



Medicom

Innovation Partner

a Phillips-Medisize Company

FROM VIAL TO WEARABLE INJECTOR

While auto-injectors are often the delivery method of choice for patient self-administration, there are occasions when a vial and syringe format is required. However, this method has a number of drawbacks such as risks of user error, dose inaccuracies and several challenging user steps. To overcome this problem, Medicom has developed a flexible, wearable patch pump which can accept a simple glass vial and provide a fully automated injection system. Directors of Front-End Innovation at Medicom, Hans Jensen, MBA, and Kate Hudson-Farmer PhD, MBA, explain how it works.

Although the vial is a well-established primary container for the delivery of injectable drugs – and is usually the quickest route to market – it is not without its drawbacks. This is particularly true for self-administered subcutaneously delivered drugs, and even more so for self-administered drugs that require reconstitution prior to injection.

Trying to promote a drug in a vial and syringe format against competition from a liquid form with a disposable auto-injector is not an easy task. The number of user steps in preparing and administering a drug product from a vial can be prohibitive to launching a new drug product, even if the drug is safer, more efficient and proven to have fewer side effects.

Healthcare professionals will, of course, assess the drug profile (efficacy, safety) and peer recommendations, in addition to personal knowledge and preferences. However, a growing number will also look at the capability of their patients to self-administer the drug – the simplicity of administration being an important factor in choosing a prescription. The many years of success for the simple-to-use auto-injectors, associated with some of the world's best-selling drugs such as Humira and Enbrel, is testament to this.

Recent user research carried out by Medicom with immunology specialists

indicates that the majority clearly prefer to prescribe self-administered biologics to patients – primarily because patients do not need to go to a clinic for infusions or injections, but can administer them by themselves in line with their daily routines. The simplicity of the self-administration provided by auto-injectors is an important consideration, as making the task easier and less prone to medication errors is associated with safety, efficacy and patient adherence.

“Being able to manage the lifecycle of a drug utilising the same primary container is a significant bonus to a pharma company from both a time and cost perspective.”

THE CHALLENGE OF PATIENT SELF-ADMINISTRATION

Changing a drug into an auto-injector formulation, at least for the two drugs already mentioned, was not an overwhelming task despite some



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challenges, as the drugs were already approved in the pre-filled syringe used with the auto-injector. Being able to manage the lifecycle of a drug utilising the same primary container is a significant bonus to a pharma company from both a time and cost perspective.

But what if you have a drug product that has not progressed beyond the vial and you still want it to be provided in some form of self-injection system? And what if you do not want to go through all the time and cost associated with the regulatory aspects of changing the primary container?

Or what if the volume is too large for delivery by auto-injector?

If the drug is lyophilised, it has to be reconstituted, usually manually by injecting a diluent into the vial and then transferring it manually to a syringe, often involving changing the needle to a thinner one before subcutaneous injection. Here it may be inserted manually into an auto-injector if the volume is relatively low, say below 1.5 mL, or injected into a reservoir in a wearable self-injection system for higher volumes. This all assumes pretty much immediate use of the drug, so that the in-use time for the injection system drug contact interface, is short enough to ensure only limited additional stability validation studies are needed.

On top of these complexities a further complication comes from repeat use of the vial. A number of drugs are provided in vials that contain a larger volume of drug than required for a single individual dose. These vials may be placed in the fridge in between use and the drug extracted using a syringe each time a dose is required, but the mandatory routines to administer manually remain nonetheless.

MEDICOM'S FLEXIBLE WEARABLE PATCH PUMP

The key inherent problems with the above scenarios relate to the risks of user error regarding correct reconstitution, risks of resulting dose inaccuracies and finally a challenging number of user steps requiring extensive patient training (and retraining). Therefore Medicom decided to develop a solution to these problems which would provide a more convenient and safe alternative to conventional manual practice (Figure 1).

