PROVIDING PHARMACEUTICAL COMPANIES WITH MARKET-LEADING WEARABLE INJECTORS, PARTNERS AND PEOPLE

This article by Stephen Allan, Senior Vice-President, Marketing & Communications, at Unilife, highlights some of the key reasons the company's customer-centric strategy is helping it establish long-term, commercial relationships with many leading pharmaceutical companies and industry suppliers.

In response to unmet and emerging market needs for the containment and delivery of injectable biologics, Unilife has created a market-leading portfolio of wearable injectors that is backed by an expert team and a strong network of industry partners to help pharmaceutical companies minimise risk and maximise brand differentiation.

Pharmaceutical companies continue to prioritise the clinical development and commercial marketing of injectable biologics such as monoclonal antibodies that target the long-term treatment of chronic or rare diseases with well-defined patient populations. Whenever feasible, companies will strive to develop these biologics in a patient-centric, subcutaneous (SC) formulation that strikes the right clinical and commercial balance between injection frequency, dose volume and drug viscosity.

Traditionally, a key gating factor has been the limitation of conventional hand-held devices such as prefilled syringes or disposable auto injectors to dose volumes of up to 1.2 mL, potentially forcing companies to compromise on sub-optimal injection frequencies or viscosity levels that may reduce rates of user acceptability or comfort.

Disposable wearable injectors, such as those which can be prefilled and supplied in a ready-to-use format like auto injectors yet pre-configured to contain doses up to 10 mL over a specific rate and duration, are increasingly being leveraged to enhance the provision of care, improve therapy adherence and maximise brand preference amongst patients, prescribers and payers.

> "A core, competitive strength of Unilife's wearable injector portfolio is the ability for any pharmaceutical company to have their drugs Pre-filled, Pre-assembled and Pre-configured for supply to patients as a fully integrated, ready-to-inject system."

Over the last year, a first wave of pharmaceutical companies has begun to market some of their lead biologics in wearable injector technologies. While such first-generation wearable systems can have technical and functional limitations, such as having to be filled and assembled by the patient prior to use, their market entry marks the beginning of a new era of innovation and growth for drug delivery.

More than a dozen pharmaceutical companies are targeting the use of

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wearable systems for new product launches or to optimise the commercial lifecycle of approved drugs via strategies such as conversion from intravenous (IV) infusion to SC injection. While some therapies will require 100% use of wearable injectors, some companies are expected to make them available as an additional option to better address the needs of patient sub-segments that are under-served by hand-held products.

Whether a pharmaceutical company has multiple drugs being targeted for use with wearable injectors, or a single therapy with multiple target indications or delivery profiles, it has become common for them to conduct upfront due diligence to select a preferred device partner and technology that can best address their long-term clinical, commercial and operational requirements. Typically, pharmaceutical companies will assess prospective wearable suppliers and their respective technologies across a range of factors which are as equally important, if not more so, than price. They include:

1) Ease of use by target patient populations
2) Flexibility for efficient customisation and scale-up across target molecules, brands or indications
3) Integration with standard filling and packaging processes, and material component preferences
4) Long-term continuity of product supply, with the potential to secure exclusive or non-exclusive access for defined drugs or indications.

In response to these and other customer requirements, Unilife has created the industry's first full portfolio of pre-filled, pre-assembled and pre-configured wearable injectors that are platform-based and leverage standard primary container materials and industry processes. The breadth and depth of this proprietary portfolio gives Unilife the flexibility to enhance virtually any wearable therapy regardless of dose volume, delivery rate, viscosity or administration duration. The market-leading attributes of this portfolio, the expertise and commitment of the people and partners behind it, and the company's commitment to helping customers enhance and differentiate their therapies under low-risk, long-term relationships, has allowed it to enter into commercial programs with many leading pharmaceutical companies.

