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PATIENT-CENTRIC REUSABLE INJECTED DELIVERY SOLUTIONS OFFER MULTIPLE BENEFITS

In this article, Bjørn Knud Andersen, Director, Front-End Innovation, and Head of Technology Accelerators and IPR, Phillips-Medisize, discusses the advantages of developing customised, reusable delivery devices in order to achieve patient-centricity.

Developments in consumer electronics and information technology are rapidly changing medical drug delivery. While manual delivery of self-administered injectables still predominates, the sector is now migrating toward more user-friendly, flexible solutions that better address patient and caregiver preferences and expectations.

Although manual delivery offers a high level of flexibility, it is often associated with being complicated and less intuitive, requiring more training for the caregiver and/or patient. In contrast, a conventional autoinjector can offer a much more intuitive injection process. However, this process is “locked” into the device structure and therefore cannot be altered without comprehensive design re-validation.

Finding a happy medium between these two options presents a challenge, not only for caregivers and patients, but perhaps most significantly for pharmaceutical companies. Too often, these companies struggle to solve the drug administration challenges of tomorrow and remain stuck with yesterday’s technology solutions. For example, many innovative injectable therapies require individualised dosages, based on factors such as body weight or surface area. With a conventional autoinjector, such individualised dosing would likely require keeping multiple units in stock to respond to variability in the target patient population, thus dramatically increasing associated development, manufacturing and inventory expenses.

In addition, while the well known pen-injector provides a good solution for managing diabetes, it does not necessarily guarantee secure operation in other therapies. For example, people with diabetes are generally highly trained and skilled in administering selected doses of insulin. However, the inherent risk of patient-related variation due to user error might critically affect results with another medicine that has a narrower therapeutic window.

ADVANTAGES OF CUSTOM- DEVELOPED DRUG DELIVERY DEVICES

Instead of remaining within the constraints of existing generic delivery platforms and struggling with patients and regulators to establish safety and efficacy within specific therapies, drug developers may be wise to consider a custom device approach. In Phillips-Medisize’s experience, custom device development provides enhanced value once patient needs move beyond the “press and fire” approach exemplified by a conventional mechanical autoinjector. More complex needs could include variable dose adjustment, lyophilised drug reconstitution or even features of dose reminding and other patient outcome measures possible when integrating with connected health services.

Developing device usability based on a patient-centric innovation process often leads to a system with significantly



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enhanced ease-of-use, where critical-to-therapy functions are deeply integrated into the device solution. Technically speaking, this naturally implies either advanced mechanical architectures or, more typically, leverage of electromechanical technology platforms customised for a specific drug preparation and its administration features, as well as user guidance and feedback.

Natural side effects of this approach include increased cost and pressure for reusability, in order to keep cost-per-injection reasonable. However, patients typically have strong preferences for the more user-friendly solutions offered by such devices and tend to embrace reusable devices from an environmental perspective. In addition, especially when frequent administration is required, there is a significant cost-per-injection incentive for companies and payers to pursue reusable devices (Figure 1).

Obviously, the price of a reusable electronic autoinjector varies with complexity and production volume. For example, assuming a price of approximately €150 (£134) results in a cost-per-injection below €1 over a four-year period of weekly administration. Products of this value constitute a market segment that includes a broad range of current biologic blockbusters.

REUSABLE PLATFORMS OFFER FLEXIBILITY

Custom device development is nothing new for bigger pharmaceutical companies servicing large therapeutic indications. Rather, it is a mandatory component of a competitive market strategy fuelled by sheer economies of scale, as well as by patient benefits. But the situation may differ substantially for smaller companies that service more specialised rare-disease indications with only few patients.

For such companies, even if applying a custom delivery device technology in a specialised segment potentially offers significant patient benefits, less competition typically means less imperative strategic incentives. Furthermore, a more specialised pharmaceutical company may often maintain a stricter focus on core drug-development disciplines and down-prioritise device technology and strategies. Relying on established technology suppliers to provide the necessary inspiration therefore often leads to single-use disposable autoinjectors as the device of choice.

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|------------------|---------|---------------------|---------|---------|
| Dosing Intervals | daily | 0,24 € | 0,16 € | 0,12 € |
| | 2 days | 0,48 € | 0,32 € | 0,24 € |
| | weekly | 1,7 € | 1,12 € | 0,84 € |
| | 14 days | 3,4 € | 2,2 € | 1,7 € |
| | monthly | 7,3 € | 4,9 € | 3,7 € |
| | | 2 years | 3 years | 4 years |
| | | Device Use Lifetime | | |

Figure 1: Device cost-per-injection examples with reusable drug delivery devices.

