DRUG DELIVERY MEETS AUTOMOTIVE ENGINEERING

Here, Thomas Mayer, Business Development Manager, Sonceboz Medical, discusses Sonceboz's activity in the world of wearable injectors and how the company's experiences in the automotive industry and its in-house development of high-quality motors provide significant advantages for the design and production of wearable devices.

Whilst at a first glance the pharma and automotive sectors have nothing obvious in common, a more detailed look under the hood reveals quite important shared requirements and challenges, such as a rigorous need for quality, reliability and safety of supply. Failing drive elements in patch-pumps can potentially cause life-threatening situations, just as failing brake systems in cars can.

To further the comparison, in both cases designs need to be user-friendly such that patient or driver errors are prevented in the first place. One way of achieving this goal is to reduce user steps and enable intuitive interaction. In addition, both industries are governed by strong norms and regulations which must be obeyed in order to maintain market access and customer trust. Last but not least, in both pharma and automotive there is strong pressure for cost efficiency. One possible avenue towards this is found in highly integrated platform designs. By reducing parts whenever and wherever possible and by utilising proven, identical design elements for different use-case specific devices, one can reduce cost while still maintaining the highest level of quality.

As a leading provider in mechatronic systems, with over 25 years of experience in medical technology and having the top 10 car makers among its customer base, Sonceboz adds value to pharmaceutical companies by enabling them to cover a broad range of injection-based therapies while leveraging a true device platform architecture. For each and every device Sonceboz designs, whether a motor with gearbox or a large volume injector, it stringently follows design-for-manufacture and design-to-cost principles, ensuring Swiss quality at world-market prices. Each year over 70 million mechatronic systems are manufactured at the company's sites in Switzerland and shipped across the globe, working reliably in cars, trucks, and dialysis machines alike.

A PLATFORM APPROACH FOR BIOLOGICS

Today's pharmaceutical landscape is characterised by an increasing number of biologic drugs being introduced into the marketplace.[1,2] These often come with challenges not only regarding the fill and finish, but also administration to the most important stakeholder – the patient. High viscosity formulations for subcutaneous administration can be difficult to inject using traditional tools, such as prefilled syringes.[3] In turn, formulations designed to mitigate increasing viscosities by diluting the same molecule payload over a higher volume of drug provide challenges as well – especially

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when using rapidly injecting delivery systems such as autoinjectors where the typical volume limit is 2.25 mL. This is mostly because of injection pain and discomfort due to either the compression caused by the injected volume or the drug's own characteristics.

Furthermore, ever increasing healthcare expenditures are a strong driver to at-home self-injection of medications previously administered in-clinic or at a doctor's office. Wearable systems enable the patient to inject the drug slowly and comfortably in a controlled fashion, thereby providing increased personal freedom and quality of life. Sonceboz's large volume injector (LVI), displayed in Figure 1 is designed to hold a prefilled and preloaded 6 mL glass cartridge with the ability to facilitate both bolus injection and complex delivery profiles that have been programmed into the device.

With biologics – often stored in a lyophilised form to enhance long-term stability – it is even more challenging for patients to carry out the complex steps required when preparing the drug for injection. The manual reconstitution of lyophilised drugs requires substantial training and care in order to avoid user errors, such as potential contamination of the drug product[4] or incomplete mixing of the drug powder and its diluent. By creating a device which automatically reconstitutes from prefilled and preloaded containers, such as a vial and a glass cartridge, prior to placement on the body, one clearly reduces the risk for user error and enhances safety and simplicity.

