a controlled manner via a compact and simple to use design.

SIMPLE – Prefilled with drug, no complex mechanics and easy to manufacture. Just apply to the body and go!



Figure 2: The ECell proprietary expanding battery is at the heart of the PatchPump®.



Figure 1: PatchPumps in (left) external cannula and (right) integrated cannula formats.

SMART – Precise electronic control allows accurate delivery of pre-programmed dose, while providing feedback to patient.

SMALL – Slim profile design, comfortable and discreet.

PRECISE – Sensor based control for accurate basal or bolus delivery of drug.

SCALABLE – The PatchPump® platform can accurately deliver a range of drug dose volumes from 1 mL to volumes over 2 mL, independent of viscosity.

SELF MONITORING - Internal sensors provide patient with dosing feedback.



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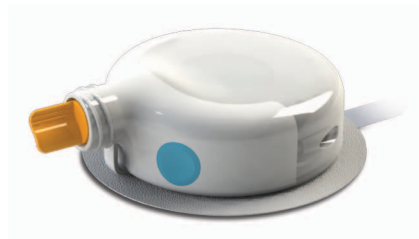
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 **PatchPump** by SteadyMed Therapeutics, Inc.

SteadyMed is about to expand the delivery limits of parenteral therapeutics with PatchPump® the world's leading pre-filled and pre-programmed liquid drug delivery platform that's not only customizable but discreet.

Learn how to get pre-filled with the confidence that will transform how parenteral therapies are delivered.

◆◆◆ Learn more at SteadyMed.com



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