



Medicom

Innovation Partner

a Phillips-Medisize Company

FAST-TO-MARKET LARGE VOLUME INJECTOR FOR SELF-ADMINISTRATION

In response to a set of very specific device objectives, Bjørn Knud Andersen, MSc, Director, Front-End Innovation, Head of Technology Accelerators and IPR, and Bjarne Sørensen, BSc, ME, Director, Front-End Innovation, both of Medicom Innovation Partner, present an electronic, connected large-volume injector concept for self-administration as the ideal solution..

In supplement to the obvious everlasting need for developing safe and efficacious medicines, the ability to accompany these with patient-centric delivery devices and monitoring systems to support home-administration, plays an increasingly relevant role in securing therapeutic outcome and patient quality of life.

More than three decades ago, the first commercial insulin pens were introduced to the market¹ resulting in greater accuracy, adherence and quality of life for diabetics compared to the common procedure of manually injecting using a vial and syringe. Since then, patient self-injection systems have become much more widely adopted, for example, in auto-immune disorders, blood disorders² and even some specific cancer-related conditions.³ Most often, the delivery system consists of a preloaded, fixed single-dose disposable mechanical auto-injector, which provides a relatively easy solution for the isolated aspect of drug-delivery. However, in recent years, the range of solutions has diversified, i.e. in response to the need to support more complex drug preparation and/or administration procedures, which

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has drawn attention towards more flexible electronic delivery systems. With the focus on such higher-value re-usable devices, the possibilities for integrating additional therapy-specific patient services – such as injection reminding, site-rotation recommendation, injection adherence monitoring as well as patient-HCP communication tools – are radically expanding.

In contrast to some common general perceptions, these higher-value re-usable device solutions typically represent a lower cost per injection than the disposable mechanical drug delivery devices. This is simply because a re-usable device represents several years of use compared with one single injection. Thus, there exists an



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excellent opportunity for the pharmaceutical industry to assess its device strategies and evaluate its application of modern drug delivery technologies and connected health services to support patient self-administration and quality of life optimally, while satisfying healthcare providers' drive for efficacious and documented treatments.

Whilst the dominant enabling factor for the commercial uptake of insulin pens was associated with changing the primary packaging from a glass vial to a prefilled cartridge, similar transitions to self-administration for other therapies have been facilitated by the development of more convenient primary containers. For example a liquid drug in a vial could undergo repackaging to be presented in a prefilled syringe (e.g. for single dose delivery). More radically, a lyophilised drug in a vial could undergo repackaging to a dual-chamber syringe or reformulation to obtain a stable liquid version presented in a vial, prefilled syringe or cartridge.

Such ease-of-use improvements in primary containers are always attractive from a drug administration perspective. However, they are typically very costly and time consuming as well as being associated with inherent risk of failure. Risks might be minor for "simple" repackaging of liquids (when retaining similar materials) but they can be much steeper, particularly where clinical equivalence data may be

required i.e. reformulating a lyophilised drug to a liquid.

Furthermore, for therapies dependent on dosing in line with weight or body-surface area, there can be a conflict between carrying an expensive large number of stock-keeping units to match individual dosing needs accurately, or accepting excessive amounts of waste from disposing of partial doses. Therefore, when targeting patient self-administration solutions, an effective alternative to drug repackaging and/or reformulation will often be to implement intelligent and advanced delivery system automation of central user steps to accompany the existing primary packaging as a means to secure ease of use.

So drug preparation may include a range of challenges e.g. transferring viscous medicines from primary containers, reconstituting lyophilised medicines, individualised dose-settings, as well as handling larger doses potentially pooled together from several (e.g. differently sized), primary containers.

Moving onto the drug delivery situation, there are several aspects influencing practical implementation, in particular whether the administration route is subcutaneous, intravenous or intramuscular (or another route), and how the combination of administration route and dosing volume may favour a handheld concept, or potentially some kind of body-mounted device.

Medicom has partnered in several

development projects for medical injection systems based broadly on the array of both drug preparation and delivery features highlighted above. A number of these systems have already reached patients, either in terms of a full commercial launch or late-stage clinical trials.

