NEW ENGINE FOR PRIMARY CONTAINER INJECTORS: A POWERFUL MICRO LINEAR ACTUATOR

In this article, Brian Li, PhD, Chief Executive Officer, Jiunn-Ru Lai, PhD Associate Professor, Tsung-Chieh Cheng, PhD, Professor, Kuang-Hsiang Cheng, Mechanical Engineer, Min-Ru Wang, Manufacturing Lead, Chia-Chi Tina Feng, Director of Business Development and Wen-Chi Huang, Specialist, all at MicroMED, introduce the company's new engine for primary container injectors, the Primary Actuator, which targets the unmet needs in the autoinjector and wearable injector market as the market shifts towards large injection volumes.

TREND OF CURRENT INJECTOR DEVICES

These days, product development for self-injectable devices is shifting towards large injection volumes. For example, the 2.25 mL autoinjector is one of the epicentres in recent market competition for cutting-edge drug delivery product development, along with many other creative products[1,2,3] under development. The other well-known biologics delivery product, the wearable injector,[4,5,6] is also moving towards large injection volumes such as 10–20 mL, or even more. Due to this new drug volume shift, the design of the primary containers used within the injectors also needs to be changed accordingly. For example, the prefilled syringe is moving from the ISO standard 1 mL to 2.25 mL, and the prefilled cartridge is moving from ISO 3 mL to 5, 10 and 20 mL. Stiction between the plunger of these large-volume glass containers is one of the key elements to maintain drug sterility, however, many engineering challenges, such as varying injection speed and risk of drug contamination, are associated with this larger container design and more complicated material interactions.

CHALLENGES IN LARGE-VOLUME INJECTION TECHNOLOGIES

Self-administration drug delivery products are limited in driving mechanism options, with springs and motors the most commonly used technologies. Within these driving technologies, spring offers large force and low cost, but comes with problems of varying flow rate (due to decrease of the spring force along with its relaxation) and high storage load (requiring more robust device housing structure making the device much bigger); motor, on the other hand, is usually quite noisy and with a limited driving force.[7] To improve device performance, many innovative driving mechanisms have been invented. Volute spring, compressed gas and linear motors are examples of the mechanisms used internally within those large-volume drug-injection devices mentioned above. These state-of-the-art delivery power sources (or "engines") offer quite large driving force, making it possible to drive large-volume, high-viscosity biologic medication fluids. However, drawbacks such as a bulky footprint and heavier weight still exist with these end products; the use of these engines as the system driving core lowers the convenience and usability of the injector systems for patient and healthcare professionals.

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THE ENGINE

MicroMED has recently developed a novel microlinear actuator, the Primary Actuator (Figure 1), targeting the unmet needs for the current autoinjector and wearable injector market. The device is specifically designed to

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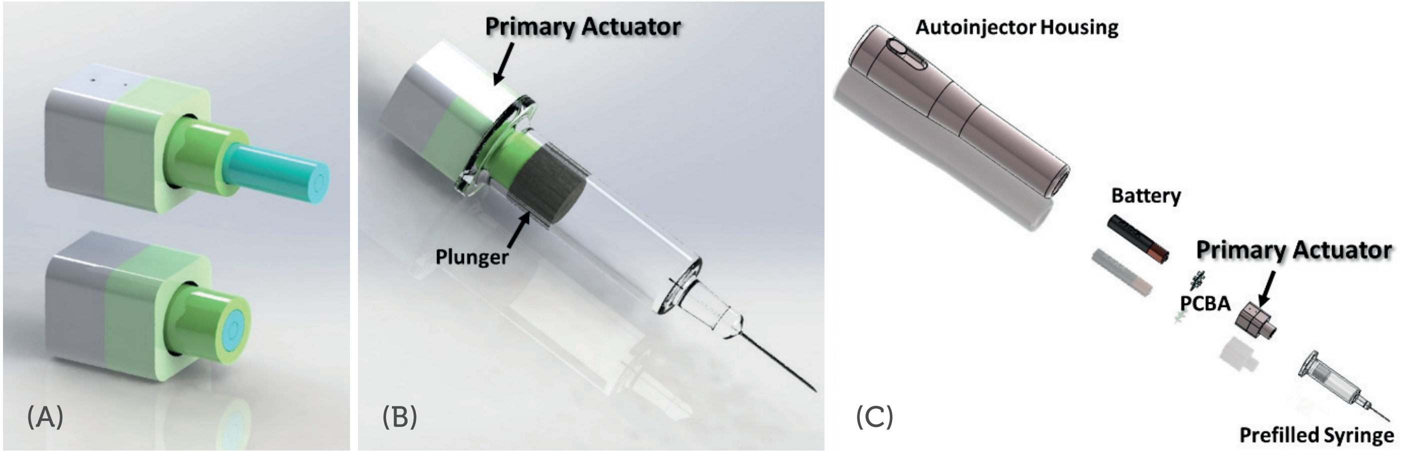
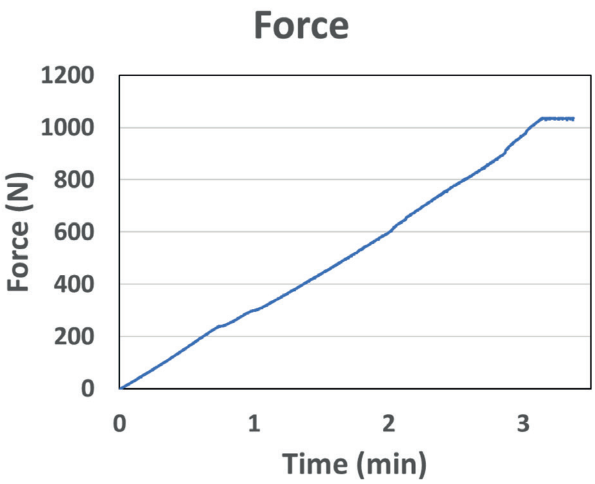