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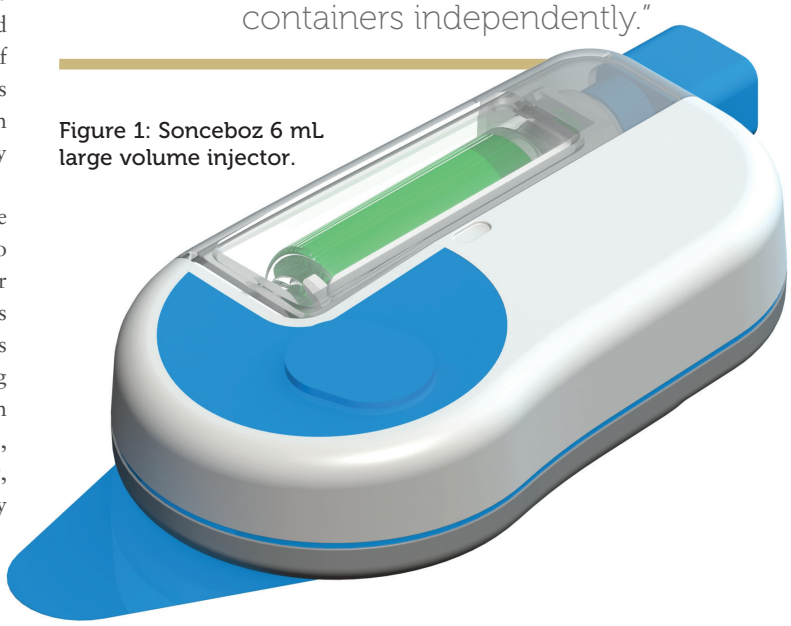

Figure 1: Sonceboz 6 mL large volume injector.

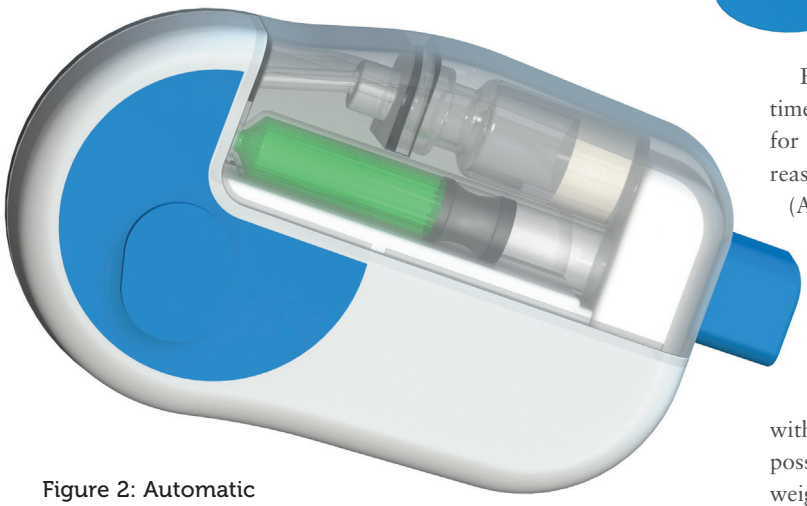

Figure 2: Automatic reconstitution injector.

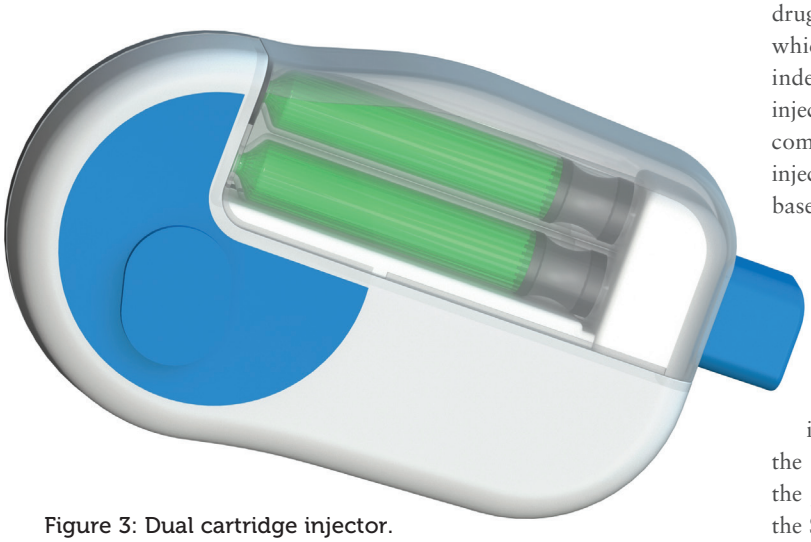

Figure 3: Dual cartridge injector.

Furthermore, such technology enables pharma to achieve a faster time-to-market, due to avoidance of lengthy stability studies with, for example, novel drug containers or liquid formulations. For this reason, Sonceboz is working on an automatic reconstitution injector (ARI), which is designed to make drug reconstitution easy, and therefore safe, for a broad spectrum of patients (Figure 2).

