



BEYOND CONNECTIVITY: ENABLE & FLEX ANNOUNCE THE ENABLE SMART DEVICE

In this article, Matthew J Huddleston, Vice-President, Research & Development, Enable Injections, and Angela Wright, Vice-President, Strategic Partnerships & Business Development, Digital Health, Flex, talk about their collaboration to integrate Bluetooth connectivity into Enable's latest Smart On-Body Delivery Device. The authors go on to describe how the partnership has also been expanded to encompass Flex's Digital Health Platform, the world's first medical-regulated, HIPAA-compliant, open architecture platform of regulated connected medical devices.

Macro trends are driving fundamental shifts in healthcare: the renewed focus on achieving the Triple Aim¹ through technology; the growth of the aging population versus the clinical infrastructure and supply of available clinicians is shifting the preferred site of care to the home; the proliferation of connected devices that are transmitting a wealth of data are enabling telehealth and remote care; and, in the near future, machine learning and predictive algorithms will be capable of generating real-time, personalised insights from collected data that will ultimately enable automated clinical decision making and drive behaviour adoption.

Today's dynamic healthcare technology landscape and connected devices are driving device OEMs and pharma companies to think about their business models differently, expanding beyond traditional device development and "the pill" to a world where smart medical devices enable real-world insights and the delivery of personalised patient experiences. For medical device technology and pharma companies, the evolution of connected devices and digital health will ultimately unlock opportunities for more direct patient engagement and improved drug adherence, while also providing insights with the potential to reduce both clinical trial costs and time-

to-market for new drugs. Smart medical devices encourage transparency and accurate information sharing between patients and their physicians, ultimately driving targeted diagnosis and effective personalised remote monitoring. All these efforts are leading to improving health outcomes and maintaining patient independence effectively, while lowering the overall cost of care.

ENABLE-ING DEVICE CONNECTIVITY

Through the use of the latest sensing and connectivity technologies, traditional mechanical drug delivery devices are being transformed into smart, connected devices.

Enable Injections has developed injection devices that enable patients to self-administer high-volume/ high-viscosity drugs, enabling and promoting patient freedom and mobility (see Boxed Text "The Enable On-Body Delivery Device" on Page 24). "Our commitment is clear – continue to develop products designed to provide the user with a safe, simple, and discreet drug delivery experience," says Mike Hooven, President and Chief Executive of Enable Injections.

Flex is the *Sketch-to-Scale*TM solutions provider that designs and builds *Intelligent Products for a Connected World*TM. Three years ago, Enable Injections



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“In our commitment to further differentiate ourselves through innovation, we’re excited to announce the development of our connected healthcare platform – The Enable Smart Device.”

and Flex partnered to develop Enable’s customised wearable injection technology. Flex and Enable Injections collaborated to develop scalable, high-volume manufacturing solutions for Enable’s core technology and have expanded that partnership to develop Enable’s next generation of devices. “In our commitment to further differentiate ourselves through innovation, we’re excited to announce the development of our connected healthcare platform – The Enable Smart Device,” says Jeannie Joughin, Vice-President of Corporate Development.

Following the strategy of designing simple systems for maximum effectiveness with minimal interaction, Enable Injections developed a smart device system to provide



Figure 1: The Enable Smart Device with the button cover in place (top) and the button cover removed showing the chip (bottom).

three key pieces of information about the operation of the drug delivery system:

1. When the device is powered on
2. When the device has started dose delivery
3. When the delivery has been completed.

“The user interaction is simple. The user opens the Enable app on their phone and the Enable Smart Device will do the rest. There are no additional steps to use the device,” Joughin explains. The core features of the Enable Smart Device (see Figure 1) include:

- Small board footprint – the entire electronics package fits inside the existing button and is less than 3/8-inch (9.5 mm) in diameter. This allows for easy removal of the electronics (button) for electronic disposal and recyclability.
- Coin-cell battery – a simple, well known power source for a long operating- and shelf-life. The battery is isolated from the electronics via the safety strip until the time of use. Removal of the safety strip by the patient activates the circuit.
- Embedded microprocessor-based system for low energy and small footprint.
- Position sensing system (IR emitter/receiver combination) to detect the location of the button within the Enable Injector to allow for state position.
- Bluetooth low power transmission for low power consumption taking advantage of the prevalence of cell phone proximity to the user.