THE P-3 ADVANTAGE

A core, competitive strength of Unilife's wearable injector portfolio is the ability for any pharmaceutical company to have their drugs **P**re-filled, **P**re-assembled and **P**re-configured for supply to patients as a fully integrated, ready-to-inject system that requires only three intuitive steps to commence therapy.

We call this the **P-3** advantage, and it provides customers with significant opportunities to optimise rates of user acceptability and product differentiation against brand-name or biosimilar rivals. By eliminating the need for users to assemble, load or pre-set the drug-device combination prior to use, pharmaceutical companies can reduce therapeutic and packaging complexity, as well as the risk of use error.

PRE-FILLED AND PRE-ASSEMBLED

Unilife wearable injectors are designed to mimic the standard assembly process used across the industry for the filling, assembly and packaging of disposable auto injectors. Standard syringe filling and inspection lines are used to fill tubs of primary drug container cartridges with a measured dose of drug, prior to the insertion of the elastomer. Low or high speed fill-finish equipment from well-known equipment suppliers can be utilised, with only change parts required. The prefilled cartridge is then assembled with upper and lower housings, electronics and a window during final assembly to complete the drug-device combination product. The process maintains container closure integrity and sterility using three barriers. Critically for the protection of the biologic, the design process enables the sterilisation of components without the need for terminal sterilisation.

PRE-CONFIGURED AND SUPPLIED READY FOR INJECTION

Unilife's wearable systems can be pre-configured to deliver a measured dose precisely at a specific rate and duration according to customer requirements. Instant, delayed or on-demand bolus or variable rates are available through the use of mechanical or electromechanical drive systems that can facilitate the controlled delivery of the dose at rates between 0.001 mL and 0.1 mL per second.

While it is most common for pharmaceutical companies to target the delivery of biologics over minutes or hours, Unilife has the capacity to customise its devices for precise delivery in less than 10 seconds or over multiple days.

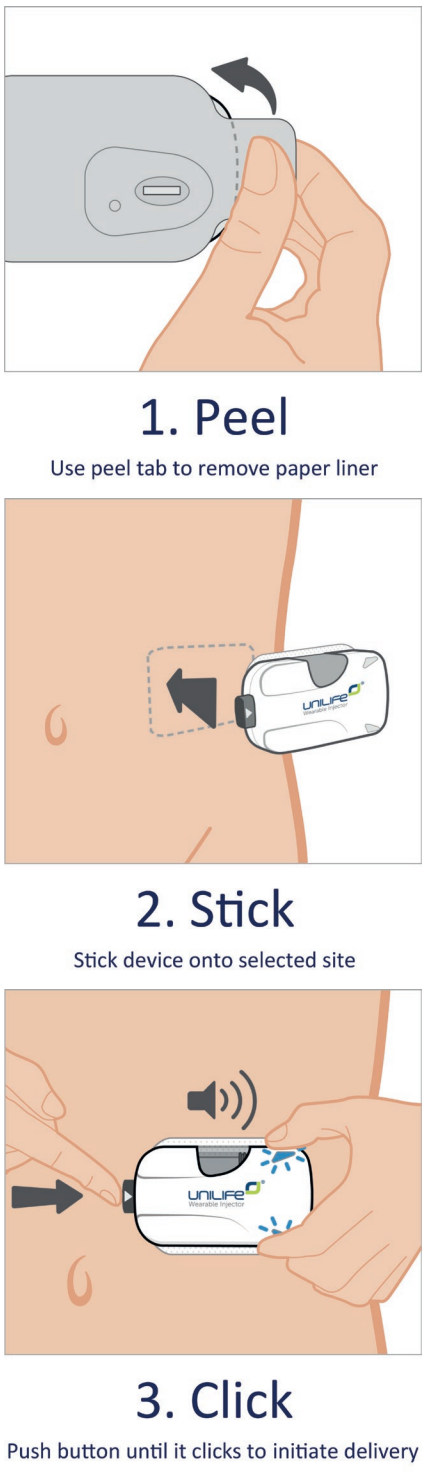

Figure 1: Prefilled, pre-assembled, pre-configured and supplied ready for injection, with only three intuitive steps required to commence therapy.

