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ONdrugDelivery Issue N° 128, December 13th, 2021

CONNECTING DRUG DELIVERY

This edition is one in the ONdrugDelivery series of publications. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field.

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ONdrugDelivery is published by
Frederick Furness Publishing Ltd
The Candlemakers, West Street, Lewes
East Sussex, BN7 2NZ, United Kingdom
T: +44 1273 47 28 28

Registered in England: Company No 8348388
ISSN 2049-145X print / ISSN 2049-1468 pdf

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TOWARDS A NEW STANDARD OF CARE WITH APTAR PHARMA'S DIGITAL HEALTH

In this article, Adam Shain, Director, Business Development Digital Healthcare, at Aptar Pharma, discusses how Aptar is building on the progress made in connected drug delivery devices to help realise their full potential by developing an open, end-to-end platform that will enable healthcare stakeholders to take a holistic view of the full drug delivery journey.

The development of drug delivery devices suitable for patient self-administration was a critical step in improving the standard of care worldwide. Instead of needing to visit a hospital or clinic to receive an injectable medication or take a slow-acting pill, now patients can often administer their own therapeutics from the comforts of home.

However, this innovation represents but a single step, as early versions of drug delivery devices offered patients no insight into whether they had used them correctly or taken the right dose. To meet this need, the market for patient support tools has evolved over time, bringing connected healthcare devices, disease management programmes, digital health applications and the latest innovation of digital therapeutics.

> "Aptar Pharma believes that the future of therapeutics is best supported by an open, end-to-end platform that hosts medical devices and digital health products, alongside the services that complement and enhance them."

Managing the vast quantity of data that emerges from this evolving ecosystem, and gleaning useful insights from it, has proven to be a tall order. Data silos, walled gardens and proprietary systems make it difficult to share information. This forces providers, payers, pharmaceutical companies and patients to make care decisions by looking at an incomplete picture of how patients take or respond to a particular therapeutic.

Aptar Pharma believes that the future of therapeutics is best supported by an open, end-to-end platform that hosts medical devices and digital health products, alongside the services that complement and enhance them. This belief has informed Aptar Pharma's growth strategy, positioning the company to push the industry towards a new standard of healthcare.

FROM DEVICES TO THERAPEUTICS: HOW DRUG DELIVERY HAS EVOLVED

The transition from standalone analogue medical devices to digital therapeutics, powered by clinically evaluated software and validated medical guidelines, represents an ongoing evolution in healthcare delivery (Figure 1). As these patient support tools have become more sophisticated, more available, cheaper to produce and simpler to use, they have improved the standard of healthcare across the care continuum.

Physicians have used medical devices for millennia, dating back to a flint-tipped

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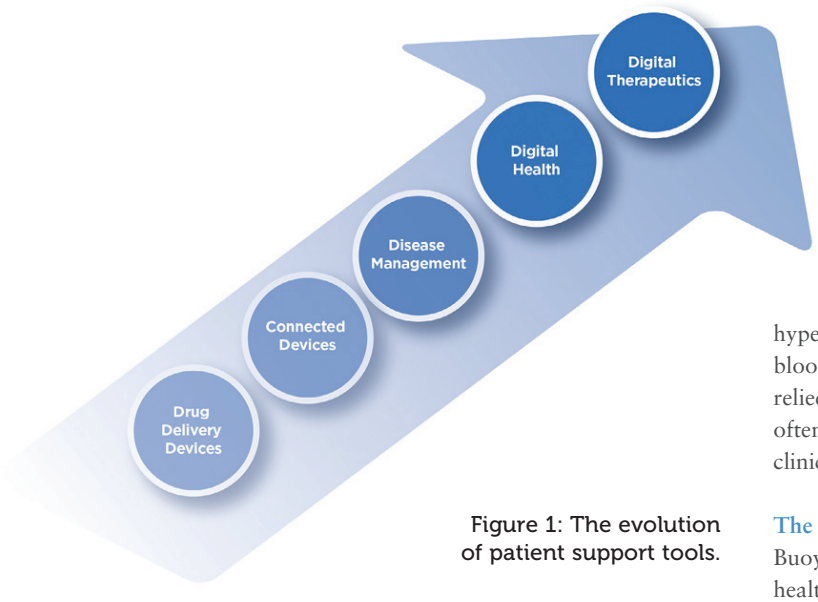

Figure 1: The evolution of patient support tools.

drill used some 9,000 years ago by dentists in modern-day Pakistan. Today, there are an estimated 500,000 medical devices on the market, according to "*Medtech and the Internet of Medical Things: How Connected Medical Devices are Transforming Health Care*", a July 2018 report by Deloitte. One key category is drug delivery devices, covering pulmonary, nasal, ocular, injectable and dermal therapies, that allow patients to administer medications at home, without the need for assistance from a physician or nurse. These provide patients with a convenient option for getting the medication they need, when they need it. The primary downfall of early-stage drug delivery devices was a lack of real-time connectivity – patients needed to record dosing data themselves and share it with a provider over the phone or during a subsequent clinic visit.

Using wired, wireless, cellular or Bluetooth connectivity, connected devices can transmit data to a computer, standalone application or data repository. This provides a tangible record of device data, saves users from needing to record and re-enter data, and reduces the likelihood of human error from misreading the device display.

Early Connected Devices

Unfortunately, early versions of connected devices ported data to standalone silos, making it difficult to share with clinical applications. Furthermore, simply seeing rows and columns of numbers in a database left clinicians and patients without the context that is critical for informed decision-making.

Disease management programmes aim to couple the benefits of continuous data collection from drug delivery devices with structured, evidence-based treatment plans for common chronic conditions. Such programmes enable care teams to recommend interventions based on what the device data tells them, such as prescribing a different medication for hypertension if the data shows that the current one is not lowering blood pressure as intended. However, the first such programmes relied on in-person care, and those that did make use of technology often relied on proprietary systems that were disconnected from clinical software and largely unavailable to patients.

> "Digital therapeutics are designed to close healthcare gaps by providing interventions when medical professionals cannot be there."

The Current Picture

Buoyed by rapid adoption of smartphones, the explosion of digital health applications over the past decade has put device data and disease management in the palms of patients' hands. This has empowered patients to self-manage their health and facilitated communication with healthcare professionals, allowing patients to become more active participants in their own care. Unfortunately, the sheer volume of digital health applications, coupled with the lack of standards for vetting their clinical efficacy, has led to understandable scepticism among many in the medical community.

The latest evolution in the standard of healthcare – digital therapeutics – aims to address these issues (Table 1). As defined by the Digital Therapeutics Alliance, these products deliver medical interventions directly to patients. They are backed by evidence-based software that is subject to an evaluation process as rigorous as that applied to the approval of new drugs or medical devices through clinical trials.

Digital therapeutics are designed to close healthcare gaps by providing interventions when medical professionals cannot be there. This increases patient access to proven therapies, allows clinical staff to provide care to more patients in less time, enables clear alignment of treatment plans and patient care goals, and makes it possible for patients to receive care in their native language.

THE VALUE OF BRINGING TOGETHER DIGITAL, DEVICES AND SERVICES

The evolution of drug delivery illustrates how digital products are positioned to boost the standard of healthcare. It is worth noting, however, that digital health solutions and digital therapeutics are just one piece of the puzzle. Devices play an important role – specifically modern drug delivery devices that work with therapeutics by helping patients administer the proper dose of treatments for

Patient Support Tool	Benefits	Drawbacks
Drug delivery devices	Enable self-administration	Analogue devices with no data to share
Connected devices	Data saved electronically	Data presented without context
Disease management	Evidence-based treatment plans	Largely in-person and proprietary
Digital health	Empower self-management	Many choices and no vetting process
Digital therapeutics	Brings approved medical interventions direct to patients	Limited adoption to date

Table 1: Benefits and drawbacks of patient support tools.