“Substituting weekly disposable autoinjectors with one reusable device will, over four years, reduce production quantity requirements by a factor of more than 200.”

In addition to being considered a nuisance to patients, a disposable device approach may carry critical consequences in terms of speed to market, thereby reducing company return on investment. For example, the time required to set up a high-volume manufacturing line, such as one that includes multi-cavity moulding tools and automated assembly stations, will be significant compared with production scaling for a reusable delivery device, due to the lower quantities of a reusable that will be needed. For instance, substituting weekly disposable autoinjectors with one reusable device will, over four years, reduce production quantity requirements by a factor of more than 200.

Obviously, the required development lead-time should also be considered. However, the reusable approach appears to offer advantages here as well. The application of software-controlled electromechanical systems allows for more design flexibility while fully respecting usability, risk and design robustness. Also, designs can be

divided into functional modules which intuitively lend themselves to support new delivery device designs through alternative combinations and therapy-specific, user-related optimisation, thus avoiding the need for a total redesign between projects.

This is the concept behind Phillips-Medisize’s Technology Accelerators, which enable extremely fast turn-around lead-time for innovation, feasibility and development processes, applying state-of-the-art technology solutions to produce optimised and individualised drug delivery device solutions. To illustrate this concept, the following example demonstrates alternative solutions to conventional mechanical autoinjectors.

PHILLIPS-MEDISIZE AUTOINJECTOR FOR PREFILLED SYRINGES

A mechanical autoinjector typically facilitates drug storage, administration and disposal. The administration is likely a straightforward “press and fire” handling

operation with simple acoustic signalling during injection. After use, the system is usually locked in a state where the needle is covered by a needle shield, which also clearly signals that the device has been used. In contrast, despite the potential benefits of reusable injection systems, they will not provide a pre-loaded dose of medicine. Instead, the patient must load the drug before administration and discard the used container afterward.

When injecting, patients will often be primarily concerned with possible pain, such as from the needlestick and drug contact, apart from speculation related to therapeutic effect and potential side effects. In Phillips-Medisize's experience with patients, adding a few minor user steps unrelated to those key concerns is typically completely acceptable. Therefore, loading and unloading a primary container is highly unlikely to pose an issue for the vast majority of patients offered a reusable autoinjector. Of course, it is important to simplify those specific user handling operations, as well as any other procedures, as much as possible.

A relevant example from the current Technology Accelerator portfolio applies a cassette concept to ensure easy loading and unloading, while providing full needle safety before and after the injection (Figure 2). The drug manufacturer installs the primary container, such as a 1 mL "long" prefilled syringe with a staked needle and needle cover, in the cassette. The cassette helps prevent needle stick injury after injection in addition to clearly signalling when it has been used by the

patient, similar to a mechanical autoinjector. However, the amount and cost of material is significantly reduced. Loading the cassette through the front provides a compact, safe, effective system with minimal user interaction.

In another device, the same injector platform is customised to support delivery from a "naked" prefilled syringe, such as the same 1 mL one with a staked needle or a standard 2.25 ml syringe with an external needle attachment. Since these approaches avoid changes around the primary container entirely, they can offer an even faster track forward in support of potential clinical trial programmes.

Regardless of conceptual direction and application, the electronic reusable autoinjector platform will manage all relevant syringe movement handling (needle insertion and retraction, programmable to desired insertion depth) and patient-controlled drug injection (injection rate, pausing, etc). The motorised architecture inherently supports higher plunger forces, up to and beyond 100 N, potentially enabling significantly reduced needle diameter. For example, whilst ensuring that the pharmacological properties of the medicine remain unchanged, the increased plunger force capabilities may be capable of supporting a needle gauge reduction from 27G to 31G, potentially reducing pain related to needlesticks.

The durable electronic devices also contain multiple sensors and connectivity features, making it easy to store and transmit data to external applications, such as a connected health service system,

further assisting patients, caregivers and healthcare professionals in improving therapeutic outcomes.