Medicom's flexible, wearable patch pump is designed to accept a simple glass vial and provide a fully automated subcutaneous injection system, without any need for reformulation and/or repackaging of the drug. It consists of a reusable electronic control module which combines with a disposable drug module containing all components with drug or patient contact. It is equipped with an integrated needle that automatically inserts prior to injection initiation and is covered after dismounting. Furthermore, it builds on standard syringe formats for the interior reservoir to leverage opportunities such as allowing existing diluent to be preinstalled in its disposable module.



Figure 1: Pump set up to initiate reconstitution (upper picture) and after removal of vial and ready to be mounted on body (lower picture).

The combination of this is a platform that achieves a number of benefits (Table 1).

Through employing its novel and optimised electromechanical drive system capable of accurately controlling the plunger movement in both directions, diluent can initially be mixed with the lyophilised drug and subsequently the reconstituted drug transferred back into the syringe ready for

injection. Depending on the specific drug properties, the user may be required to swirl the mixed substance manually as part of the reconstitution process and here the electronic pump module will help monitor and interpret or guide when sufficient physical agitation has been provided.

After visual control and confirmation, the pump will draw back the accurate

amount of drug ready for injection. Additionally, a novel drive system supports a compact form factor, not least from a length perspective, whilst still using standard syringe sizes of up to 5 mL or even 10 mL.

If faced with a drug already formulated into a stable liquid, the system naturally also allows such liquid in a vial to be

Benefit	Associated Attributes
Automated preparation and dosing of lyophilised drug in vial	<ul style="list-style-type: none"> • Reconstitution of the drug in the vial is performed automatically preferably with diluent in pre-mounted prefilled syringe • Pre-set dosing back into syringe, e.g. patient adjusted • Automated needle insertion following pump mount on skin and activation • Pre-programmed dosing duration, e.g. patient controlled
Automated single or multiple dosing from liquid in vial	<ul style="list-style-type: none"> • Transfer of the drug from vial to interior syringe and subsequent injection etc. • Pre-set dosing volumes either pulling one single or several individual doses from a vial
Reduced regulatory time, risk and cost	<ul style="list-style-type: none"> • Standard vial and syringe and commercially available vial adaptor etc. • Intelligently automating already approved manual preparation and administration processes • Final pump system based on platform adjusted to specific patient population and dosing volumes

Table 1: Key benefits associated with Medicom’s flexible, wearable patch pump.

Design Parameter	Device Details
Cost efficient	<ul style="list-style-type: none"> • Device consists of low-cost, disposable module and a higher-cost reusable electronic control module, allowing cost-efficient support of chronic diseases through reuse of expensive pump components • Low-cost disposable module contains all drug and patient contact components
Motor controlled electronic platform	<ul style="list-style-type: none"> • Bi-directional motorised plunger operation supports automated reconstitution process or simple withdrawal of drug product from a vial • Controlled and consistent injection speed and time (i.e. independent of temperature, viscosity, variability, inner needle dimension tolerances etc.) • Extended user interface opportunities (controls and feedback, e.g. audio, visual, tactile, user steps guidance etc.)
Wearable	<ul style="list-style-type: none"> • Pump attached to body using adhesive during injection, e.g. for extended injection procedures • Integrated needle with automated insertion and post-injection needle protection • System optimised for medium to large subcutaneous dose volumes (e.g. up to 10 mL) • Due to a novel plunger interface system, the device length is kept minimal even with a standard syringe installed
Connected health	<ul style="list-style-type: none"> • Interface to connected health systems from reusable module • Detection of critical process parameters (e.g. orientation, temperature, occlusion etc.) to monitor and assist use • Link to specific app or other interface to enable patient engagement, learning, training

Table 2: Attractive features and functionalities of Medicom’s flexible, wearable patch pump.