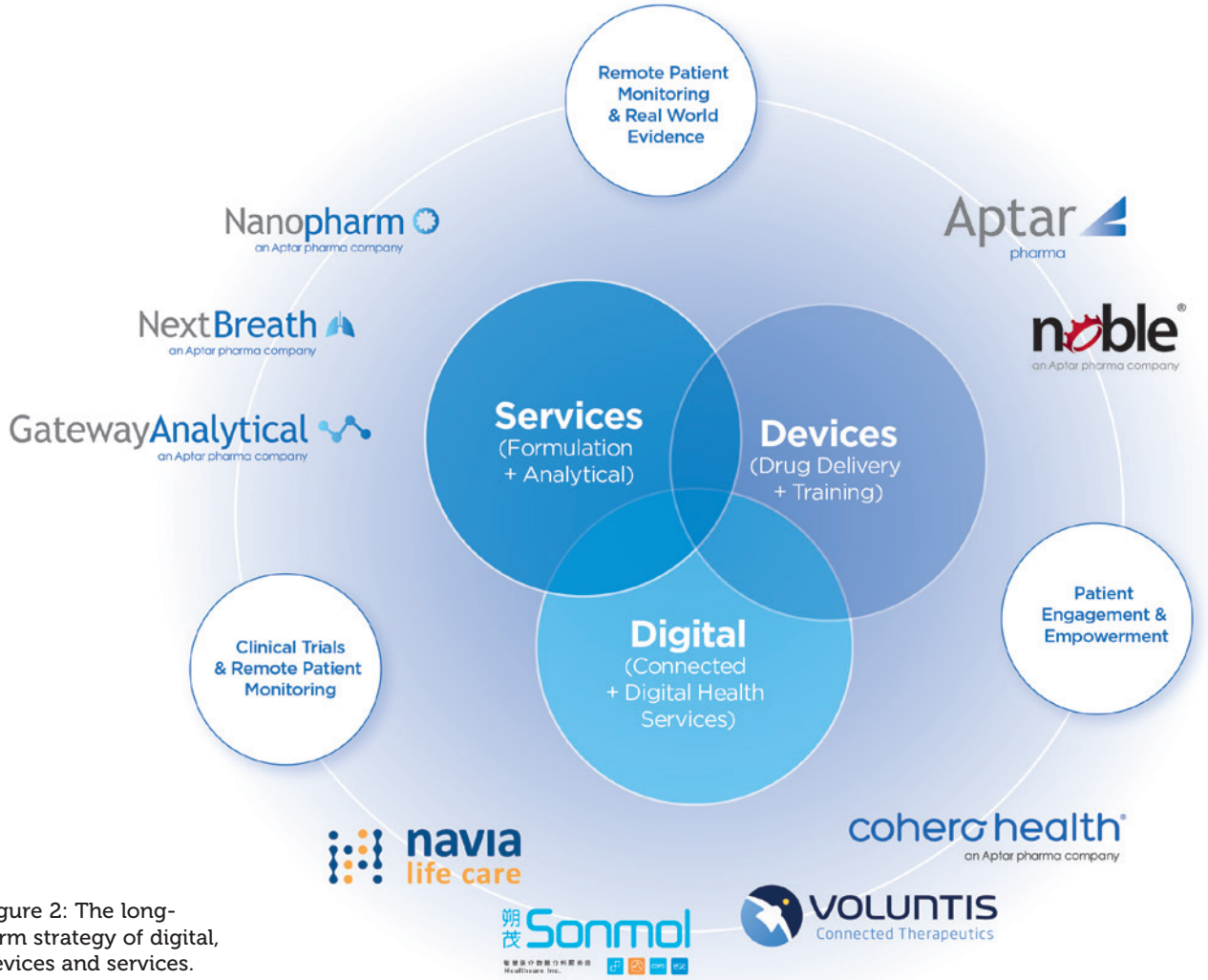

Figure 2: The long-term strategy of digital, devices and services.

common chronic conditions. There are even specialised training devices that can help familiarise patients with how to use injectables, sprays or eye drops so they are confident once they have their actual therapies in hand.

Services, meanwhile, assist pharmaceutical companies with the design, development, formulation and testing of therapeutics. Analysis is a critical service for pharmaceutical companies to ensure that products adhere to quality and regulatory standards, meet customer expectations and deliver the right dose to a patient the first time and every time.

Each of these three components is important on its own, but the true value of digital, devices and services is realised when they work in combination. This is the theme in Aptar Pharma's growth strategy (Figure 2) – most recently complemented by the acquisition of Voluntis (Paris, France) and reflected in previous acquisitions ranging from Nanopharm (Newport, UK) and NextBreath (Baltimore, MD, US) to Noble (Orlando, FL, US) and Cohero Health (New York, NY, US).

THE BENEFITS OF HOSTING DIGITAL, DEVICES AND SERVICES ON AN OPEN, END-TO-END PLATFORM

As discussed, the new standard of healthcare depends on the ability of all healthcare stakeholders – provider, payer, pharmacy, pharma manufacturer and patient – to have access to the longitudinal data necessary for them to make informed healthcare decisions. This cannot be done if data remain in silos, regardless of who has created them, be it software vendors, device manufacturers or healthcare institutions.

> "Each of these three components is important on its own, but the true value of digital, devices and services is realised when they work in combination."

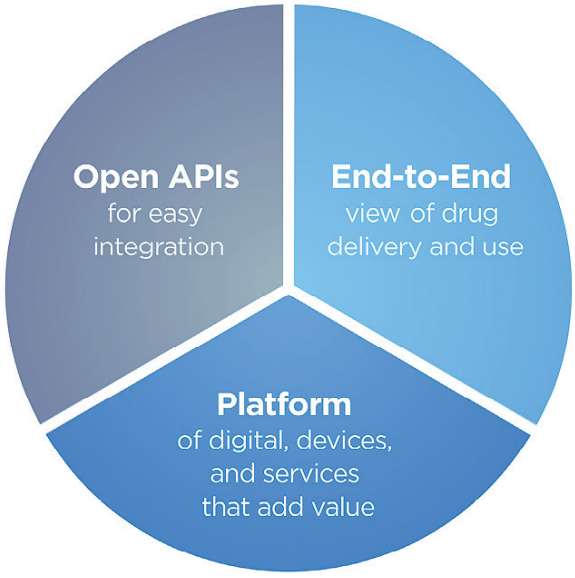

Figure 3: The benefits of an open, end-to-end platform API.

"When an end-to-end platform is in place, patients and their care teams can finally realise the high standard of care that healthcare has sought for so long."

The new standard of healthcare demands a new, unified experience for engaging with digital, devices and services. Aptar Pharma believes that this can only be done through the adoption of an open, end-to-end platform that paints a more complete picture of drug delivery and use for the entire healthcare ecosystem. There are three key phrases in the description of Aptar's vision, "open", "end-to-end" and "platform" (Figure 3). Let's unpack what each one means and see how, together, they offer a level of insight into the use of therapeutics that has not been possible before.

Open

Healthcare has had walled gardens for too long. Leveraging open application programming interfaces makes it possible to connect digital, devices and services without writing custom integrations. Any healthcare stakeholder with value to add, whether it is a diagnostic device, digital therapeutic, data aggregator or clinical application, should have the ability to connect and integrate with other solutions.

End-to-End

Today, key data about each stage of using a therapy resides with a different stakeholder. The manufacturer makes the therapeutic, the physician prescribes it, the pharmacy fills the prescription, the insurer pays for it, the patient takes it and the care team follows up to see how it is working. An end-to-end view is necessary to get a more complete picture of drug delivery and use – to identify what obstacles prevent patients from getting the therapy they need, from adhering to the prescribed dosing requirements to achieving the desired therapeutic outcome.

Platform

Drug delivery devices become even more powerful tools when it is possible to layer digital health applications and services on top of them, especially when these tools have been created by trusted third-party partners with expertise that the designer's organisation lacks. For example, the manufacturer of an inhaler can add a sensor that measures whether a full dose was inhaled, if the angle of inhalation was correct or whether the inhaler was shaken appropriately prior to actuation.

ABOUT THE AUTHOR

Adam Shain is Global Business Development Director for Aptar Pharma's Digital Healthcare team and is responsible for driving the new business agenda with pharma, payers and hospital network partners to reinforce the division's leadership in the digital healthcare space. Mr Shain previously worked for Promius Pharma (NJ, US), a subsidiary of Dr Reddy's Laboratories (Hyderabad, India), where he was instrumental in the development, commercialisation and launch of many of its branded combination products.

The End-to-End Platform in Action

When an end-to-end platform is in place, patients and their care teams can finally realise the high standard of care that healthcare has sought for so long. Care teams can provide patients with personalised digital therapeutics backed by clinical evidence, as well as the latest in predictive analytics.

Voluntis – a digital therapeutics company recently acquired by Aptar Pharma – has received 14 regulatory approvals in North America and Canada, amassed 13 years' worth of clinical trial data and managed deployments covering more than 100,000 patients. The company's approach to delivering patient-centred care in three key clinical areas demonstrates the power of the end-to-end platform in action:

- **Oncology**: Helping patients self-manage symptoms related to cancer treatment through communication, shared decision-making and personalised real-time recommendations can improve quality of life while limiting exposure to harmful treatments.
- **Diabetes**: Automated insulin dose recommendations coupled with coaching messages let care teams monitor patients remotely while meeting payers' requirements for reimbursable telemedicine services.
- **Anticoagulation**: Using a solution developed in collaboration with Roche Diagnostics (Basel, Switzerland), patients on anticoagulation therapies are connected to diagnostic testing facilities that monitor the ratio of the self-administered vitamin K antagonist treatment.

CONCLUSION

The evolution of the market for patient support tools closely mirrors the evolution of Aptar Pharma's business. Through organic growth, as well as mergers and acquisitions, the company's focus has transitioned from drug delivery devices to connected devices to disease management to digital health to digital therapeutics.