In 2015, it was estimated that 69% of the population in advanced countries own a smartphone.² To leverage this existing platform, Enable Injections felt utilisation of Bluetooth communications was the most efficient and effective means of providing data to the user, and selected Bluetooth Low Energy (BLE) as the optimal system to integrate into this product.

BLE is a newer version of the Bluetooth specification, introduced in Bluetooth v4.0, and has seen wide adoption in applications such as wearable fitness sensors. BLE is designed for low power, low cost applications that require lower data throughput rates than traditional Bluetooth connections such as audio streaming or hands free phone connections. There are two major types of connections defined in the Bluetooth standard: standard (bonded) mode and

broadcast (also known as “beacon”) mode. In standard or bonded connections, a host (smartphone with installed app) creates a saved connection with a peripheral (e.g. a drug delivery device).

In this scenario, through the pairing process, both the host and the peripheral share data to create a permanent connection that allows sharing between only one host and one peripheral. This method has the advantage of a secure connection allowing the exchange of encrypted information that cannot be decoded without the encryption key. However, a major disadvantage to this method is that the pairing process can be cumbersome, requiring user interaction as well as increased power consumption from the peripheral, as both the receive and transmit radios require power for communication.

In broadcast mode (also called a “beacon”), the peripheral sends out data at regular intervals that can be read by any nearby host. In this scenario, the peripheral only broadcasts data; data is never received. There are several advantages to this mode:

- Only the transmit radio on the peripheral device is powered, minimising power consumption.
- As the device does not need to listen for data from the host device, further power savings are achieved through lower power, sleep mode, waking up only when new data needs to be broadcast.
- Additionally, as the device is a transmit-only mode, the hardware can never be hijacked or loaded with malicious software. This eliminates the risk of unauthorised remote control of the device.
- The software is loaded onto the device in the factory, preventing unauthorised alteration once deployed.

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While it is possible that other Bluetooth-enabled devices could listen to the broadcast from the Enable Smart Device, without the proper application installed, the data would simply consist of an unusable list of binary numbers, lacking any text or other readable identifiers. Because of this, the lack of an encrypted connection does not expose any sensitive user information. The data will also never contain any identifying patient information – such as names or identification

numbers – which could be associated with a specific individual, thus allowing full compliance with the US Health Insurance Portability and Accountability Act (HIPAA).

An important attribute of the connected healthcare implementation within the Enable system is that

it doesn't affect the essential performance functions of the drug delivery device. The electronic feature of the device only reports the status of the device and in no way alters the mechanical drug delivery function. Even in the event of a critical failure of the Bluetooth components, such as the battery, the device will complete the delivery of the drug and provide the user with visual feedback as to the device status.

Utilising the BLE broadcast mode and through a tiny electronic chip in the button of the device, Enable Injections can deliver real-time device performance information in a small, low cost, convenient package.