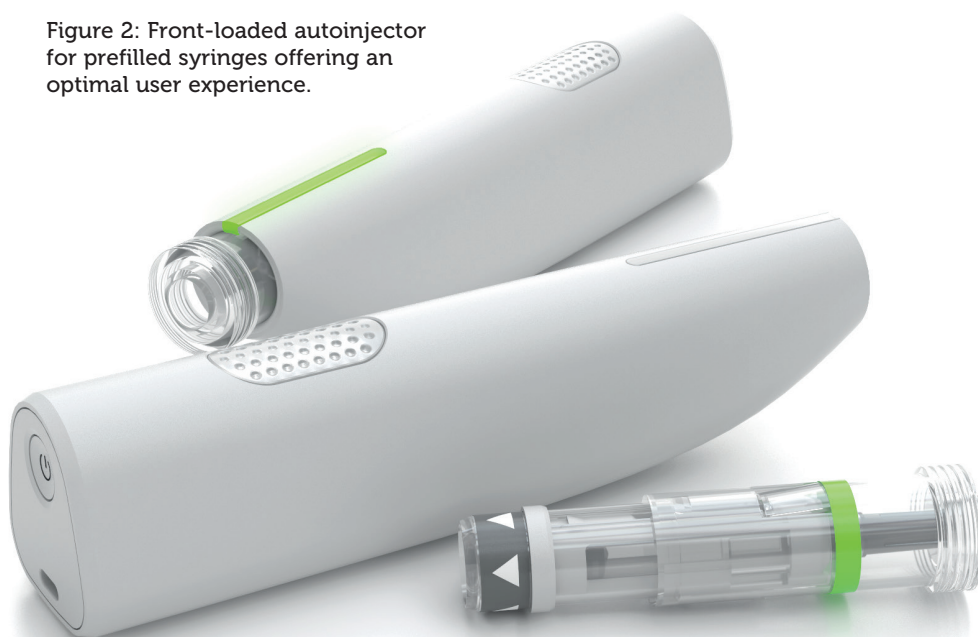
A PROMISING NEW OPPORTUNITY

Reusable electronic drug delivery devices have been around for many years, primarily in professional care segments. Historically, companies have had valid concerns about deploying such systems into patient self-administration settings. However, recent developments in electronics and information technology, along with emerging needs in the pharmaceutical industry, are driving change. Modern electronic reusable drug delivery systems offer a wealth of potential in terms of usability and flexibility, as well as tangible cost-per-dose reductions, making them an obvious choice for patient-centric injected drug delivery solutions in global pharmaceutical markets.

ABOUT THE COMPANY

Phillips-Medisize, LLC, a Molex company, is an end-to-end provider of innovation, development, manufacturing and post-launch services to the pharmaceutical, diagnostics, medical device and speciality commercial markets. Post-launch services include a connected health app and data services. Backed by the combined global resources of Molex and its parent company Koch Industries, Phillips-Medisize's core advantage is the knowledge of its people to integrate design, moulding, electronics and automation, providing innovative high-quality manufacturing solutions.

Figure 2: Front-loaded autoinjector for prefilled syringes offering an optimal user experience.



ABOUT THE AUTHOR

Bjørn Knud Andersen has been with Phillips-Medisize since 1997 and is part of the Front-end Innovation team responsible for innovation to translate pharmaceutical drug delivery needs into competitive patient-centric device solutions. As part of that role, he also heads activities related to developing the Phillips-Medisize Technology Accelerators. Mr Andersen is an industry expert with more than 20 years of experience within medical diagnostics, electronic drug delivery devices and connected health systems.

5 THINGS TO CONSIDER WHEN MANUFACTURING CONNECTED DRUG DELIVERY DEVICES

The estimated number of connected drug delivery devices continues to increase and the impact of this trend could be significant, explains Phillips-Medisize



While digital connectivity or connected health can improve the coordination and delivery of patient care, original equipment managers need to keep these five things in mind when creating connected drug delivery devices:

- 1 Development strategy and design consideration**
- 2 Situation analysis and patient compliance**
- 3 Connectivity ecosystem**
- 4 Wireless subsystem**
- 5 Security of device and information**

As the Internet of Things continues to become an integral part of people's lives, the opportunity to use it within drug delivery device applications remains promising. The manufacturers and device designers must identify, investigate and overcome these challenges so that the implementation of wireless and other related smart technologies can be achieved. When done successfully, connected systems enable the patient and caregivers to have a 360° view of both the patient and the disease – not only to manage adherence, but to improve results by understanding the effect of the regimen.