At the same time, Aptar Pharma is building an open, end-to-end platform to host the devices, digital applications and services that make it possible to see the complete picture of drug delivery and use. Not only does this serve the needs of the company's partners, it enables it to support the healthcare ecosystem in providing a new standard of personalised care backed by evidence-based digital interventions. For patients managing chronic conditions, this leads to better outcomes and a better quality of life.

ABOUT THE COMPANY

For pharma customers worldwide, Aptar Pharma is the go-to drug delivery expert, providing innovative drug delivery solutions across a wide range of delivery routes, including nasal, pulmonary, ophthalmic, dermal and injectables. Aptar Pharma Services provides early stage to commercialisation support to accelerate and de-risk the development journey. With a strong focus on innovation, Aptar Pharma is leading the way in developing connected devices to deliver digital medicines. With a global manufacturing footprint of 14 GMP sites, Aptar Pharma provides security-of-supply and local support to customers. Aptar Pharma is part of AptarGroup, Inc. (NYSE:ATR), a global leader in the design and manufacturing of a broad range of drug delivery, consumer product dispensing and active material science solutions.

eFLOW TECHNOLOGY NEBULISERS WITH DIGITAL THERAPY MANAGEMENT: THE PARI CONNECT ECO-SYSTEM

Here, Carola Fuchs, PhD, Director e-Health Solutions, and Simon Buchner, Usability and Product Compliance Manager, both at PARI, describe PARI's new nebuliser and digital Connect eco-system and how it supports patients, directly and indirectly, through carefully considered device usability in combination with digital therapy management solutions.

While it is obvious that successful inhalation therapies require efficacious drugs, they are also heavily reliant on efficient delivery systems that address a patient's ability to follow their treatment regime. The easier it is for a patient to follow their treatment regime and use their device, the more likely it is that their therapy will be effective. The usability of a device can affect the delivered dosage in a given therapy session, as well as overall therapy acceptance in the long run. Despite being an important factor for positive real-world outcomes, therapy acceptance and adherence have been found to be as low as 36% for some inhaled therapies.[1]

According to internal market research with over 250 patients, physicians and pharma company employees, both device usability and the possibility to transfer and share data between a patient and their physician are key features for improving the success of inhalation therapies. As such, connectivity for providing feedback on patients' inhalations will have a significant role to play in the sector going forward.

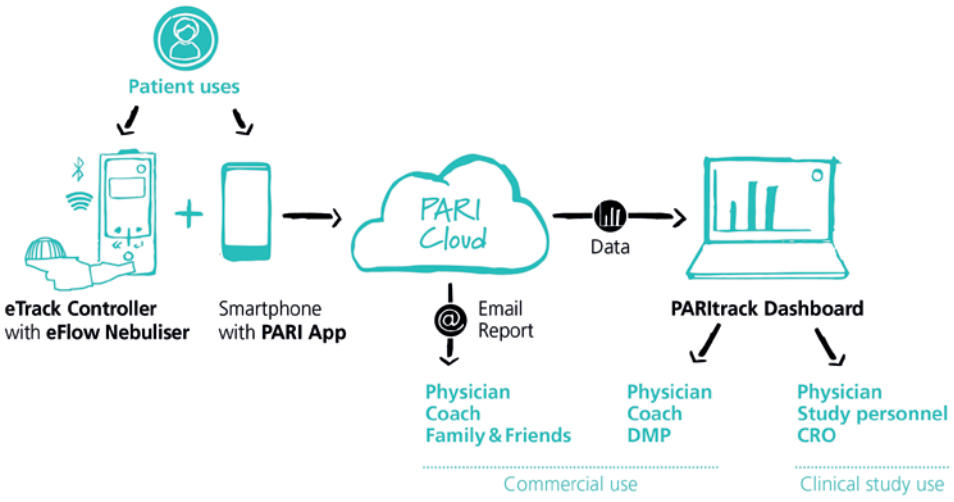

Figure 1: eTrack Controller in the PARI Connect eco-system.

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"PARI has recently updated the eBase and eTrack Controllers, with a special focus on improving usability and implementing better therapy support features."

Figure 2: The new eTrack Controller with eFlow Technology nebuliser and PARI Connect app.

THE PARI CONNECT ECO-SYSTEM

PARI is a provider of customised vibrating membrane nebulisers, supporting its clients during the clinical development, regulatory approval and commercial phase of their product development. PARI's devices always consist of a drug-specific, customised nebuliser handset and a controller. Depending on the target patient population and their specific needs, three types of controller are available:

- eLete®, without any display or connectivity functionality
- eBase®, with a display but without connectivity functionality
- eTrack®, a Bluetooth and wi-fi ready controller.

PARI's nebuliser devices are complemented by digital supporting products that are part of the PARI Connect eco-system – a proprietary app that enables data transfer from eTrack Controllers to secure cloud storage coupled with the PARItrack Dashboard, which aggregates and displays the data stored in the cloud (Figure 1).

PARI'S NEW CONTROLLERS FOR eFLOW® TECHNOLOGY NEBULISERS

PARI has recently updated the eBase and eTrack Controllers, with a special focus on improving usability and implementing better therapy support features. The new eTrack Controller, together with the corresponding app, will be available in summer 2022 (Figure 2). This update focused on human-centric design by following a comprehensive human factors engineering process – not only to comply with regulatory requirements but also to ensure safe and effective use and a positive user experience that enables a smooth transition into future partner collaborations and clinical studies.

Knowing that there is a broad range of potential patient populations for future drug and device programmes, PARI tested the device setup across a range of indications throughout the development phase, including considerations of respective limitations that may be concomitant with certain respiratory diseases. The challenge was designing a device that enables patients with a wide range of user characteristics, such as age, physical limitations or limited experience, to effectively perform their therapy and, simultaneously, create a user interface that implements connectivity using cutting-edge digital tools.

General improvements were made that emphasise the mobility and user-friendliness of the device, for example, both controllers had their weight and size significantly reduced, alongside the addition of an integrated rechargeable battery pack that is designed to last for 90 minutes after three years of normal use. Further to this, the data transfer feature of the new eTrack Controller was improved by implementing both Bluetooth and wireless LAN connectivity. This feature allows for the automatic transfer of nebulisation data without the need for the patient to actively transfer the data after each treatment, enabling regular, instant data sharing with a telemedicine centre or a physician. Additionally, an inhalation detection function was implemented in the eTrack Controller to optimise the monitoring feature.

PARI also focused on the re-design of the user interface. The target was to develop self-explanatory pictograms that are readily comprehensible without additional text. To this end, simplified lateral graphics of device components were used to inform the user about device status or malfunction (Figure 3).

Another challenge was to design buttons that are robust and easy to clean on the one hand, but that allows users with limited dexterity, or even a tremor, to successfully push them on the other. The use of a keypad that covers the front of the controller makes cleaning and disinfection methods, such as chemical wipe disinfection, as simple as possible. Again, this requires finding the optimal haptic feedback, and so the push forces required by the controller buttons were iteratively adjusted according to user feedback.

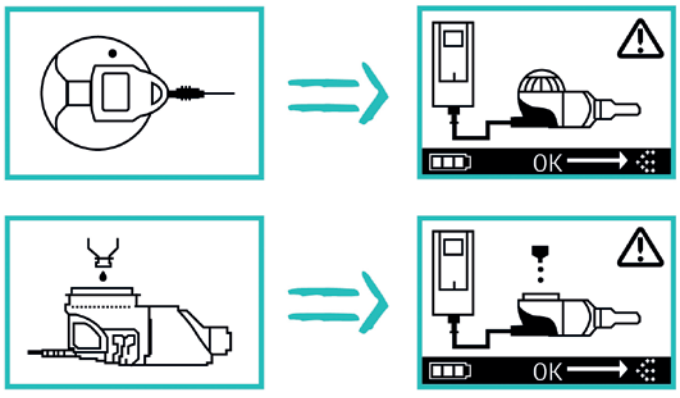

Figure 3: Evolution of exemplary error screens – current controller (left) versus new controller (right).

During the early development stage, participants that are familiar with the current eFlow Controller gave input regarding their expectations on a new device. As a result, PARI incorporated a settings menu within the new interface that allows patients to adapt their therapy feedback to their needs. For example, some users described being annoyed when constantly receiving audio feedback and would prefer to mute the device, whereas parents were positive about the way that audio feedback kept them informed while their child was performing a therapy. In the later stage of human factors engineering, users were observed in comprehensive simulated-use scenarios, including performing a complete therapy to validate the safe and effective use of the device.

PARI also tested if users were able to connect to the eTrack Controller via an app. By iterative adaption of the user interface, PARI developed a simple setup process that connects the nebuliser to the app using only the symbols on the eTrack Controller. Once the connection is established, further configurations can be done within the app itself. This allows PARI to offer different app functionalities and levels of complexity. On the one hand, simple automatic data transfer to the PARI cloud ensures a successful transfer for clinical studies and patients with limited affinity to digital tools. On the other hand, detailed analysis and visualisation of nebulisation data can be offered to patients wanting to get more involved.

