

WEARABLE INJECTORS: LATEST DEVICES & RECENT TRENDS

Tom Oakley, Director of Drug Delivery Device Development at Springboard, discusses recent trends in wearable injection devices. He also takes a look at devices currently on the market and considers the future of wearable injectors.

There are big changes underway in the market for wearable injection devices. In this article, we shall examine:

- The changing needs and competition
- Strategies for designing a wearable injector
- The current state of wearable injectors
- Progress on international standards
- A look to the future of wearable injectors.

THE NEEDS AND COMPETITION HAVE CHANGED

Wearable injection devices have been around in one form or another for decades, ranging from relatively small devices such as insulin infusion pumps to large injectors like the Freedom60 (Figure 1) from KORU Medical Systems (Chester, NY, US). Now there are many small wearable injection devices in development for drugs other than insulin, and some have reached the market.

The need for new wearable injectors has been driven by several factors, for example:

- Many new high-value drugs are biologics, and some biologics have either a viscosity or a volume (or both) that are too high for other delivery devices such as autoinjectors.
- Some new drugs require specific dose timing, for example the start time, or flow rate.

Wearable injectors (sometimes also called patch pumps, on-body delivery systems, or bolus injectors) were predicted to be widespread in many indications, but that has not happened yet. Why not?

Pharmaceutical companies tend to prefer to deliver drugs orally if possible, because the oral route has high patient acceptance and relatively low costs. If a drug must be injected, then pharmaceutical companies tend to look at packaging in vials and prefilled syringes, and then autoinjectors or pen injectors for increased usability. Wearable injectors tend to cost more and involve more user interaction, compared with the options above, so there needs to be a clear case to use them, such as a use case or viscosity or volume that other device options cannot support.

A few years ago, there appeared to be a trend towards high viscosity drug formulations (many tens of cP and above), primarily driven by new monoclonal antibody therapies. However, few of the

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Figure 1: The Freedom60 syringe infusion system from KORU Medical Systems.



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very high viscosity drug formulations that were in development have been continued. Peers in pharmaceutical companies have said that manufacturing very high viscosity formulations is challenging, for example filtering and dosing.

In addition, autoinjectors have been upgraded to deliver volumes greater than 1 mL. For example, Teva's antimigraine treatment, Ajovy (fremanezumab-vfrm) is available in the 2.25 mL capacity Ypsomed YpsoMate autoinjectors.¹ Mylan's EpiPen (epinephrine) stores 2 mL and other autoinjectors, such as Midas Pharma's (Ingelheim, Germany) NISInjector, can deliver 3 mL or more.

There remains a strong case for wearable injectors where:

- The stored volume is greater than 3 mL, even if less than 3 mL is delivered
- The timing of dosing is important, for example with Amgen's granulocyte colony-stimulating factor (G-CSF) analog, Neulasta (pegfilgrastim), or
- The dosing regime is unusual, for example delivering drug from more than one container.

STRATEGIES FOR DESIGNING A WEARABLE INJECTOR

Designers of wearable injectors know that the device is the interface between the patient and the drug. Many user studies, questionnaires and surveys have shown that ease of use is high on the list of requirements for wearable injectors. This tends to promote the design of very compact form factors, which often need custom primary drug containers.

On the other hand, pharmaceutical companies are often reluctant to use non-standard primary containers. For wearable injectors, this means that the primary drug container is very often a standard pharmaceutical cartridge with a septum seal at one end and a standard plunger at the other.

Whatever the primary container, the designer has a fundamental choice to make: whether to push the drug out of the container or pull it out.

Most pushing concepts push a standard pharmaceutical plunger, such as with a telescopic or bending plunger rod. Some concepts push drug out of a non-standard drug container such as the Trevyent PatchPump (Figure 2) from United Therapeutics (Silver Spring, MD,



Figure 2: Trevyent PatchPump from United Therapeutics uses an expanding battery to push drug out of a semi-flexible container.

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US), which was developed by SteadyMed Therapeutics until 2018 when United Therapeutics acquired SteadyMed. The PatchPump uses an expanding battery to push drug out of a semi-flexible container. The advantages of pushing concepts include:

- The drug does not contact different materials on its way to the patient
- There is minimal risk of damage to the drug
- No vacuum is created, which minimises the formation of air bubbles.

Pulling concepts tend to have some sort of reciprocating piston, or peristaltic or other pump between the drug container and the needle (or cannula). The advantages of pulling concepts include:

- The pump features can be physically separate from the container, which allows for different device layouts
- A single design of the pump module could support different primary drug containers such as vials, syringes or cartridges
- Some pumps can be used to pump in both directions, so the pump could fill the drug reservoir from a standard pharmaceutical vial before being attached to the body
- A pump could extract drug from more than one drug container.