“Having a device that enables not only automated reconstitution of a drug, but also its transfer and injection administration, significantly benefits the user.”

applied – it does not have to reconstitute a drug. It also allows partial transfer of the drug into the device, e.g. supporting an administration setting where the patient needs to withdraw a number of individual doses from a vial over a number of days. A vial could therefore be attached and part of the drug transferred to the device ready for injection. The vial containing the remainder of the drug can be stored between uses and reattached for another administration. This provides a solution addressing user errors associated with manual drug transfer to devices, in addition to wastage issues.

Furthermore, if during lifecycle management the drug should be reformulated into a prefilled syringe presentation, the pump will still be supportive as the prefilled syringe can be installed in the disposable pump module. The patient will be able to benefit from the easy administration but is completely free from even the minor complexities of handling the vial as part of the injection preparation – simply mount and activate the pump.

The split reusable and disposable platform offers a wearable, low-risk and

low-cost approach with a wide range of flexible design opportunities to be optimised towards individual diseases and patient populations. These include the ability to optimise delivery of medium to larger volumes, adjust plunger speeds and dose volumes, supportive graphical user interfaces and safe needle handling etc. (Table 2).

APPLICATION OF CONNECTED HEALTH SERVICES

Apart from the advantages more directly related to drug preparation and delivery, a key aspect is the ability to add connected health features to the device. These could aid not only adherence monitoring, but longer-term patient engagement through the use of associated apps and other platforms that could assist with training, education and data transfer from and to the patient.

Services supporting self-administration with the device, such as reporting of symptoms and side effects, allow healthcare professionals to focus assistance and therapeutic intervention on patients who really need this.

CONCLUSION

Medicom’s flexible wearable patch pump provides a range of key benefits that differentiate it from a market perspective. Having a device that enables not only automated reconstitution of a drug, but also its transfer and injection administration, significantly benefits the user.

Simply attaching the vial to the device and allowing the device to perform reconstitution and transfer cuts out

the need for the user to engage with syringes, and particularly needles, and decreases the total number of user steps, as well as addressing potential reconstitution and transfer inaccuracies and risks. In addition, the fact that the vial remains the same and that standard components are used throughout the drug path – i.e. a prefilled syringe with water for injection – cuts down on both regulatory costs and time.

This makes Medicom’s pump ideal not only for an initial launch device but also for the initial lifecycle management update of an already marketed drug in a vial indicated for patient self-administration.

ABOUT THE COMPANY

Medicom Innovation Partner (a Phillips-Medisize Company) is a leading global innovation, development and low-volume production provider focused on drug delivery devices and connected health solutions. Medicom Innovation Partner was established as a technology venture of Bang & Olufsen A/S in 1989 and the company has been a dominant player within the drug device world for more than 25 years. Medicom holds a dedicated staff of more than 90 high-calibre innovation specialists, mechanical, hardware, software, quality assurance, regulatory and production engineers based in Struer, Denmark, and Cambridge, UK. Medicom has experienced considerable growth over the last five years.

As of May 31, 2016, Medicom became part of Phillips-Medisize Corporation. Phillips-Medisize is a leading global outsource provider of design and manufacturing services to the drug delivery and combination products, consumable diagnostics and medical device, and specialty commercial markets. The company has annual sales of over US\$700 million with 80% of the total revenue coming from drug delivery, medical device, primary pharmaceutical packaging and diagnostic products such as disposable insulin pens, glucose meters, specialty inhalation drug delivery devices, single-use surgical devices and consumable diagnostic components.

Together Phillips-Medisize and Medicom are becoming one of the leading players within the growing drug delivery device and connected health market.