During the development of the PARI Connect system, the accompanying app also underwent human factors evaluations. This started with remote user tests on basic wireframes to create a clearly arranged user interface in the app, after which further studies were performed to observe users entering and managing therapy plans and extracting reports, as well as analysing the effect on adherence. By doing so, PARI was able to focus on the essential user needs for daily therapy management – throughout this process PARI always kept the benefits for the patient in mind.

> "With the progress in digitisation in other areas of their lives, the expectations patients place on digital tools in the medical field is rising."

PARI CONNECT® APP

With the progress in digitisation in other areas of their lives, the expectations patients place on digital tools in the medical field is rising. Chronically ill patients appreciate a digital tool that helps to collect all relevant information about their disease. Thus, the new eTrack Controller can be connected to an app on a patient's mobile phone to document all nebulisations and information related to their disease. The PARI Connect app has the following features:

- A comprehensive plan encompassing all therapies, such as pills, inhalation and physiotherapy
- Individual reminders for all therapies
- Automatic transfer of data from the eTrack Controller and a home spirometer to the PARI cloud
- Manual documentation of vital parameters, such as lung function, glucose, oxygen saturation and BMI
- Both short daily queries and validated quality-of-life questionnaires
- Graphical visualisation of stored therapy data to see long-term trends for adherence and vital parameters
- Exportable reports for physicians, coaches, parents and friends
- Automatic message generation in case of decreased adherence or lung function to a selected person
- Diary function
- Support from family and friends ("Buddy-System").

When opening the app, the patient immediately sees the next therapy they need to take and can track the nebulisations that they have already done, as was shown in Figure 1. For use in clinical trials a special version, PARI Study Connect, is available to consider corresponding requirements.

Figure 4: PARItrack Dashboard gives access to the data for the physician and helps to focus on the patients that need support: web portal (A), list of patients (B), exemplary adherence report (C).

"The PARItrack Dashboard is a web portal for physicians to access the data transferred from the app and the connected devices, based on six years' experience with use of eTrack Controller and PARItrack within clinical trials with more than 2,000 patients across Europe, the US, Canada and the UK, available for both commercial and clinical settings."

Data is collected, encrypted, securely transferred and stored in the PARI cloud considering all requirements for data privacy according to the EU General Data Protection Regulation. For commercial use, the patient has control over who they share their data with. They can either share a report via email with any person of their trust or give access to their data to their physician via the PARItrack Dashboard. Within a clinical study, the data are shared according to the study protocol, which needs to be incorporated into the patient information and consent form. The app is a tool for documenting and transferring data and therefore not a medical device from a regulatory perspective, however, this might change in the future if more features are integrated.

PARITRACK DASHBOARD

The PARItrack Dashboard is a web portal for physicians to access the data transferred from the app and the connected devices, based on six years' experience with use of eTrack Controller and PARItrack within clinical trials with more than 2,000 patients across Europe, the US, Canada and the UK, available for both commercial and clinical settings. PARI understands that to maximise the benefit of using the system, it is important that physicians have easy access to aggregated data and can gain a good overview with only a quick check.

When accessing the PARItrack Dashboard, physicians can immediately see all their patients alongside their therapy adherence data and, if applicable, can also see their vital parameters, allowing them to focus on the patients that most need support (Figure 4). Additionally, they can investigate the details of each of their patients, featuring lists with all the aggregated information on inhalation sessions, including the date, time and duration of each nebulisation, the switch-off criterion, the corresponding drug and the graphical analysis of therapy adherence. Notifications for drops in adherence or lung function can be adjusted and activated.

In a commercial setting, an attending physician can set up their practice in the PARItrack Dashboard and invite their patients with an eTrack Controller to share their data. If a patient agrees and decides to share their data, the data will be available in the PARItrack Dashboard, but the patient can withdraw whenever they so wish. Data access can also be given to a physiotherapist, a therapy coach or nurses as part of a telemedicine programme. For use in clinical studies, the structure of the PARItrack Dashboard reflects the organisation of patients in study centres, with different access roles for physicians, study personnel, contract research organisations and sponsors.

The advantage of this system is that the setup and technical solution for use in clinical studies is the same as for commercial use, thereby enabling an easy transfer from use within clinical development to the commercial phase. Storing the data in the secure PARI cloud allows country-specific requirements to be met easily with local branches in the corresponding countries. If necessary, this also enables worldwide use of the system.

BENEFITS OF ADHERENCE MONITORING AND THERAPY MANAGEMENT SUPPORT

The benefits of using the system in clinical trials have been demonstrated in recent years. Patients who are less adherent can be directly contacted by clinicians and other healthcare professionals to assist with device handling or for training and motivation. This has resulted in very high mean adherence rates – between 99 and 76% for studies with a duration of two to six weeks and up to two years, respectively.[2] Monitoring also supports improved evaluation of study outcomes with respect to the efficacy and safety of a medication by correlating efficacy with adherence. In total, this can result in cost and time savings as higher rates of non-adherence necessitate greater numbers of participants and elongated recruitment periods.[3]

eTrack Controllers have also been used within studies considering the adherence of chronically ill patients in respect to their daily treatments in real-world settings. The adherence to standard therapies is known to be approximately 34%. Recent research shows that it is possible to achieve significantly higher objectively measured adherence to inhaled medications (sustained over 12 months) with an absolute difference of 18% at 50 weeks in the largest self-management intervention trial in cystic fibrosis (CF) to date (607 adult participants, 19 UK-based test centres).[4] Interestingly, the intervention group showed a lower perceived CF treatment burden than the control group with usual care and lower adherence. This is the only trial thus far to demonstrate a sustained difference in adherence versus a control group using a theory-based approach including habit formation. eTrack Controllers with eFlow Technology nebulisers were used in this trial to accurately record participants' inhalations. Intervention participants additionally had access to the CFHealthHub digital platform via an app where they saw their adherence data alongside motivational and educational material.

OUTLOOK

In another ongoing multi-centre study sponsored by the innovation grant of the German statutory health insurances, telemonitoring adherence in combination with lung function, together with coaching of non-adherent patients by staff trained in patient psychology, is being evaluated with respect to adherence increase, health outcomes, quality of life and economic impact in a randomised controlled trial.[5] The study is using PARI's eTrack Controller, the PARI Connect app and the PARItrack Dashboard.

ABOUT THE COMPANY

PARI is a world leader in the development of aerosol delivery devices. PARI Pharma focuses on pharma licensing partnerships that use the company's eFlow Technology nebulisers optimised for specific drug products and formulations. eFlow Technology is an aerosol delivery platform that enables efficient nebulisation of liquid medications via a vibrating perforated membrane. eFlow devices are

designed to reduce the burden of treatment for patients with severe respiratory conditions. Several inhaled medicinal products have already been launched in combination with optimised eFlow nebuliser systems for different therapeutic indications in North America, Europe and Japan.

REFERENCES

1. *Daniels T et al, "Accurate Assessment of Adherence: Self-Report and Clinician Report vs Electronic Monitoring Of Nebulizers". Chest, 2011, Vol 140(2), pp 425–432.*
2. *Koehler Y, Fuchs C, "Monitoring Nebuliser Usage & Lung Function in Clinical Trials". ONdrugDelivery Magazine, Issue 87 (Jun 2018), pp 66–70.*
3. *Alsumidaie M, "Non-Adherence: A Direct Influence on Clinical Trial Duration and Cost". Applied Clinical Trials, Apr 2017.*
4. *Wildman MJ et al, "Self-management Intervention to Reduce Pulmonary Exacerbations by Supporting Treatment Adherence in Adults with Cystic Fibrosis: A Randomised Controlled Trial". Thorax, 2021, Online as thoraxjnl-2021-217594.*
5. *Thee S, "A Multi-Centre, Randomized, Controlled Trial on Coaching and Telemonitoring in Patients with Cystic Fibrosis: conneCT CF". BMC Pulm Med, 2021, Vol 21, Article 131.*

ABOUT THE AUTHORS

Carola Fuchs, PhD, leads the e-Health department at PARI and is responsible for development, lifecycle management, business development and management of all e-Health activities for the PARI Group. She joined PARI after working for Sanofi and a biotech start-up in 2006, starting her work on connected devices as a project leader at PARI Pharma. Since then, Dr Fuchs has established digital solutions and an international network of contacts in the field of digital health. She has a Master's degree in Mechanical Engineering from the Technical University of Munich (Germany) and a PhD from the Technical University of Hamburg-Harburg (Germany).