THREE STEPS TO THERAPY

To initiate dose delivery, a patient has only to undertake three device-related steps that are popularly summarised as "Peel, Stick

Figure 2: A 1 mL product configuration from Unilife's wearable portfolio designed to enhance biologics constrained by the limitations of conventional hand-held systems.

and Click" (see Figure 1). By comparison, other wearable injector technologies that require loading and assembly with the drug can take up to nine device-related steps or more to initiate dose delivery, significantly increasing preparation times and the risk of user error.

One example of Unilife's design commitment to safe, simple patient use is the inclusion of an on-body sensor that automatically prevents the risk of premature activation until the sensor has depressed against the body. A safety guard, which covers the sensor during packaging, is removed by the patient as they peel off adhesive liner.

CLEAR, CONFIDENT AND COMFORTABLE USE

Unilife has created various features available across its portfolio of wearable injectors that are designed to provide patients with clear, confident and comfortable use during all stages of therapy.

- **Single push activation:** On standard Unilife wearable injectors, a single button is situated on the side of the device to reduce the sense of downward pressure being applied onto the body during activation. Minimal force is required to push the button, with the start of dose delivery occurring virtually simultaneously to help build user confidence.
- **Audible & visual status alerts:** Clear audible and visual alerts inform the patient of dose initiation, in-progress status and completion. Should pharmaceutical companies identify that patients may desire discretion during therapy use, Unilife can configure the device so that users can easily turn off these alerts.

> "Unilife has developed wearable injector configurations with integrated Bluetooth LE that provides customers with significant opportunities to improve connections with patients, prescribers and payers. Together with smart phone apps developed by Unilife, patients can receive injection reminders and prompts, access to historic data regarding their therapy regime, and access to technical or steps of use information."

- **Wide medication viewing angle:** A large window provides a clear, unobstructed view of the medication prior to and during use.
- **Medical-grade adhesive skin patch:** The medical-grade adhesive patch that is applied against the skin is designed to provide comfort and security over periods of up to one day across a range of normal physical activities.
- **No needle visibility:** Upon activation, a soft cannula is automatically inserted into the administration site at a pre-configured depth to initiate drug delivery. No needle is visible during any stage of use, with patients able to dispose of the device safely and conveniently as per recommended guidelines.

SMALL DOSES FROM 0.5 ML TO 2 ML

Unilife has created various device configurations designed to enhance the containment, portability, delivery and disposal of injectable therapies that might traditionally be administered in prefilled syringes, disposable auto injectors or insulin pumps (Figure 2). One device configuration developed by Unilife for the bolus delivery of doses up to 1.2 mL is approximately 25% smaller in volume, 60% shorter in length and 90% lower in height than a popular disposable auto injector with an equivalent dose.

Another Unilife configuration combining constant basal infusion with on-demand bolus represents the world's first prefilled, disposable insulin patch pump.

The small size, ergonomic shape and robust materials utilised with Unilife's small dose wearable devices can optimise user portability prior to use, as well as discreet, under-clothing wear during use. With the ability to pre-configure the delivery of the dose over a specified number of minutes, hours or days, Unilife also has the potential to assist pharmaceutical companies seeking to minimise the sense of patient pain or sense of discomfort that occur with the rapid injection of a dose with some auto injector technologies.

LARGE DOSES FROM 2 ML TO 10 ML

Unilife has created a broad portfolio of wearable injectors for the delivery of injectable biologics with dose volumes between 2 mL and 10 mL. The Precision-Therapy platform (Figure 3) leverages a mechanical drive system for immediate bolus injections, and is designed for use with therapies where the specific dose delivery volume helps to determine clinical outcomes. The Flex-Therapy platform

Figure 3: Precision-Therapy wearable injectors are designed to optimise the bolus delivery of injectable biologics with dose volumes greater than 2 mL.