In recent years the interest in larger volume delivery devices, for both subcutaneous and intravenous home administration, has become increasingly significant to Medicom's innovation and development focus. In response to this, Medicom is continuously strengthening its technology base to be able to implement and validate innovative concepts to address this market need quickly and efficiently with, for example, end-users and stakeholders.

The Medicom Technology Accelerators (see Figure 1) are key in providing mature building blocks, e.g. physical components, modules combined with relevant technical and regulatory expertise etc, to be combined into virtually any type of injection delivery system, thereby speeding up development execution timelines and mitigating technology and project risks.

DESIGN OBJECTIVES

The example discussed here provides a more detailed illustration of the turn-around opportunities with the Medicom Technology Accelerators, and although a few details are examples only, the complexities

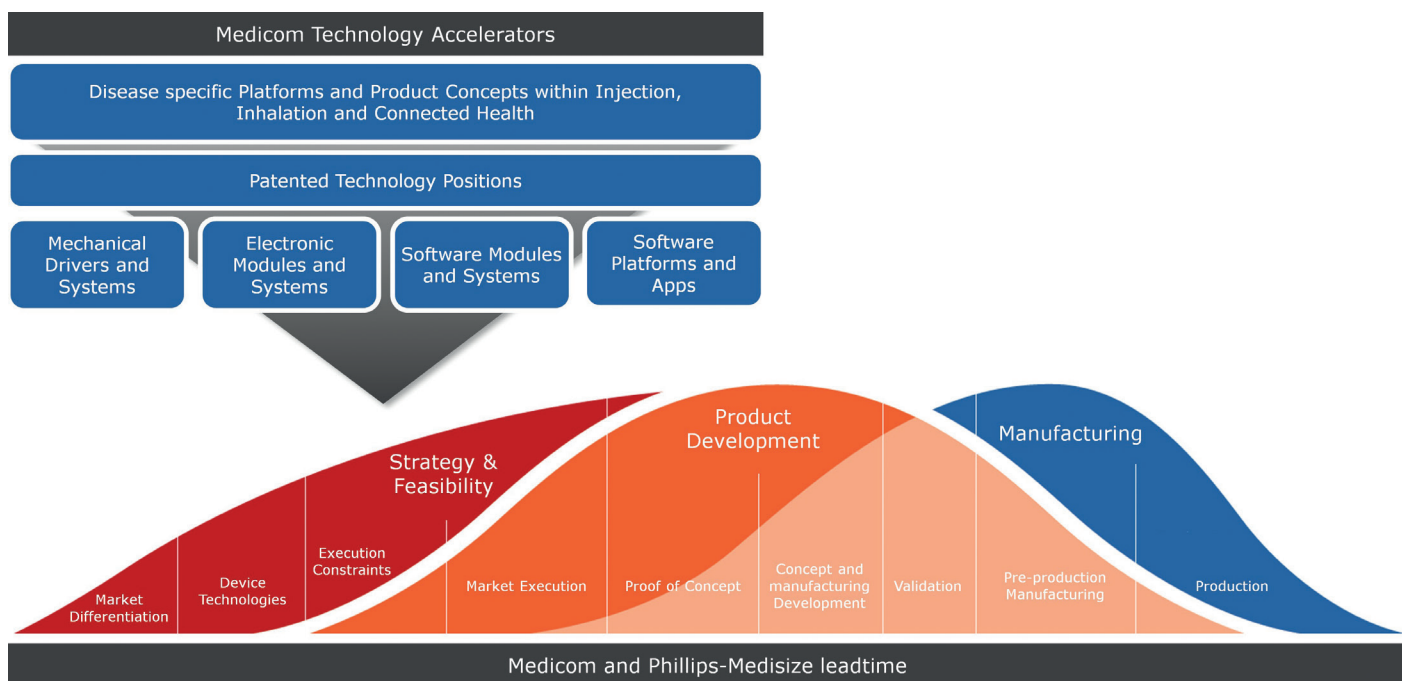


Figure 1: Medicom Technology Accelerators speed up and de-risk the development process.