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MATERIAL SELECTION FOR NEXT-GENERATION CONNECTED MEDICAL ELECTRONICS

Here, Miriam Kingsley, Marketing Communications Manager, Marcus Jarman-Smith, Marketing and New Business Development, and Thomas Billings, Senior Application Development Engineer, all at Victrex, highlight the growing array of applications for high-performance polymers in electronic and connected medical devices and how proper material selection is crucial, providing a guide to successful material selection, going on to showcase its APTIV™ PEEK polymer film, which is well suited to meet the specific demands of next-generation connected medical devices.

Consumer demands for the latest electronic devices, coupled with emerging radio frequency (RF) technologies, such as 5G, are creating constant pressure for more innovation. To stay ahead of the competition, products must offer more functionality, more durability, and faster and more powerful performance, all at an acceptable cost.

Crucial to this is choosing the right material. High-performance polymer technology provides the versatility and high performance necessary. Now it is possible to have the design freedom to meet today's challenges and deliver the next generation of electronic drug delivery devices. Material selection is critical for medical device designs. This includes drug delivery – whether the device is implantable or not. There are, in fact, quite a few materials available on the market that are successfully used in drug delivery devices, and selecting the right materials can be a bigger challenge than originally thought.

MEETING MULTIPLE ENGINEERING REQUIREMENTS

Designers often define multiple key engineering requirements (KERs) when looking at developing components for next-generation drug delivery devices. For example, we know that demands for higher structural integrity, reliability, mobility and connectivity are all shaping the way that electronic components are

> "Increasingly, designers are looking to high-performance polymers for answers. Without a doubt, PEEK is one of the highest performing polymers, and one that can support multiple KERs."

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designed. Increasingly, original equipment manufacturers (OEMs) are specifying high-performance polymer solutions to reach new levels of device performance and enhance the user experience. Some of the unique drivers for change include:

- **Increased connectivity:** Devices are now expected to deliver an enhanced user experience with seamless connectivity, improved interactivity and high reliability.
- **More chips for smarter and smaller devices:** Semiconductor fabricators are under constant pressure to produce higher performance chips in a faster cycle and with fewer defects.
- **Energy efficiency and sustainability:** Device manufacturers are challenged to enhance the lifespan of their products and make the manufacturing process more efficient in terms of energy consumption and waste.

Traditional materials, such as commodity polymers and metals, can be used for some applications, but what happens when there are multiple engineering requirements for components that have complex designs and need to operate with precision over a long lifetime?

Increasingly, designers are looking to high-performance polymers for answers. Without a doubt, poly-ether-ether-ketone (PEEK) is one of the highest performing polymers, and one that can support multiple KERs. PEEK has been used to achieve improved safety and durability, greater design freedom and patient comfort, and increased cost efficiency in the production of medical devices.

WHEN TO SELECT HIGH PERFORMANCE POLYMERS

- **High-temperature environments:** VICTREX™ PEEK polymers can withstand continuous-use high temperatures and harsh chemicals; surviving anodising, wave soldering and other harsh fabrication processes.
- **Mechanical strength:** Superior bond strength, high strength and stiffness, good metal adhesion, allowing more design freedom with better structural integrity.
- **Weight reduction:** Replacing metal with VICTREX PEEK can help pack more performance into a lighter package.
- **Miniaturisation:** The development and production of smaller and smarter chips with more data storage and increased functionality is an ever-present trend driving the semiconductor industry.

CHOOSING THE RIGHT POLYMER FORM

PEEK-based films, fibres, coatings and composites incorporate all of the outstanding properties of VICTREX PEEK polymer in multiple formats, enabling customers to meet increasing performance demands and providing design freedom to drive innovation. Regulatory compliant implantable and non-implantable biocompatible grades enable safe, long-lasting solutions for drug delivery devices.

> "Providing all the benefits of VICTREX PEEK polymer in a thin film, APTIV films can give provide the versatility and high performance needed to address complex demands and design next-generation electronic devices."

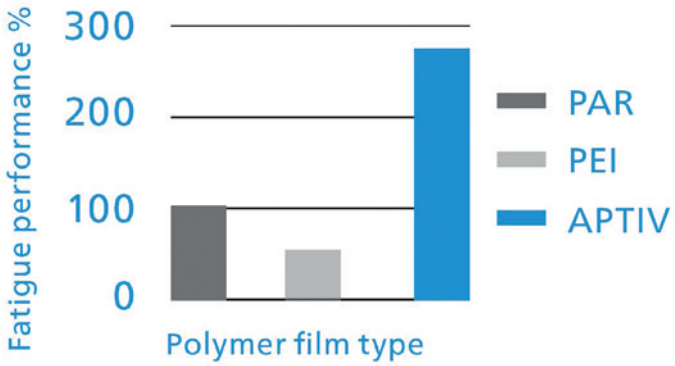


Figure 1: APTIV films have around three times the lifetime of other polymers such as PAR or PEI films.

In addition to natural, unfilled PEEK, the polymer is also available compounded with fillers, including glass fibre and short and continuous carbon fibre, each with different characteristics for different environments.

PRODUCT SHOWCASE: APTIV™ FILMS

Providing all the benefits of VICTREX PEEK polymer in a thin film, APTIV films can give the versatility and high performance needed to address complex demands and meet the design requirements of next-generation electronic devices, including connected drug delivery devices. APTIV films have been used in over four billion mobile devices for acoustic performance and reliability.

- APTIV films can meet specific needs of different electronics applications, with a range of thicknesses from 3–360 µm ultra-thin for wear and insulation.
- APTIV films have around three times the lifespan of other polymers, such as polyarylate (PAR) or polyetherimide (PEI) films (Figure 1)
- Lower moisture absorption versus polyimide – APTIV Films provide more stable electrical properties, especially at higher (RF) frequencies.
- More ductile and less brittle compared with liquid-crystal polymer – APTIV Films have similar high (RF) frequency electrical and mechanical properties, but are more ductile and less brittle (e.g. in injection-moulding processes).

APPLYING HIGH-PERFORMANCE POLYMER ADVANTAGE IN DRUG DELIVERY APPLICATIONS

There are limitless applications, such as insulin pens, wearables and inhalers, that can take advantage of the light weight and high durability of high-performance polymers, from battery insulations to gears and pumps, but let us focus on two:

1) Integrated Structural Electronics and Flex Circuits

Integrated structural electronics is a space-saving concept that uses laser direct sintering into a compatible material. Figure 2 shows the concept of a casing for a wearable patch pump where the electronics are sintered directly into the casing to create an antenna to communicate wirelessly via Bluetooth. This eliminates the need for a printed circuit board (PCB), thereby increasing the available space within the device so that it can hold larger volumes of drug or be further miniaturised.

PEEK has good dielectric properties with a very low dissipation factor, with only small amounts of electrical energy absorbed by the PEEK material. The stable dielectric properties (Dk, Df) over a wide range of temperatures, humidities and RFs enable internet of things and bluetooth support. This makes PEEK radio transparent and allows the design to have an antenna on the inside for connecting to a smartphone or other device. The advantage of adding antenna tracks directly onto the surface of the material is that these antennas have great operational stability. They are not in a separate component with its own assembly tolerances, but instead are part of the device's casing with a consistent thickness of material between them and the outside world.

2) Precision Sensors and Capacitive Switches

For many years PEEK films, such as Victrex's APTIV film, has been used to create tactile switches and touch sensors. Again, the dimensional stability of PEEK makes switches reliable, able to retain their strength even after repetitive depressions. In the patch pump concept, the touch sensor could be used to dispense the drug precisely, using pressure to dictate the strength or volume of drug to be released. By applying PEEK film behind an LED, the capacitive switch could be made into a smart switch, perhaps by blinking to notify the user of changes to temperature, battery life or connectivity. As designers are faced with new challenges, high performance polymers, such as PEEK, offer additional choice and options for new solutions.