(Figure 4) has an electromechanical drive system for delayed bolus, variable or intermittent bolus injections, and is designed for use with therapies where the specific delivery rate profile helps to determine clinical outcomes.

Figure 4: Flex-Therapy wearable injectors are designed to optimise the variable rate delivery of injectable biologics with dose volumes greater than 2 mL.

PRIMARY CONTAINER DESIGN AND MATERIALS

Unilife's primary drug container is designed with industry standard borosilicate type 1 glass and well characterised lubrication oils and elastomers for long-term drug containment and sterility assurance. A sterile path to the prefilled container is only opened when the user has pressed the button to initiate drug delivery.

Unilife has established a broad, flexible supply chain to provide customers with access to preferred materials from various component suppliers that are well known across the industry. Unilife is also able to provide pharmaceutical companies with primary drug container cartridges, together with other technical information regarding container closure integrity and sterile barrier integrity, separate from its full wearable injector system, for testing and evaluation purposes.

DEVICE CUSTOMISATION

All product configurations across Unilife's platform-based portfolio of wearable injectors are based upon a modular system designed to allow the customisation of one element without creating a need to redesign the others. This provides customers with a modern, flexible, and easily scalable technology platform that can be efficiently tailored to specific drug, patient or brand requirements with minimum risk or incremental cost. In addition to standard customisation options relating to size, look, shape and materials, a number of advanced customisation options are also available (see Table 1).

For example, Unilife has developed wearable injector configurations with integrated Bluetooth LE that provides customers with significant opportunities to improve connections with patients, prescribers and payers. Together with smart phone apps developed in collaboration with Unilife, patients can receive injection reminders and prompts, access to historic data regarding their therapy regime, and access to technical or steps of use information. When combined with RFID or Quick Response (QR) codes, use of the correct prescribed dose and expiration status may also be verified. To improve monitoring of therapy adherence rates by specific patients or entire patient populations, data, including successful dose delivery, may be sent in real-time to secure data hubs.

CONTINUITY OF SUPPLY AND SPECIAL ACCESS

Unilife's business is structured to provide pharmaceutical customers with long-term continuity for production and supply to minimise risk and maximise choice during the clinical development, approval and commercial marketing of the drug-device combination. Partnerships are in place with a range of global industry leaders that are regularly utilised by pharmaceutical companies for production and commercial supply, elastomers, glass forming, injection moulding, equipment automation, contract filling, electronics and sterilisation.

In addition to a provision of supply-chain continuity, Unilife is open to long-term business relationships that provide customers with some level of exclusive or non-exclusive access to its proprietary technology, including a customised look and feel, for use with specific drugs or drug areas.

Such mutually favourable access rights, where it does not conflict with other customers, can allow pharmaceutical companies to leverage the benefits of Unilife's technology fully, to differentiate its therapies from brand-name or biosimilar competition.

Unilife's team of industry professionals is ready to serve the needs of pharmaceutical companies seeking to enhance and differentiate the delivery of their small or large volume biologics.

Unilife Wearable Injector Portfolio Customisation Options		
Shape, Look and Feel	Materials and Components	Advanced Customisation
Ergonomic shape	Glass or plastic tubing (material / supplier)	Bluetooth LE or other
Activation button (Nº, size, force, position)	Elastomer (material / supplier)	Smartphone apps
Adhesive design (Nº and size of tab)	Silicone oil (material / supplier)	RFID scanning
Viewing window design	Rigid needle or soft cannula	Drug warming
Pad printed label / Laser marked		Temperature sensing
Rubber grip		
Removable electronics		
Lighting (Nº, colour, size, position)		
Sounds (tones, sequence)		
Tactile (clicks, vibration)		

Table 1: Unilife wearable injectors are platform-based with a variety of customisation options available, enabling the efficient tailoring of one element within the system without the need to redesign others.