Also, recent trends in combining multiple biologic drugs, so called drug-combination therapies, are becoming increasingly important – especially in immuno-oncology.[5] Although today these drugs are often injected intravenously in a hospital setting, novel formulation options and better tolerability in combination with modern devices could make subcutaneous administration possible. In addition, personalised medicine with individual and weight-based dosing and drug combination is becoming more prominently discussed in literature.[6]

By utilising a small piston pump to apply a vacuum to the drugs' primary containers, Sonceboz is able to provide a device which is able to pump from two primary drug containers independently. This technology is called a dual cartridge injector (DCI) and will empower patients to administer complex combination therapies in their own home by conveniently injecting two drugs sequentially in a bolus or programmed fashion based on their individual needs. Also, this technology can be helpful when an injection site needs to be prepared using hyaluronidase in cases where a co-formulation of the enzyme and the drug aren't possible or such is undesirable for other reasons. Last but not least, a wearable device holding two containers can be an asset if a drug is already approved on the market in, for example, 3 mL cartridges and a new indication or lifecycle management update requires doubling the drug volume (Figure 3). In such cases, one could keep using the proven container and its filling equipment and place them into the Sonceboz DCI.

HUMAN FACTORS, STANDARD CONTAINERS AND A MOLECULE-FRIENDLY PUMP

The unique pump architecture allows for omnidirectional flow of the pumped liquid depending on the programmed parameters, for example from vial to cartridge or from cartridge to cartridge. The pump is made of three different parts:

- a pump piston
- a valve piston
- a pump cylinder.

The valve piston has the function of selecting one of the three ports to enable pumping from one port and injecting from the other. Simply put, it creates a vacuum in the primary drug containers and is thereby actively drawing the liquid in a non-turbulent and gentle fashion, like filling and emptying a syringe. This is of particular importance when considering drug integrity with sensitive large molecule biologics. First data suggests the compatibility of this pump design with large molecule drugs. Test results with TNFα monoclonal antibodies revealed both molecule integrity as well as activity – showing no signs of shear damage. In addition, our material selection and manufacturing processes are designed to be compatible with biologic drugs.

The independent pump plungers are driven using proprietary low-noise slimline-stepper motors, which are placed directly on the circuit board in a solderless fashion, helping to reduce cost and potential weak points of the system. Patients prefer devices which seamlessly integrate into their daily routine, which is why low-noise emission is as important as a compact footprint. Due to the flat shape of the motors, the device thickness can be kept low.

Using closed-loop controlled motors enables load monitoring and helps achieve extraordinary flow accuracy of about ±2%. Since Sonceboz is in the advantageous position of manufacturing its own quality motors (200,000 per day in case of the slimline-stepper), it is not required to build its platform around low-cost motors, often running at high revolutions per minute, contributing to noise (Figure 4).

The common brain of all the platform devices is found in the smart electronics on the circuit board, which helps patients in receiving their required dose of medication the way they need it. From bolus injection to patient-specific profiles, many different dosing regimens are possible thanks to a dedicated microprocessor. For data transfer and user feedback, Sonceboz integrated a Bluetooth Low-Energy chip on the board designed for digital health applications.

In order to enhance patient comfort and help prevent needlestick injuries, the dynamic needle-insertion system (DNIS) uses a solid needle in combination with a soft-cannula made from PTFE. Once the device is triggered by the user and satisfactory skin contact is established, the DNIS releases the needle and directly retracts leaving behind only the soft-cannula.

In order to minimise the burden of validating novel types of drug containers, Sonceboz focused on designing its device around existing and proven containers, such as glass cartridges of different sizes. In general, it was able to adapt its drug container interface to the container a pharma company intended to use. The only requirement is that the device needs to be able to actively draw liquid from the container using vacuum. If required, the platform integrates containers in a prefilled and preassembled fashion, which is important in avoiding potential user errors during drug handling, insertion and filling. In collaboration with its partners, Sonceboz will provide an assembly process that seamlessly integrates into current fill-finish infrastructure.