Figure 2: Structural electronics integrated into a PEEK enclosure, eliminating the need for a PCB. This enclosure is designed by Tricas (Bromsgrove, UK) to maximise the potential of VICTREX PEEK. (Image © Copyright 2021 Victrex plc)

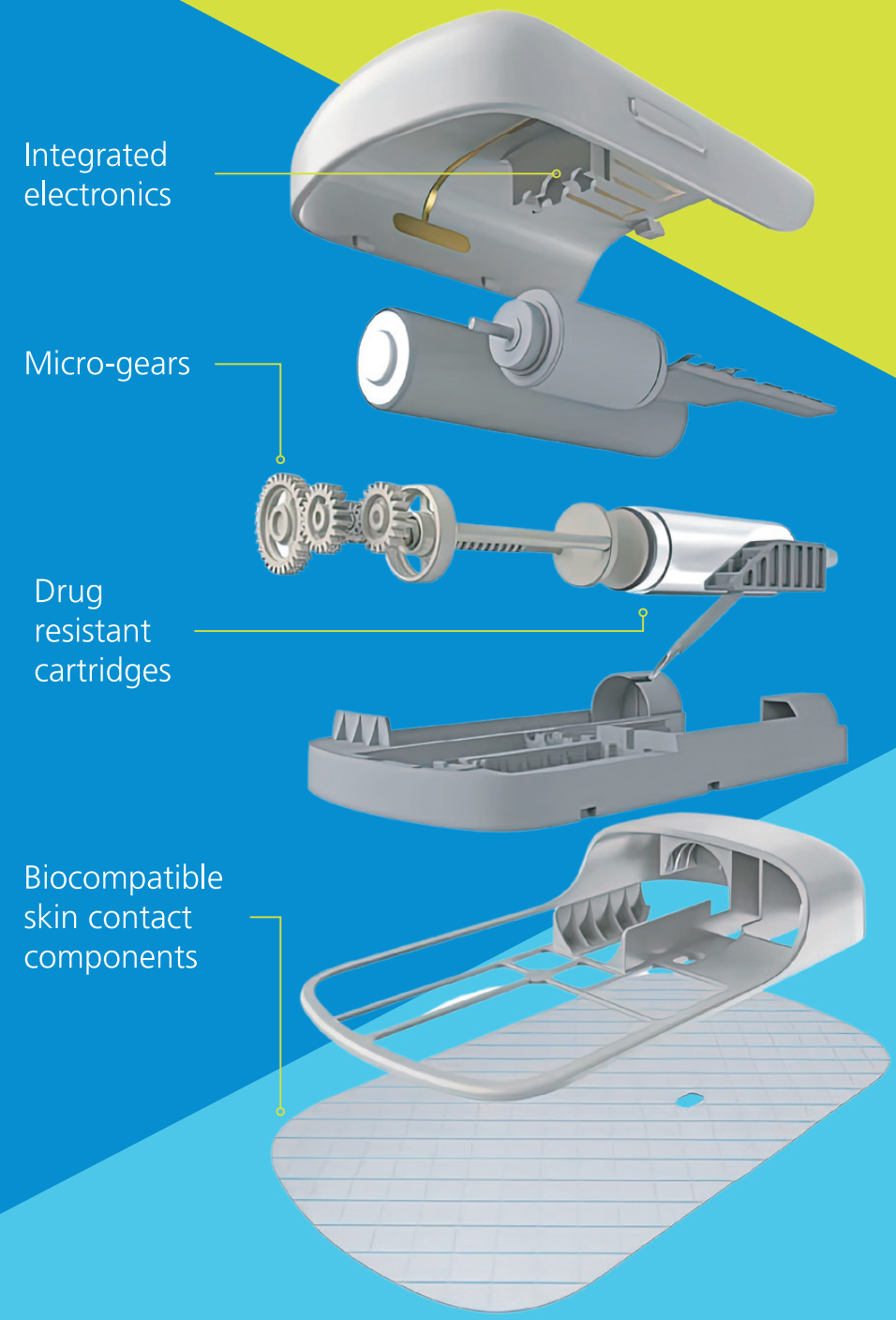
ABOUT THE AUTHORS

Marcus Jarman-Smith supports developments across the multiple market segments including medical devices and most recently in scouting for breakthrough technologies as well as supporting the development of Victrex's Additive Manufacturing offering. Marcus's expertise is in PEEK in medical and dental applications as well as food contact, materials and technologies for Additive Manufacturing and 3D printing.

Thomas Billings is a mechanical engineer with specialist expertise in injection moulding of thermoplastics, and high performance PEEK and PAEK polymers. At Victrex, he has supported commercial programmes in hybrid composite overmoulded polymers for the aerospace industry, and projects in medical implants and drug delivery devices.

Miriam Kingsley has 15 years' experience in health technologies and medical devices. At Victrex, she collaborates with OEMs and KOLs involved in the launch of applications made with high-performance PEEK polymers, including food contact applications, biocompatible orthopaedic implants, prosthetic dental implants and drug delivery devices.

Wearable insulin patch pump device design concept made with VICTREX™ PEEK polymers



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HIGH PERFORMANCE VICTREX™ PEEK POLYMERS

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ON drugDELIVERY

2022 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
February	Prefilled Syringes & Injection Devices	Jan 13, 2022
March	Ophthalmic Drug Delivery	Feb 10, 2022
April	Pulmonary & Nasal Drug Delivery	Mar 3, 2022
April/May	Drug Delivery & Environmental Sustainability	Mar 17, 2022
May	Delivering Injectables: Devices & Formulations	Apr 7, 2022
June	Connecting Drug Delivery	May 5, 2022
July	Novel Oral Delivery Systems	Jun 2, 2022
August	Industrialising Drug Delivery	Jul 7, 2022
September	Wearable Injectors	Aug 4, 2022
October	Prefilled Syringes & Injection Devices	Sep 1, 2022
Oct/Nov	Drug Delivery & Environmental Sustainability	Sep 15, 2022
November	Pulmonary & Nasal Drug Delivery	Oct 6, 2022
December	Connecting Drug Delivery	Nov 3, 2022

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"SOFTWARE AS A MEDICAL DEVICE" FROM A HUMAN FACTORS PERSPECTIVE

In this article, Natalie Shortt, Principal Human Factors Specialist at Harvey Medical Consulting, discusses the considerations and steps to take when planning usability engineering efforts for "software as a medical device".

A quick search online will show that guidance relating to "software as a medical device" (SaMD) is sparse, particularly when it comes to applying usability engineering to software. When a client approaches with what might be SaMD, it is important to run through a series of questions to determine exactly what will be required for that piece of software.

The client might be a traditional medical device manufacturer or a pharmaceutical company that has decided to develop a connected technology to accompany their treatment pathway. However, occasionally there are software developers that have found their innovative software is encroaching on medical territory, and so are bound by medical regulations. In any situation, the same initial stepping stones help to understand what activities are required. This article maps out a range of considerations and steps, from a human factors perspective, that enable you to plan your usability engineering efforts accordingly.

CONFIRMING IT IS SAMD

First and foremost, it is necessary to determine which of the following the software is:

- Software that is not a medical device
- Software that is integrated into a medical device (Figure 1)
- Software, independent of any hardware, that contributes towards medical care.

The last of these is SaMD. The International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world, has developed guidance that can help to determine what the software should be classed as.

The IMDRF defines SaMD as "software intended to be used for one or more medical purposes that performs these purposes without being part of a hardware medical device",[1] whereby "without being a part of" means software that is not necessary for a hardware medical device to achieve its intended medical purpose. To this end, to determine whether your software is SaMD, you need to craft an intended use statement. This will help to understand if the intended use is integral to the overall use of a medical device. If this intended use statement indicates that the software is standalone from the device, the software is more likely to be SaMD.

> "To determine whether your software is SaMD, you need to craft an intended use statement."

The IMDRF suggests an intended use statement should consist of three major points:

1. A clear and strong statement about intended use, outlining whether the device is used to:
   - treat or diagnose
   - drive clinical management
   - inform clinical management.
2. The state of the healthcare situation or condition, either:
   - critical
   - serious
   - non-serious.
3. A description of the software's core functionality, identifying critical features essential to the intended significance of the information the software provides.

As an illustrative example of an intended use statement, consider "a piece of software that provides information regarding insulin uptake in people newly diagnosed with Type 1 diabetes, so that they can observe whether they are calculating their insulin correctly per meal. The software reviews data pertaining to insulin levels pre-meals, post-meals and post-administration of an insulin dose, and provides an outline of any discrepancies in the maths".

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Figure 1: A woman using her phone to review the data being collected by her continuous glucose monitor. The monitor requires the mobile app to function, and the mobile app may influence the patient's decision making in monitoring their glycaemic index. Therefore, this could be considered "software integrated into a medical device".

"The intended use statement can be used to determine if the software meets the definition of SaMD or if it is an integrated part of the overall medical device."

The intended use statement can be used to determine if the software meets the definition of SaMD or if it is an integrated part of the overall medical device. In both cases, the device is subject to usability engineering, but what that will look like may change according to the overall objective. Additionally, for software to be considered a medical device, it must meet the criteria for a medical purpose. The IMDRF suggests taking the definition of the term "medical device"[2] into account. This definition will vary, depending on the market. In the EU, it is best to review the definition of a medical device as per the Medical Device Regulation, whilst in the US it would make sense to review the formal terms provided by the US FDA.

CLASSIFYING THE LEVEL OF RISK

Once you have discussed the intended use of the software and feel confident that it is SaMD (or at least a part of a medical device), there is a framework for determining what level of risk may be associated with the SaMD.

Within the EU, at least, SaMD is automatically considered Class IIa (generally a low-medium risk device) by default, so initial assumptions should be that manufacturers will at least have to perform some usability engineering, develop usability documentation and demonstrate compliance with a usability engineering file. To get a better idea of exactly what level of effort is required, a systematic process can be followed.