“The device concept supporting all of the above requirements takes the shape of a re-usable miniature syringe pump equipped with a standard disposable subcutaneous infusion set.”

draw directly upon actual implementation challenges experienced across a range of past Medicom projects.

This example explores the automation opportunities associated with preparing and administering a large-volume, lyophilised drug provided in a glass vial together with a prefilled syringe containing diluent. The dose – typically 8-20 mL – is to be calculated based on the patient’s body weight, and doses are potentially combined from two vials of medicine. When reconstituted, the drug is to be injected subcutaneously over 15-30 minutes.

Since an automated device (for cost reasons, for example) is not envisioned for all markets, the existing primary packaging should remain fundamentally unchanged.

Moving the administration procedure to the home-setting, there exist clear opportunities for simplifying



Figure 3: Large volume injector interacting with drug vial.

the drug preparation procedure. Examples include adding automation assistance for drug reconstitution, as well as for accurate dosing preparation, this being of significant benefit to patient’s ease of use. For the reconstitution process, a motorised platform may provide automation of the mixing of drug powder and diluent, reconstitution and dose withdrawal simply based on mounting the prefilled syringe and vial connected by an inline vial adaptor. During withdrawal of the final dose, the device-user interface may actively guide the patient to hold the device upright (vial septum pointing down) as well as controlling it by integrated orientation sensing.

In relation to accurate dose preparation, the device may be equipped to provide an integrated dose calculation based on patient’s body weight. The patient could specify their weight in Kg instead of the dose in mL or, optionally, the device could have such a dose setting accessible only to the healthcare professional. The device would then automatically measure off the exact dose, based on patient weight, during withdrawal into the syringe prior to injection, and for doses combined from two vials, it will automatically guide the patient and control the amount pulled from each vial taking into account aspects of overflow and tolerances etc.

In the case of several different drug presentations, perhaps with varying dose sizes, then individual labelling of the vials combined with automatic vial detection may further guide the patient e.g. to select appropriate vials based on the required total dose. Labelling of vials could for example be done using a visual 2D barcode or colour marking, alternatively using radio frequency identification (RFID) or near-field communication (NFC) short-range wireless technologies.

LARGE-VOLUME INJECTOR

The device concept supporting all of the previously mentioned requirements takes the shape of a re-usable miniature syringe pump equipped with a standard



Figure 2: Industrial design example of a large volume injector.

disposable subcutaneous infusion set (see Figures 2 & 3). With this concept, the patient can initially prepare the device and dose while, for example, sitting at a desk or table, then connect and prime the infusion set and subsequently continue with injection either while still sitting at the desk or table or after having moved to a more comfortable location, a cosy armchair or a bed, all to their personal preference.