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THE CURRENT STATE OF WEARABLE INJECTORS

Here we present an update on selected wearable injectors, but cannot cover all of the devices in development.

West Pharmaceutical Services' SmartDose (see this issue, Page 36) was approved for Amgen's Repatha (evolocumab) (a 3.5 mL dose) in July 2016. Since then, West has:

- signed a development agreement with scPharmaceuticals (MA, US) for a 10 mL variant
- started offering a preloaded variant, and
- rolled out a fill-finish service.²

Insuler's (Acton, MA, US) Omnipod[®] Insulin Management System (Figure 3a) was repurposed for the delivery of Amgen's Neulasta as the Onpro on-body injector (Figure 3b) which was launched in April 2017.³

Enable Injections (see this issue, Page 28) has announced various development agreements for its enFuse platform with partners such as CSL Behring (King of Prussia, PA, US) and UCB (Brussels, Belgium). A transfer system which can pump drug formulation from a vial into the wearable enFuse injector is in development.

(A)



(B)



Figure 3: Insulet's Omnipod® Insulin Management System (a) was repurposed for the delivery of Amgen's Neulasta as the Onpro on-body injector (b).

In March 2020, SHL Medical acquired Weibel CDS, whose LyCaJect patch injector can reconstitute lyophilised drugs *in situ*. We have seen various handheld injectors that can reconstitute, such as Ypsomed's LyoTwist platform, but it is unusual to see explicit support for lyophilised drugs in a wearable device. LyCaJect's drug delivery mechanism is purely mechanical (spring based) but electronic sensors monitor the injection and display progress.⁴

Ypsomed's YpsoDose is motor-driven and based on a standard 10 mL cartridge, which can be filled to lower volumes to support any injection up to and including 10 mL.

Subject (see this issue, Page 32) is developing a very small, prefilled, wearable injector that does not incorporate electromechanics. Instead, it is driven by salt-water osmosis which allows it to be compact and inexpensive. Subject is performance testing a moulded concept model of the device in order to demonstrate stability of the base technology.

Sensile Medical's micropump system is based on a reciprocating rotor and has been approved for delivering apomorphine to treat Parkinson's Disease.⁵ Sensile Medical, which was acquired by Gerresheimer in 2018, has been adapting the pump for various indications and drugs including under a strategic alliance with Sanofi and Alphabet subsidiary Verily Life Sciences (South San Francisco, CA, US), to develop and commercialise a connected insulin patch pump.⁶

In July 2020, Sorrel Medical (see this issue, Page 20) signed a partnership agreement with an undisclosed pharmaceutical company to further develop its pump system,⁷ and has opened a new cleanroom manufacturing site for the manufacture of hundreds of thousands of units per year.

Other companies that have publicly announced their wearable injector projects include Elcam Drug Delivery Devices, E3D (see this issue, Page 24), Phillips-Medisize (see this issue, Page 15), Becton Dickinson, Sonceboz, and CCBio (see this issue, Page 12).

PROGRESS ON INTERNATIONAL STANDARDS

ISO 11608-6 "Needle-based injection systems for medical use – Requirements and test methods – Part 6: On-body delivery systems" is still in development, currently in its enquiry phase. It is expected to:

- Define physical, functional, biological, electrical safety and software, and drug compatibility requirements

- Define test methods for adhesion of the injector to the body
- Give guidance on methods for measuring the dose profile
- Define methods for measuring needle or cannula displacement.

Meetings during most of 2020 have been postponed due to the covid-19 pandemic and the next meeting is unlikely to be held before March 2021.

A LOOK TO THE FUTURE OF WEARABLE INJECTORS

In our experience, all the pharmaceutical companies that are developing injectable drugs are considering wearable injectors in their device strategies. Anticipating this demand, all established injectable device manufacturers that we are aware of have at least one form of wearable injector in their portfolio. Additionally, there are many specialist wearable injector companies.

The use case and cost of wearable injectors mean that they are not likely to

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replace prefilled syringes and autoinjectors. Yet wearable injectors do allow self-administered delivery of some drugs that would otherwise require clinical support and/or admission to a medical facility.

The device concepts which push drug from standard pharmaceutical cartridges are likely to feature strongly in the future marketplace, primarily due to risk aversion by pharmaceutical companies. Alternative devices will have a bright future where they can demonstrate an advantage such as a smaller or more elegant form factor or better usability.

ABOUT THE COMPANY

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

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ABOUT THE AUTHOR

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



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