Start with the IMDRF guidance N24, "Possible Framework for Risk Categorization"[2] – this will give an indication of the level of risk that may be associated with the device, and therefore what level of usability engineering should be applied during development. This categorisation is independent from regulatory classification and the two should not be confused.

To get an idea of what level of risk the SaMD is, return to the intended use statement from before. Risk associated with SaMD is considered through two variables:

- Significance of information provided by SaMD to healthcare decision
- State of healthcare situation or critical condition. IMDRF N24 lays this out as a table (Table 1).

State of healthcare situation or condition	Significance of information provided by SaMD to healthcare decision		
	Treats or diagnoses	Drives clinical management	Informs clinical management
Critical	IV	III	II
Serious	III	II	I
Non-serious	II	I	I

Table 1: SaMD risk classification (IMDRF N24).

From the intended use statement, you can reason the type of information that the SaMD will provide. You can also infer the state of the healthcare situation or condition (e.g. the state the patient is in when receiving care with the SaMD). The combination of these two variables gives an indication of how much risk may be associated with normal use, with I being low risk and IV being high risk. In the case of the diabetes management example, we know it provides information relating to a serious healthcare condition. Therefore, it would be somewhere between low and low-medium risk. Although these categories are not regulatory categories, the level of risk can be used to gauge what formal class the SaMD should be – whether to stick with the automatic Class IIa or not.

MANAGING THE DOCUMENTATION

At this point, you should be confident about whether or not your software is SaMD and what pathway to consider. Let's assume the device is Class IIb – perhaps the SaMD is intended to drive clinical management in a serious healthcare situation – there will be an expectation to conduct full usability engineering and demonstrate compliance with a usability engineering file.

For hardware devices, this is already quite a task – but changes are implemented slowly, which means documents are only updated periodically, perhaps at the conclusion of each milestone or once or twice a year. For SaMD, this is not the case. Software benefits from being easily edited or updated based on design decisions – you can enter a meeting with one iteration and make some design changes within the meeting, go to another meeting with that iteration and then make some more design changes within that meeting! This is great for refining the device, but is problematic for usability engineering because these changes should technically be documented. At the rate of software development, someone would have to update usability documentation on a daily basis, which is impractical.

To reduce the impact quality management can have on the creative design process for software, manufacturers can benefit from setting some internal rules or processes that trigger the need to update documentation. This could be included in a "usability engineering plan", a document that contributes to demonstrating compliance. Within the plan, specify what magnitude a design change needs to be to trigger a document review, then ensure that all team members who have the capacity to make interface changes understand the triggers.

> "One of the immediate difficulties is developing a test plan for something that is frequently changed."

Additionally, the plan should include a periodic timeframe for updating documents, with an agreement on how versions of the software are managed. For example, this plan could specifically outline that documents will be reviewed every three months. On the xth day of that month, the most up-to-date version of the software will be considered the current version and all documentation will be updated with that iteration. This is a structured approach that implements the methodological practices that are typical to medical device risk management, whilst trying to maintain the creative processes common in software development.

CONDUCTING USABILITY STUDIES

Similarly, one of the immediate difficulties is developing a test plan for something that is frequently changed. In usability studies, it is typical to define the use flow within the protocol and describe what is being assessed at each point in the use flow.

Furthermore, these documents can take weeks or months to develop. However, in software development a lot can change in the space of a few weeks, let alone a few months, so the protocol author needs to take this into account. The author needs to develop a protocol that is flexible to meet the needs of prospective study changes. The author may therefore need to be involved in various meetings to gain a greater understanding of the plans for the SaMD over the following weeks. This will give them some insight for developing a protocol with moving goalposts.

Participant interpretation of software has been shown to be largely different from hardware and this must be taken into account when developing the study script as well.

Participant Interpretation of Software Versus Hardware

Users interact with software completely differently from hardware. Imagine you are given a comprehensive blueprint of a house. Quite easily, you could see all the rooms and understand the design of the house. Now imagine you were placed at the front door of a house you've never been into and asked to find the bathroom on your first attempt. Would you be able to find the bathroom on your first attempt? Maybe not!

In late-stage usability studies, participants are traditionally given one attempt to get something correct, which makes sense if you have the blueprints (in this case, a physical product and all components) but not so much if you have no idea what's inside – looking at the log-in screen for software does not indicate the internal functionality that is waiting. So, how does one comply with usability engineering requirements and also give users a fair chance at using the product? One answer is to build in some exploratory time with the app to give participants an opportunity to become familiar with the "inside of the house". Ensure that you build this into the most realistic portion of the session – typically this is once the user has logged in for the first time.

Also, key to late-stage usability testing are the success and failure criteria for each isolated task. Hardware usually has a very limited number of logical actions, whilst software has more, and the list grows greater with the more features that are included in the software. For example, to use a pen injector a user must remove the cap. They can either remove the cap correctly, not remove it at all or remove it in such a way that it damages the device. This is a limited scope of logical actions. However, with software a user could click the right option or one of several incorrect options. Once they have made a choice, they are faced with the opportunity to click the right option again or several incorrect options. Recording all the missteps generates a lot of data, so success and failure criteria need to

be designed to encompass an entire activity, rather than the sub-tasks that contribute to the overall activity. This option is only appropriate when it reflects the context of use – if there are sub-tasks that can have effects later in use, these tasks would need to be assessed independently.

SUMMARY

So, to drive effective usability engineering for software, make sure to determine early on whether it is indeed software **in** a medical device, software **as** a medical device or simply software, by developing an intended use statement. Once you have this, consider possible risk categories for software and use this to help understand what class of device you are developing. Finally, use this knowledge to tailor the usability engineering effort to meet the needs of the software development process, remembering to make sure that your study protocols are tailored to using software rather than hardware.

ABOUT THE COMPANY

Harvey Medical is a consultancy providing services in human factors and market research for medical devices and combination products. The company has an in-house multidisciplinary team of human factors and market research specialists, providing research services that cover the entire product development cycle. This ensures that, in human factors studies, Harvey Medical always has a commercially sensitive mindset, whilst it ensures product safety and usability is at the forefront when conducting market research studies.

REFERENCES

1. *"Software as a Medical Device (SaMD): Key Definitions". IMDRF, Dec 9, 2013.*
2. *"Software as a Medical Device: Possible Framework for Risk Categorisation and Corresponding Considerations". IMDRF, Sep 18, 2014.*

ABOUT THE AUTHOR

Natalie Shortt has worked exclusively within usability engineering for medical devices and combination products for over six years and prior to that completed a BSc in Human Factors (Ergonomics) at Loughborough University (UK). She is the principal specialist at Harvey Medical, championing all work related to the regulatory requirements for usability engineering. SaMD is a particular interest for Ms Shortt, recognising the growing number of healthcare software platforms and unique challenges that come with the usability engineering process for software compared with hardware.

INTERVIEW

In this exclusive interview with ONdrugDelivery, Mr Guillet discusses Mallya, Biocorp's connected clip-on for pen injectors, including Mallya's successful launch in multiple countries this year, the factors that have played into Mallya's success, and the future for Mallya, Biocorp and connectivity in the drug delivery industry.

ARNAUD GUILLET

BIOCORP

Arnaud Guillet is Vice-President, Business Development at Biocorp, in charge of finding partnerships and licence opportunities for Biocorp's range of connected devices. Previously, Mr Guillet worked for a healthcare consulting firm with a strong focus on connected health strategies for pharma and insurance companies, and he has additional past experience in the pharmaceutical industry with Sanofi (Paris, France) and the insurance industry with AXA (Paris, France). He graduated from HEC Paris (France), a major European business school.

"Rather than design a whole new device with all this built in, we wanted to capture that data with a wide variety of different pens, which means dealing with a variety of designs and geometries – and we've achieved it with a single technology that leverages electromagnetic sensing technology."

Q Regular readers will likely already be familiar with Mallya, but as a refresher, please could you provide a brief introduction to Mallya and how it fits into Biocorp's overall offering in the connectivity space?

A At the most basic level, Mallya is a clip-on device that turns regular pen injectors into a connected solution (Figure 1). Mallya captures the dosage, and time and date stamps each time the injector is used, with the highest level of accuracy. It can differentiate priming from an actual injection, and confirm that the dose selected was actually triggered by the patient. However, rather than design a whole new device with all this built in, we wanted to capture that data with a wide variety of different pens, which means dealing with a variety of designs and geometries – and we've achieved it with a single technology that leverages electromagnetic sensing technology. Mallya is able to capture the critical information we want on various lines of pen injectors and send that via Bluetooth to a companion app or other related software.

Biocorp's goal here is to position itself as the leading player for solutions that bring connectivity to regular drug delivery devices. The central principle of the add-on approach is that it produces easy-to-use, reliable and cost-effective solutions to connect drug delivery devices. Mallya is Biocorp's top add-on product, but we have two other products that really illustrate this.