Figure 1: Device 3D photos showing: (a) working principle for the Primary Actuator, (b) an actuator assembled into the space behind the plunger of a prefilled syringe and (c) a simple modulisation design of the actuator with other autoinjector components.

drive primary containers, such as a prefilled syringe or cartridge. This small micro-electromechanical systems (MEMS) engine (22 mm in length, a small but powerful MEMS microchip and micro-integrated control circuitry inside) can provide the injection force/speed for the most challenging specifications required by high-viscosity, large-volume biologics injections. The real-time force output of MicroMED's actuator was measured using a load cell force sensor (Figure 2). The peak driving force exceeded 1,000 N at around three minutes (the data saturated at around 1,000 N due to the measurement limit of the sensor). The actuator can easily achieve higher force if required, but the 1,000 N force measured already surpasses most of the current driving technologies (springs or motors) by more than 10 times.

Figure 2: Real-time force output measured by a force sensor. The data saturated at around 1,000 N due to the measurement limit for the sensor, not the limit of the actuator.



MicroMED has also introduced a 2.25 mL prefilled syringe with 28 cP simulated fluid through a 26G needle with injection time of about nine seconds. Figure 3 shows this testing result measured by a commercial flow sensor. The flow rate was stable throughout the whole injection process and the injection volume increased steadily, demonstrating excellent delivery control of the primary drug container. The total capacity needed from the battery was about 5 mAh. This means a small lithium battery would be able to drive the microactuator, which also helps to lower the overall drug delivery device footprint (with this MEMS actuator as the core engine), making it superior to many current injection driving technologies such

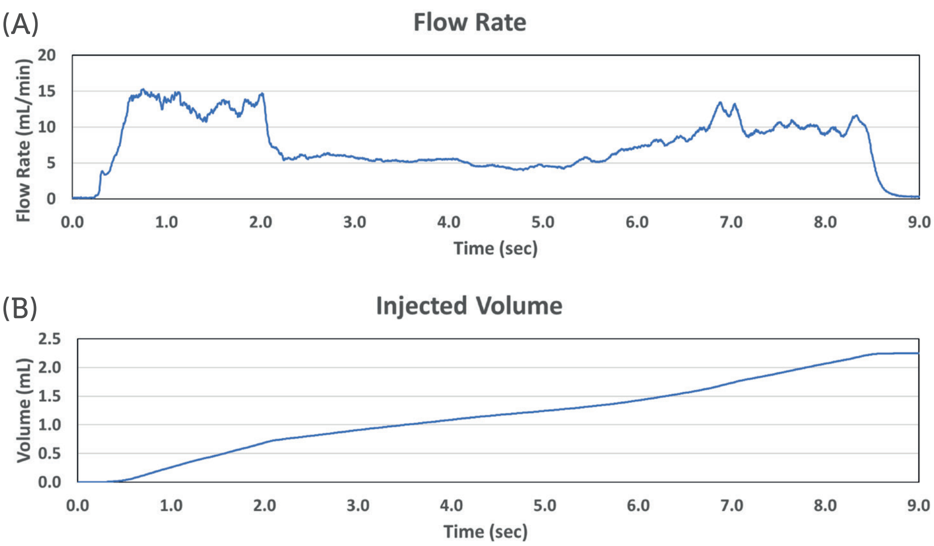


Figure 3: The injection performance (a: flow rate and b: injected volume) of the MicroMED Primary Actuator using a 2.25 mL prefilled syringe with 26G needle and 28 cP viscosity simulated fluid.

> "The Primary Actuator is an innovative, small, low-cost engine solution for the application of large-volume, high-viscosity medication injection. This engine technology is well suited to address the growing needs for the subcutaneous protein drug therapies."

as spring, compressed gas and motor (see Table 1 for the performance comparison and Table 2 for the specifications of MicroMED's engine product).

The Primary Actuator is an innovative, small, low-cost engine solution for the application of large-volume, high-viscosity medication injection. This engine technology is well suited to address the growing needs for the subcutaneous protein drug therapies. The Primary Actuator has demonstrated its capability as a smart solution for drug delivery that will benefit all stakeholders in the subcutaneous injection market. A successful partnership between the strategic collaborators and MicroMED will enable this engine technology to be developed into a superb commercial injector product meeting the true needs for today's large-volume biotech injectables.