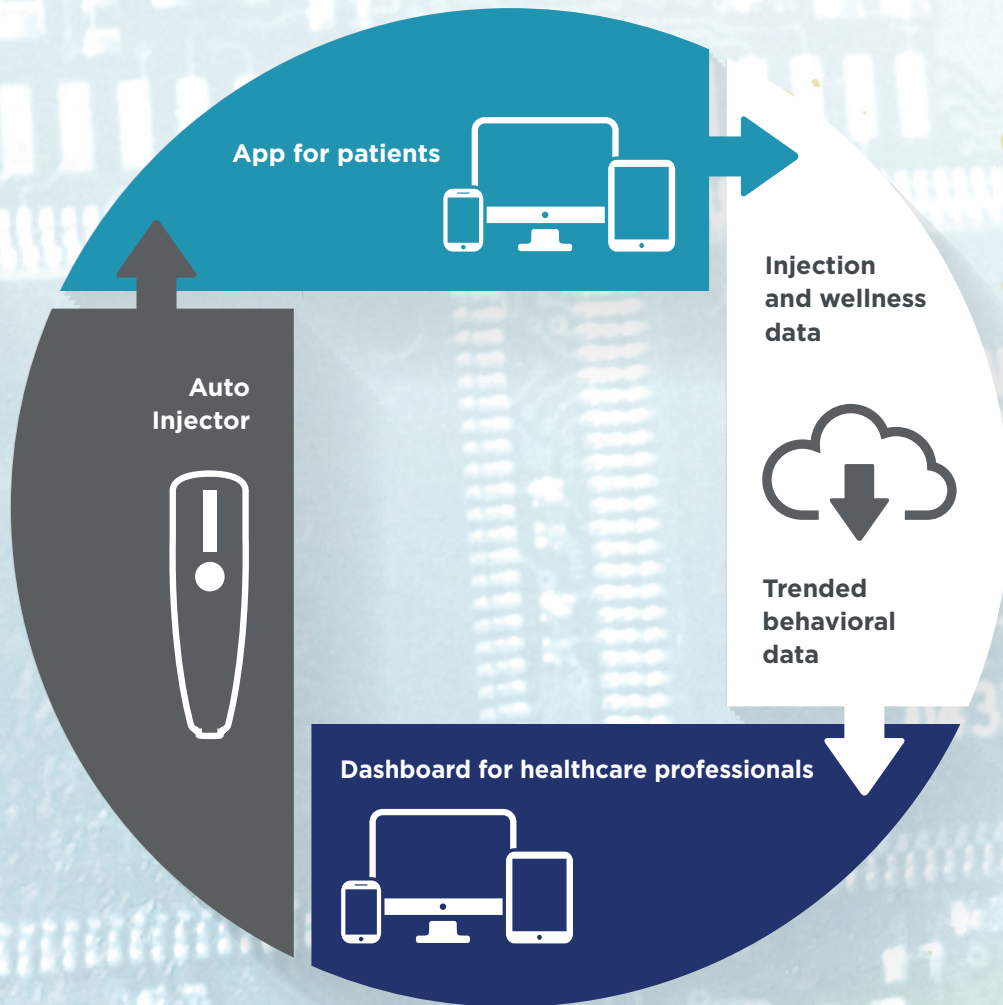
In addition to the drug delivery device aspects, the electronic device approach also enables connectivity options from the delivery device to a patient app and onwards to a secure cloud data structure capable of facilitating data sharing between the patient, healthcare provider and other relevant stakeholders. Beyond, adherence data etc, the mobile app is able to provide guidance and assistance including patient training, thereby helping to mitigate

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remaining risks such as those associated with non-compliance.

Such interactive services in correct and compliant use of self-administration with the device, and reporting of symptoms and side effects, allow a more focused effort for healthcare professionals, allowing additional assistance and therapeutic intervention to be focused on those patients who really need it. Thus, a connected health service approach directly supports patient empowerment and hence quality of life while at the same time ensuring that patients in need will never fall below the radar.

The ability to execute an initial lifecycle-management device extension in line with this example very rapidly often overrules any potential ambitions for a more compact patch pump with, for example, integrated needle handling, especially because such further advancements could be activated at a later point in time.

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CONCLUSIONS

Based on Medicom's Technology Accelerators and substantial experience, the speed of execution for the above exemplified device development could be reduced to 18-24 months, including the initial strategy and concept phase, additional detailed feasibility and development, validation

etc, and including a small-scale manual-validated production line. As needed, the establishment of a scaled-up full production-volume manufacturing line is an option to be activated anytime following design validation, for example in response to further expanding capacity requirements from additional markets and/or product therapeutic indications.

Automated drug delivery solutions remain key in driving therapeutic procedures out of the clinics and into patients' homes to the benefit of patients, healthcare professionals and payers.

Historically, practical examples have often been defined by the opportunities vested in primary packaging formats but pressure for faster lifecycle-management updates due to, for example, intensified competition may be incompatible with realities such as minimum reformulation and/or repackaging timelines. Instead, the approach of applying intelligent technology to automate otherwise manual user steps may bridge needs and thus provide a fast track to market with higher-valued, re-usable device solutions while realising a lower cost-per-dose compared with conventional and unconnected, mechanical delivery devices.

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 (a Molex company) 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.

The combined Phillips-Medisize and Medicom organisation is becoming one of the leading players within the growing drug delivery device and connected health market.

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