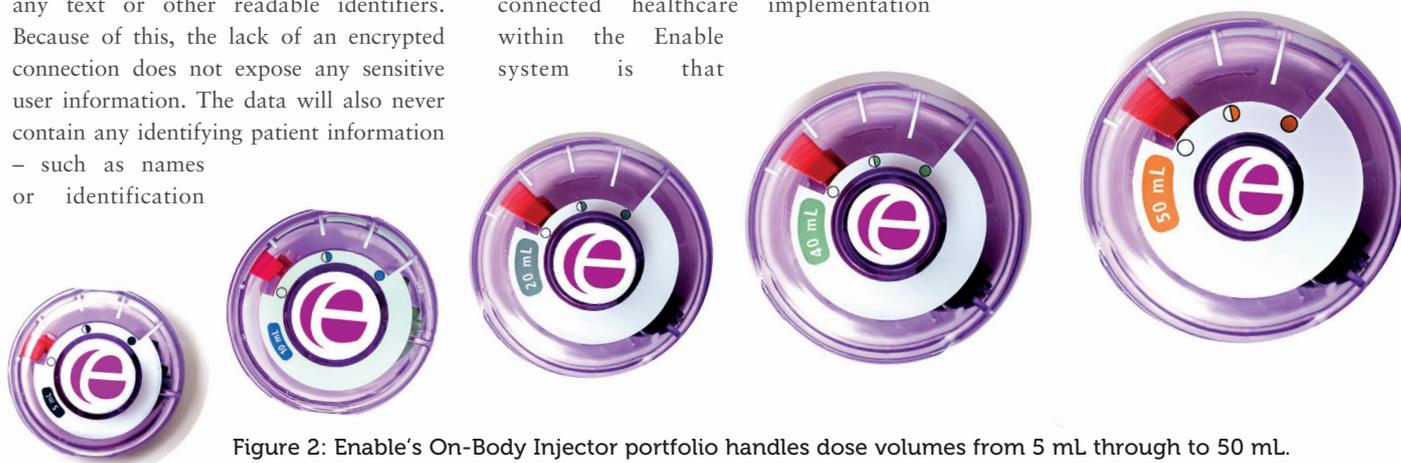


Figure 2: Enable's On-Body Injector portfolio handles dose volumes from 5 mL through to 50 mL.

THE ENABLE ON-BODY DELIVERY DEVICE

The right balance between dose volume, viscosity and in particular delivery duration is becoming increasingly important to pharmaceutical and biotechnology companies for SC injection therapies.

Enable Injections' wearable high volume injectors (see Figure 2) are capable of delivering higher volume – 5 mL, 10 mL, 20 mL, 30 mL, 40 mL, and 50 mL all available – at a desired flow rate over periods suitable for a particular product, minimising pain and delivering product in a predictable manner.

The injector design is based on over 12 years of research in minimising injection pain with numerous human factors studies conducted. The Enable Injector incorporates a unique pause function that allows the user to pause the injection at any time.

The Enable injector and transfer system are customised to the specific product characteristics. By using three different transfer platforms, which utilise established primary containers (syringe and vial), the advantages to the product manufacturer include cost savings and shorter time to market.

Minimising user error is an engineering and design challenge for wearable injector developers. Today's most advanced injector minimises any confusion by requiring only a few simple steps for patients – the “3 P's” of Enable Injections are:

- Place the injector onto the skin
- Pull the safety tab
- Press one button.

Enable Injections provides the smallest profile, wearable device for large volume product delivery, and is ready to partner with the biopharmaceutical industry to enable and empower patients requiring chronic administration of lifesaving or life enhancing therapies.

Updated from the article, “Pharma Company Innovation & Lifecycle Management: Delivery Devices as the New Key to Product Success” by Jeannie Joughin, which appeared in ONdrugDelivery Magazine, Issue 70 (Sep 2016), pp 34-37.

EXPANDED PARTNERSHIP FOR REGULATED DATA PLATFORM

To progress along the full healthcare continuum, medical device and pharma companies need capabilities that extend well beyond adding connectivity to a device, requiring a digital health software stack that is “medical grade” to support clinical use cases, diagnosis and treatment, as well as data privacy and security. Maintaining scalability and flexibility for such a solution requires ongoing monitoring and maintenance, including preventing security threats. The functional components of such a solution would, at minimum, require user management and preference, patient and physician engagement and patient and medication data management. A home-grown, siloed solution like this can be cost-prohibitive to build and maintain, and could take over two years to implement.

Flex has a unique view of the world, being on the leading edge of technology development in virtually every industry, and having evolved from a long tradition of high-tech/electronics hardware design and manufacturing. “Given our engagements on the xmedical device side, we quickly recognised the need for our partners to harness their new data sources and convert these into insights. Our partners leverage these insights not only to drive positive behaviour adoption, but also to fully understand the value of their products,” says Kal Patel, Senior Vice-President of Digital Health at Flex.