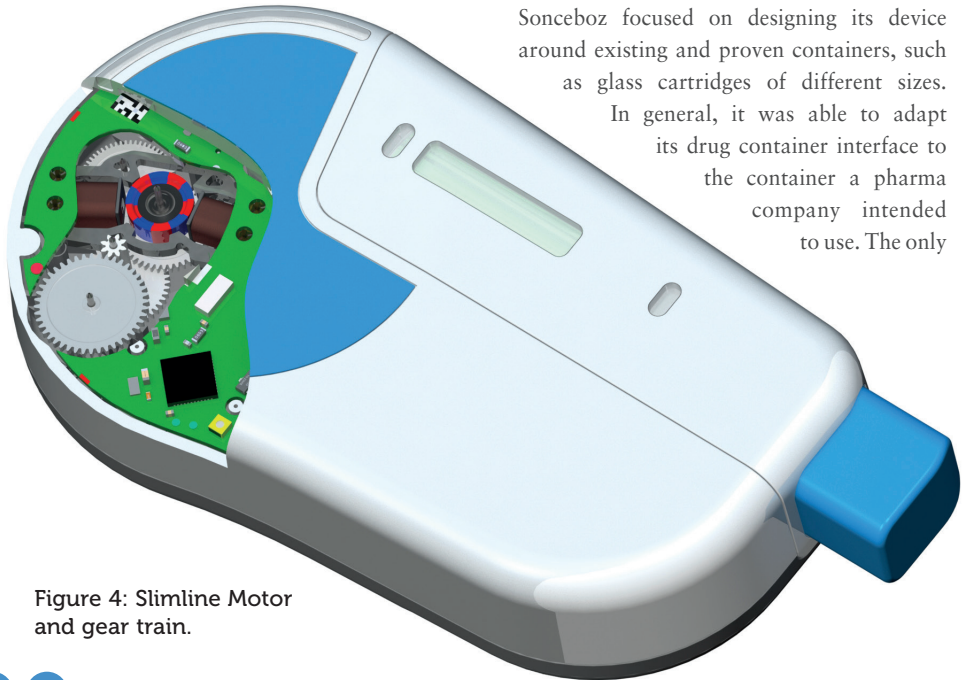

Figure 4: Slimline Motor and gear train.

> "From the very beginning, the platform was designed with user friendliness in mind, which means that user steps should be intuitive and reduced wherever possible."

From the very beginning, the platform was designed with user friendliness in mind, which means that user steps should be intuitive and reduced wherever possible. This is one of the main drivers to enable a prefilled and preassembled device configuration. Also, size, weight and feedback are important to achieve patient acceptance. In order to have a platform which can be adapted to different use-cases, Sonceboz decided to design for one of the most challenging applications – self-injection in rheumatoid arthritis (RA). Patients suffering from RA often have difficulties with dexterity and extreme pain in their joints.[7] The design is continuously tested and iterated upon with patients suffering from RA by performing formative studies. The use steps for the device are:

- Take the device out of the package
- Activate the patch-pump by pushing the activation button inwards
- Remove the adhesive tape
- Place the device on the skin
- Start the injection by pushing the inject button on the top of the device (see Figure 5).

SUMMARY

Sonceboz is working on a wearable device platform aimed to cover the most challenging applications for large volume self-injection systems, with the intention of empowering patients in self-injection

