
Pre-filled,
Pre-assembled,
Ready-to-Inject.
Peel,
Stick,
Click.
UNILIFE
Wearable Injectors
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These products have not yet been evaluated by the FDA

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 devices, 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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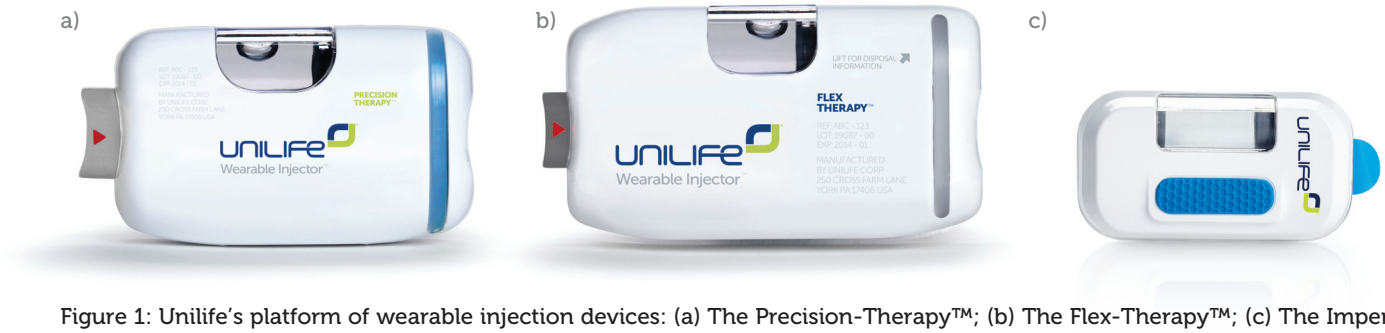

Figure 1: Unilife's platform of wearable injection devices: (a) The Precision-Therapy™; (b) The Flex-Therapy™; (c) The Imperium™.

- 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

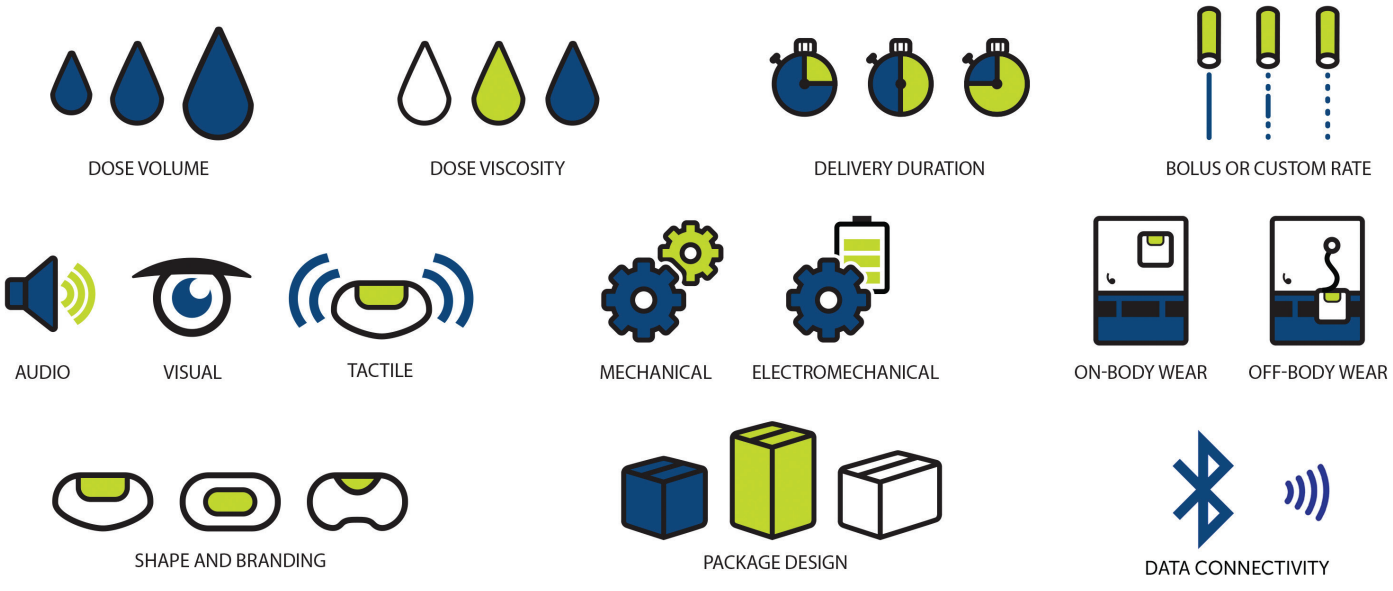

Figure 2: Wearable technology customisation options.

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 preset 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.

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.

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

"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"

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 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 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."

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.