Flex recently introduced Digital Health solutions to its portfolio of products and services, offering the world’s first medical-regulated, HIPAA-compliant, open architecture platform of connected medical devices tied to a complementary, cloud-based software stack for commercialisation and scale (see this issue, Page 60, for more details). The Flex Digital Health Platform as a Service captures medication adherence data and relays bioinformatics data, enabling the conversion of raw data into actionable insights to enable clinical decision making, accelerate patient health engagement, and drive better health outcomes.

Enable Injections and Flex are expanding their collaboration to include

the Flex Digital Health platform. Enable’s Smart Device will be pre-integrated to connect to the Flex Digital Health ecosystem, offering Enable’s pharma partners the ability to integrate with this open platform easily to gain immediate access to patient data across multiple devices, gaining more direct engagement with patients to drive adherence, while avoiding the high upfront development and ongoing maintenance costs.

“Enable Injections is excited to expand our partnership with Flex to leverage this added capability, offering our pharma partners a solution beyond device connectivity, with the ability to plug into this ecosystem,” Hoooven commented.

CONCLUSION/SUMMARY

Building on their existing three-year collaboration, Enable Injections and Flex are developing The Enable Smart Device, integrating Bluetooth Low Power communication and IR sensing into Enable’s On-Body Injector in order to provide three pieces of information about the system: when it’s powered on; when it starts delivery; and when it completes delivery.

The integrated electronics are small, fitting inside the button of the device, and low cost; communication is broadcast-only and thus saves power and is wholly secure and HIPAA compliant. User interaction with the smart system is simple and intuitive – the patient simply opens an app on their phone and the device does the rest. The patient just uses the device to deliver their medication exactly as normal.

Building on their existing three-year collaboration, Enable Injections and Flex are developing The Enable Smart Device, integrating Bluetooth Low Power communication and IR sensing into Enable’s On-Body Injector in order to provide three key pieces of information: when the device is powered on; when drug delivery begins; and when delivery is complete.

The integrated electronics are small, fitting inside the button of the device. Communication is enabled by low cost broadcast, providing secure, HIPAA-compliant data transmission and minimising device energy usage. User interaction with the smart system is simple and intuitive – the patient simply opens an app on their phone then uses the device to deliver medication

as normal. The data transmission is automatic.

Beyond device connectivity, the Enable Smart Device is pre-integrated into Flex’s Digital Health Platform, the world’s first medical-regulated, HIPAA-compliant, open architecture platform of connected medical devices, giving Enable’s pharma partners the ability to integrate with this open platform easily to gain immediate access to patient data across multiple devices, gaining more direct engagement with patients to drive adherence, while avoiding the high upfront development and ongoing maintenance costs.

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ABOUT THE COMPANIES

Enable Injections is a late stage start-up company that has developed a disposable wearable injector to deliver high-volume, high-viscosity drug biological products (up to 50 mL) to the subcutaneous tissue. The system utilises standard container closures (syringes or vials) and can automatically mix solutions or solubilise lyophilised product. Founded by medical device veterans the company has R&D, operations and manufacturing facilities in Cincinnati, OH, US.

Flex is the *Sketch-to-Scale™* solutions provider that designs and builds *Intelligent Products for a Connected World™*. With approximately 200,000 professionals across 30 countries, Flex provides innovative design, engineering, manufacturing, real-time supply chain insight and logistics services to companies of all sizes in various industries and end-markets. Flex partners with a broad spectrum of healthcare OEMs to provide complete solutions that make its customers more competitive in the areas of medical devices, drug delivery, diagnostics and medical equipment.

ABOUT THE AUTHORS & CONTRIBUTORS

Matthew J Huddleston serves as Vice-President, Research and Development and Feasibility for Enable Injections. He is an experienced medical device professional with over 20 years' experience in start-up environments with emphasis in project management, design, development, manufacturing, regulatory and intellectual property. He has several issued and pending patents in the medical device field including soft tissue and cardiovascular fixation devices and delivery instruments, histologic automated embedding systems, laparoscopic visualisation devices, and automatic injection devices. He is a professional engineer and a licensed patent agent. Mr Huddleston holds a Bachelor of Science in Mechanical Engineering from Purdue University (West Lafayette, IN, US) and a Master of Science in Biomedical Engineering from The Ohio State University (Columbus, OH, US).