Large-Volume Engine Mechanism	Spring	Compressed Gas	Micro-Motor	Primary Actuator
Maximum Driving Force	**	**	*	***
Storage Load	*	**	***	***
Varying Injection Speed	*	**	**	***
Device Size	*	*	*	***
Leakage of Gas	***	*	***	***
Drug Contamination	***	*	***	***
Noise	**	***	*	***
Modular Design	**	**	***	***
Connectivity Integration	*	*	***	***
Cost	***	**	*	**

Table 1: Comparison of the current driving technologies for the large-volume primary container injectors. Performance scale: *** Excellent, ** Good, * Normal.

Model #		PA-1W	PA-6W
Input Voltage (VDC)		3.0	3.0
Input Power (W)		1	6*
Max Load (N)		200	1200
Max speed (mL/min)**		1.5 mL/min	9 mL/min
Stroke (mm)		35	35
Ingress Rating		IP67	IP67
Weight (g)		15	20
Dimension	**Body**	12 x 12 x 22 mm	15 x 15 x 25 mm
	Shaft	25 (L) x 9.5 (D) mm	25 (L) x 9 (D) mm

Table 2: Product specifications for the MicroMED Primary Actuator: (a) 1W model and (b) 6W model.

* Customisation engine with up to 24W is also available.
** The speeds were measured using a 2.25 mL prefilled syringe with 1 cP of saline and 30G needle.

ABOUT THE COMPANY

MicroMED is a MEMS microchip design house specialising in the development of microinjection devices targeting unmet needs in the most challenging drug delivery applications. MicroMED has established a proprietary high-precision MEMS drug delivery engine system, capable of delivering broad flow rate from 1 nL/min to 10 mL/min (eight orders of magnitude) with driving force up to 2,000 atm (29,000 psi) of pressure. MicroMED welcomes all types of business connections/relations in the PDA drug delivery value chain (pharma, biotech, medical injector developer and insurance payer) with the goals below (but not limited to):

- Purchasing of the current micro-engine products
- Co-development of advanced injector products
- Licensing of the micro-engine proprietaries/intellectual properties.

MicroMED has established a strong and experienced supply chain for the development of injection devices from raw material suppliers, semiconductor foundries and component providers to contract manufacturers in both the US and Taiwan. These valuable partners have required regulatory certifications and years of experience in supporting medical device design and manufacturing. MicroMED applies its quality management system, providing the necessary structure and controls to help its value-chain supplier team develop products that meet defined safety and performance requirements for high-value drug delivery customers.

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ABOUT THE AUTHORS

Brian Li, PhD, Chief Executive Officer at MicroMED, has over 18 years of experience in both business and engineering development with medical device and drug delivery start-ups in ophthalmology and biotechnology in both the US and Taiwan. Dr Li has co-led fundraising activities and M&A deal negotiations resulting in successfully closed deals with leading pharmaceutical/biotech firms. Dr Li has 30+ technical articles and 40+ granted patents worldwide in biomedical microdevices. His research in ophthalmic implantable micropump was awarded Best Paper at a major MEMs conference.

Jiunn-Ru Lai, PhD, leads the microcircuitry development in MicroMED. Dr Lai is an Associate Professor with the Department of Electrical Engineering at National Kaohsiung University of Science and Technology, Taiwan. Dr Lai received the Best Paper awards from the Taiwan Academic Network Conference in 2016 and 2018. His research interests include embedded system, mobile and wireless networking, internet of things and network protocol performance analysis.

Tsung-Chieh Cheng, PhD, leads the MEMS microchip production in MicroMED. Dr Cheng is a Professor with the Department of Mechanical Engineering at National Kaohsiung University of Science and Technology, Taiwan, and has over 25 years of experience in the field of MEMS manufacturing, heat and mass flow, and material characteristics. Dr Cheng has published more than 130 technical papers and 12 patents worldwide in MEMS and materials science.

Kuang-Hsiang Cheng is a mechanical engineer and leads the medical device product design in MicroMED. His work involves early-stage research and development for design and manufacturing. Mr Cheng specialises in 3D modelling and is an expert in product development for medical device microcomponents. He graduated with a Bachelor's degree in mechanical engineering from National Yunlin University of Science and Technology, Taiwan.

Min-Ru Wang leads the production team in MicroMED. She has over 12 years of experience in drug-development research in a hospital research centre, collaborating with physicians in cell culture, molecular biotechnology and animal experiment in fundamental medical sciences. Ms Wang has a Bachelor's degree in food and nutrition from Providence University, Taiwan.

Chia-Chi Tina Feng has over 10 years of experience in business development and financial management in the US and Taiwan. In her business management career, she served as financial manager and sales specialist in multiple industries: medical device, furniture, automobile and hotel. Ms Feng received her MBA degree from the University of California, Riverside, US.

Wen-Chi Huang is responsible for the project management of the product development in MicroMED. She has over four years of experience in high-end tea branding and sales activities in the tea production industry and has a Bachelor's degree in economics from the National Central University, a top-ranking business school in Taiwan.