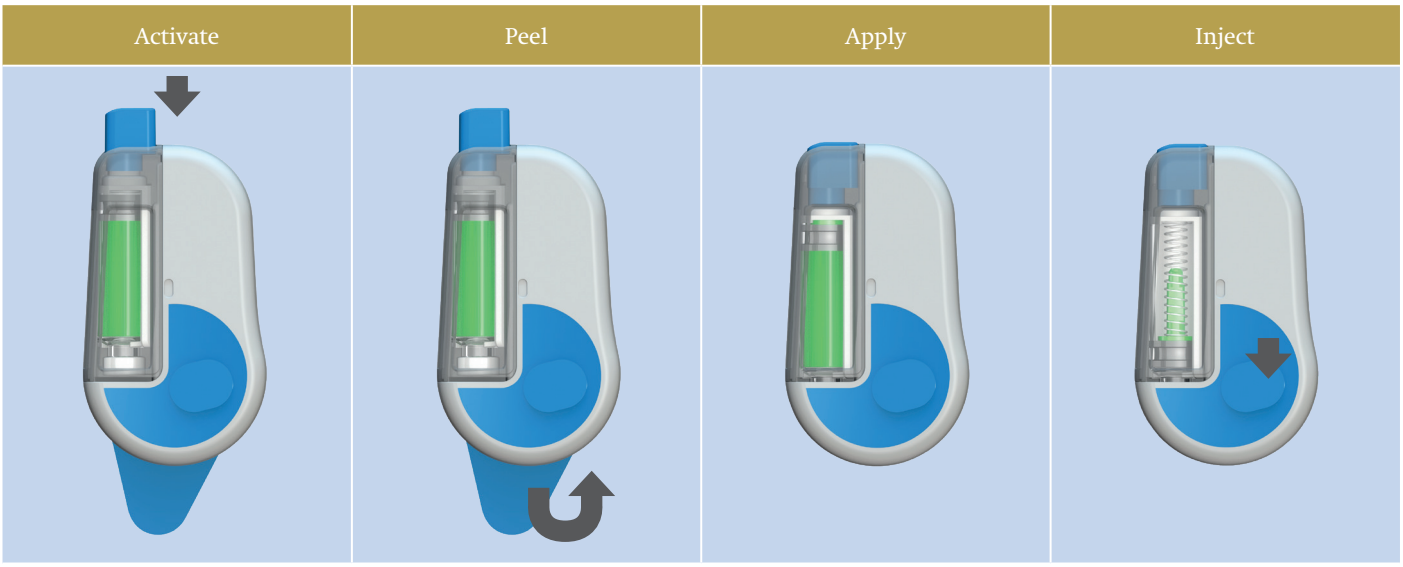

Figure 5: User steps to injection.

applications that weren't possible before. Figure 6 illustrates the Sonceboz platform architecture with its different device arms and the associated stakeholders influencing and contributing to the design.

Sonceboz differentiates itself by its versatile platform built around a piston pump which provides omnidirectional, highly precise flow and connects multiple containers at once. This technology allows for novel device designs such the DCI and ARI. Thanks to a programmable microcontroller, Sonceboz offers a device platform that truly adapts to a drug's intended therapy profile. There is also the option to have a prefilled/preloaded device design without the need to change to a special container type, shape or material, which substantially reduces time to market, risk and ultimately cost. By using proven high-quality components and leveraging high-volume automotive production, Sonceboz provides the highly integrated, cost efficient and low noise drug delivery devices of tomorrow.

Figure 6: Sonceboz device platform architecture.

ABOUT THE COMPANY

Sonceboz's core competencies consist of design, development and production of mechatronic drive systems. Since 1936, the company's focus has been on innovation, and best-in-class quality and service, which is key to success for worldwide OEM customers. Sonceboz is ISO 13485 certified and active in wearable drug delivery, medical devices and laboratory industry.

Pharma companies looking for large volume injectors for high viscosity drugs, dual cartridge or auto-reconstitution injectors will find interesting solutions in Sonceboz's new drug delivery device platform. Customised technology modules like motor-drives, electronics, pumps and needle insertion systems are available for medical device manufacturers.

Sonceboz's activity in medical devices is based on a long experience in automotive where top quality, reliability and cost effectiveness is key.

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ABOUT THE AUTHOR

Thomas Mayer is responsible for Business Development at Sonceboz Medical. Prior joining Sonceboz in 2016, Mr Mayer held various management positions at Boston Scientific's cardiac rhythm management division. His first interactions with the pharmaceutical industry came early during his apprenticeship at Uhlmann Pac-Systeme in Laupheim, Germany. Mr Mayer holds a Diploma degree in Medical Engineering from Furtwangen University (Germany) and an MBA with honours from FOM University in Munich.

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We provide the platform for tomorrow's wearable injection devices. With a Swiss quality spirit, we engineer and manufacture your cost-effective patient centric solutions for:

- Reliable precision dosing
- High viscosities and volumes
- Safe drug combination therapies and automatic reconstitution

LARGE VOLUME INJECTION

DUAL CARTRIDGE INJECTION

AUTOMATIC RECONSTITUTION INJECTION