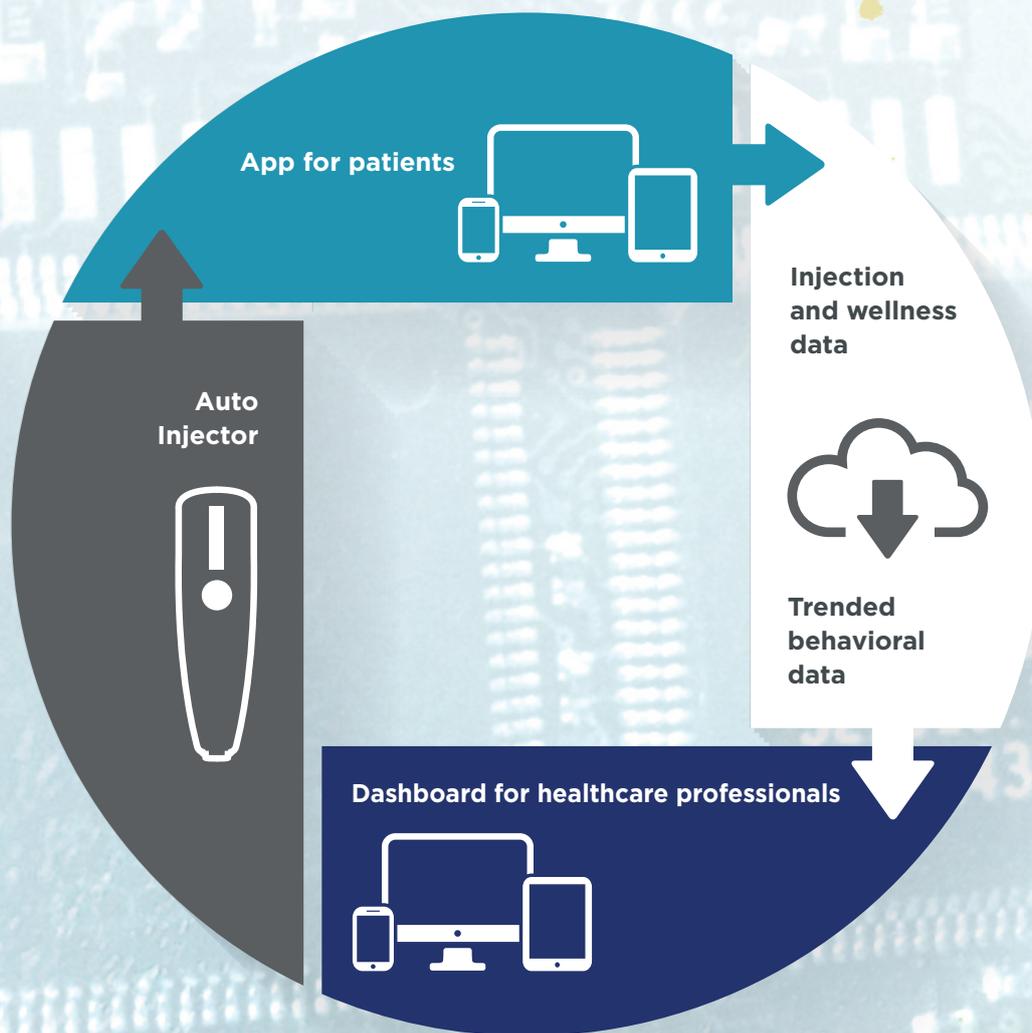
ABOUT THE AUTHORS

Hans J Jensen has been with Medicom Innovation Partner, a Phillips-Medisize company, since 1991, and is responsible for managing Medicom’s sales activities as well as managing front-end projects developing drug delivery device strategies and design concepts. He is an industry expert with more than 25 years of experience working with advanced electronic auto-injectors and connected health systems, wearable injectors and pharmaceutical markets and strategies.

Kate Hudson-Farmer is responsible for working with companies to develop drug delivery strategies and innovative solutions that improve patient outcomes and strengthen competitiveness. She has over 15 years’ experience and has worked extensively at the front-end of drug delivery, in addition to conducting numerous strategic, technology and commercial consulting assignments across the pharmaceutical and medical device industry. She has held senior consulting positions, in addition to business development roles for both industry and academia.

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