Angela Wright, Vice-President of Strategic Partnerships & Business Development for Digital Health at Flex, is responsible for developing strategic partnerships for Digital Health solutions and driving new business growth.

With more than 11 years at Flex, Ms Wright has deep expertise working closely and strategically with a range of customers across every industry including healthcare, enterprise infrastructure and consumer technologies. She has led several strategic initiatives whereby leveraging Flex's range of cross industry capabilities and global solutions delivered Flex customers with creative and innovative solutions to drive competitive value. Upon joining Flex in 2006, Wright was focused on one of Flex's top five largest accounts. She drove collaboration across 30 sites globally, supporting 15 product lines driving US\$2 billion in business annually. As Vice-President of Business Development and Innovation for the account, she led innovation and business expansion delivering value aligning with customer growth initiatives. Angela holds a Bachelor of Business Administration in Business Management and a Master of Business Administration degree with a concentration in Entrepreneurship from St Edward's University (Austin, TX, US).

Jeannie Joughin, PhD, Vice-President of Corporate Development at Enable Injections, is responsible for business development, strategic alliances, alliance management, marketing and clinical activities. She previously held various scientific positions including Senior Research Scientist, Post-Doctorate and Senior Post-Doctorate positions in Australia at The Alfred Hospital, The Walter & Eliza Hall Institute, as well as internationally in Austria (University Clinic, Innsbruck) and Switzerland (Ludwig Institute for Cancer Research, Lausanne). Dr Joughin began her career in the pharmaceutical industry in 1992 as a Clinical Research Manager with Bristol-Myers Squibb.

After successfully completing several marketing roles in the National Stroke Foundation, MediMark International and Mayne Pharma, Dr Joughin joined CSL Biotherapies in 2005 as Director, Pharmaceuticals Marketing and In-licensing. She assumed responsibility for a portfolio of pharmaceutical products from several licensing partners in various therapeutic areas. As Vice-President, Business Development at CSL Behring, Joughin was responsible for managing business licensing arrangements and relationships. This involved close liaison with CSL Behring's Commercial Development Team in the US, Germany and Switzerland.

Mike Hooven, President & Chief Executive Officer, Enable Injections, has more than 30 years of experience in the medical device industry in a broad variety of technical and clinical areas. He is the founder of five medical device companies and holds over 100 issued and pending US patents.

Mr Hooven is the founder, and a director of AtriCure, Inc (Nasdaq ATRC), a medical device company that manufactures and sells surgical devices to treat the most serious forms of atrial fibrillation. AtriCure has grown rapidly to become the market leader, with over 200,000 procedures performed. AtriCure completed a successful IPO in 2005. He previously held positions as the Chairman and CEO of AtriCure, and the Founder and Chairman of Enable Medical, a surgical device manufacturer that was acquired by AtriCure in August of 2005. Hooven founded Enable in 1994 and, prior to that, he headed up all internal product development at Ethicon Endo-Surgery from 1988 to 1994. He held engineering positions at Siemens/Pacesetter from 1986 to 1988, and at Cordis Corporation from 1981 to 1986. He earned a BS in Physics and an MSc in Mechanical Engineering from the University of Michigan (Ann Arbor, MI, US).

Dr Kal Patel, Senior Vice-President of Digital Health at Flex, has held a variety of leadership roles across biopharma, healthcare delivery and digital health. Prior to joining Flex, he served as Chief Commercial Officer at Doctor on Demand (San Francisco, CA, US), a leading video telemedicine provider, where he was responsible for all business and commercial functions, including marketing, business development, partnerships, implementations, operations and account management. Prior to Doctor on Demand, Dr Patel founded and led Amgen Digital Health, with responsibility for setting and executing a strategy focused on incubating and commercialising a portfolio of digital health products and programs that supported Amgen's drugs. Previously, he held leadership positions at Novartis and The Boston Consulting Group. Patel has a Bachelor's degree in Economics from the University of Chicago (Chicago, IL, US), an MBA from its Booth Graduate School of Business, and an MD from its Pritzker School of Medicine.



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