The first one is Injay, which is a solution to bring connectivity to regular prefilled syringes (PFSs). Injay is, in essence, a combination of two components: a customised piston rod with a near field communication (NFC) tag for storing product info and a customised finger flange featuring an activator for detecting a complete injection. So, in practice, Injay records the key product information, such as drug concentration, batch number and expiry date, and confirms that the injection has been completed. The data can then be time-stamped and transferred to a smartphone via NFC. We have also developed a variant of this technology that is compatible with PFS equipped with needle safety systems, keeping the same simplicity and value proposal.

Figure 1: Biocorp's Mallya, a connected Bluetooth add-on device for pen injectors, which was commercially launched for diabetes in 2021.

Looking at a completely different delivery route, another example is Biocorp's Inspair device, which is a smart cap for pressurised metered dose inhalers (pMDIs). With Inspair, we not only collect data on the actuation of the device with time and date, but we also want to collect information on the quality of the inhalation technique – using a pMDI correctly frequently proves to be difficult for patients, so if we can give them real, tangible feedback on their technique that's hugely valuable. Specifically, it's co-ordinating actuating the device with their inhalation that patients tend to struggle with, which has a major impact on the efficacy of the device if not done exactly right. We collect this information and send it to a mobile app so that patients can review it and, if they want to, share it with their HCP.

"We have to make it smart, make it easy and make it commercially viable, all while ensuring that it's acceptable for users as well."

These two products are not commercialised yet, but are in a mature stage of development and we care getting good traction from the market.

At Biocorp we develop one specific device for one specific area. While there are some transferable ideas, you have to approach each device and mechanism on its own terms; with pen injectors, for example, we know that we need to collect accurate dosage information with an exact time and date because this information is critical for insulin management – you have to follow your units carefully, so this is a key functionality Mallya focuses on. Whereas, with Injay and PFSs, recording the exact dose delivered doesn't really matter – PFSs contain a single fixed dose, so the question is whether you fully inject it or not.

These specific characteristics also impact the choice of connectivity technology we use for each device. For instance, Mallya uses Bluetooth Low Energy (BLE), which is relatively expensive when compared with its peers. However, because Mallya is designed to be transferred between disposable pen injectors for two years or more, BLE is actually the cost-effective option. Injay, on the other hand, uses NFC because it's cheap and incredibly simple to integrate into a PFS. So, as you can see, it's not always the same recipe; we have to make it smart, make it easy and make it commercially viable, all while ensuring that it's acceptable for users as well. For instance, making Injay something you swap between devices every time is a no-go. It's one thing with a pen injector which you'll use multiple times, but with a one-and-done PFS this is not going to work.

"2021 has been the launch year for Mallya in the diabetes field, which is massive – we're hitting the market in both Europe and the rest of the world."

Q Looking back at 2021, it's been a busy year for Mallya, and an incredibly successful one, with major deals both in diabetes and other areas. Can you give us a rundown of the year's Mallya highlights?

A First of all, 2021 has been the launch year for Mallya in the diabetes field, which is massive – we're hitting the market in both Europe and the rest of the world. I'd say one of my highlights there was the initial launch of Mallya back in May with Roche Diabetes Care France, our local distributor. Mallya became available in French pharmacies and connected to the Gluci-chek app, delivering a really great service to patients, who could their insulin injection data from their Mallya, their glucose data from their Roche Accu-Chek device and see it all together in their Gluci-chek app. It was a very exciting launch with a strong value proposal for patients, and we had a great partner in Roche Diabetes Care.

Another highlight was the Taiwan launch with Sanofi. In this case, we were leveraging the Health2Sync platform, which is a famous diabetes management platform that's already widely used in Asia – specifically in Taiwan, with hundreds of thousands of users. The app is well implemented in clinics and hospitals, so we launched Mallya connected to their platform, and we already have a lot of patients on board, communicating with their doctors on a daily basis to analyse the data and receive recommendations.

These launches have also been supported by collaboration with software partners, which is one of the things we really wanted to have in place. We don't plan to reinvent the wheel, there are already a number of great software platforms in the diabetes space that are used by patients on a daily basis, so we really wanted to integrate Mallya with these existing platforms. We initiated this process with AmalgamRx last year and have reinforced our netowrk this year through integrations with Health2Sync, which I mentioned before, and Social Diabetes, which is very good in Europe and Latin America and features the SmartBolusCalculator, which is a very helpful tool for patients. With these two integrations, we have the potential to reach nearly one million users. Of course, that's not going to materialise overnight, but we have a step-by-step approach in place and the potential is there, which is really exciting.

And then there are the great partnerships we've made with major insulin manufacturers this year. We've strengthened our relationship with Sanofi and made progress on specific development of Mallya for its pens, which is going really well, to the point that we're expecting a lot of launches in the upcoming months. We've also signed a deal with Novo Nordisk to adapt Mallya for its FlexTouch pen, which is a very specific pen requiring a totally new approach, and we're partnering up with Novo Nordisk to develop it further and push it to market.

The last very important highlight of 2021 was our first major partnership outside of diabetes. We've partnered with Merck to develop Mallya for its growth hormone applications, which is very exciting because Merck is a pioneer in the connected drug delivery device area. It has been very ambitious with its connectivity strategy – EasyPod Connect launched a few years ago, which is really early in the connectivity space. Merck has real knowledge, expertise and

"First and foremost, I think that the user-friendliness is an obvious factor. But I think that, if we look back and compare Mallya with its peer competitors, the key to Mallya's success on the device side is its focus on one key function – the dosage timestamp."

understanding when it comes to patient needs and connectivity, so it's a privilege to work with the company on a solution for its growth hormone applications. We're very excited about this partnership, and I think it's going to be a massive help for patients and HCPs. We also have intense internal discussions and active programmes going on in other therapeutic areas outside pen injectors that I'm really excited about, but I'm not able to disclose any details on those just yet.

Q What do you think are the features of Mallya that explain this success?

A First and foremost, I think that the user-friendliness is an obvious factor. But I think that, if we look back and compare Mallya with its peer competitors, the key to Mallya's success on the device side is its focus on one key function – the dosage timestamp. It's tempting to try and cram in as much functionality as you can think of, for example maybe I want the temperature, and I also want the angle of injection, and then there's always another thing and another and another. Instead, we sat ourselves down and asked, "What exactly do we want to achieve here?" The answer to which is that we want to help patients keep track of their injection data, and what really matters there is what dose is injected at what time, so we focused on just capturing that, and did it very simply.

The result of this approach is that, for pharma companies, implementation of Mallya doesn't require any modification of their regulatory dossier or their pen and, for patients, there's no modification to the user process. Once you attach Mallya and pair it all with your phone, there's no more you need to do, it's totally passive, totally effortless for the patient. With that key functionality and simplicity, we can really work on the user-friendliness. That's really the key, I think, Mallya does one thing very simply and very well.

Of course, in Mallya's case doing "one thing very well" means measuring the injected dose very accurately, which is where we leverage the magnetic technology, because it provides, by far, the highest level of accuracy. Using this technology, we've reached very close to 100% accuracy, which has been demonstrated through verification testing. It's extremely reliable and reputable technology that has made us successful with benchmarking, which I think has been a significant factor for the companies who've partnered with us. Really, it's a key element for all stakeholders, pharma partners, patients and, of course, HCPs – if they're going to base healthcare recommendations off the data Mallya is providing, it absolutely has to be accurate. Add in the user-friendliness and simplicity we discussed before, and I think you have a good picture of why the market has really embraced Mallya.

Then there's also the compatibility – Mallya is easily replicable from one pen to another. Of course, you have to adapt to the different geometries of the pens, the specific movements of the knob, that sort of thing, but we always have a solution for that.

> "With Mallya, we brought our own software solution, which was a just a basic mobile app, but we built the system so that it could integrate very quickly with any partner's system directly and flawlessly."

What never changes is that guarantee of accuracy, the principle of detection using magnetic sensing technology. Through all the programmes we've worked on, we've pretty much seen all the different form factors, which means we've developed a really solid understanding of all the various pen injector mechanics and we can transfer the Mallya technology easily from one to another and provide the same guarantee of accuracy.

Q How about on the software side of things? Can you give us some insight into what the demands are on that aspect of connectivity, and which stakeholders are driving it?

A Here my thinking is mostly defined by the diabetes sector, which is where our focus has been for the launch of Mallya. I would say that interoperability and flexibility are the things you really have to deliver. So, with Mallya, we brought our own software solution, which was a just a basic mobile app, but we built the system so that it could integrate very quickly with any partner's system directly and flawlessly. This approach made sure that we didn't cut ourselves off from opportunities just because we wanted to push our own software. As I mentioned before, there are plenty of really good software platforms already in use in the diabetes space. Instead, when we talked to our partners, we could say that we have some assets that they could leverage if they wanted to, but if they had their own system we could integrate with it – we can propose our system, but we never push it. We don't present Mallya as a device-and-software package that's all or nothing; we're always open to integration with other software. With diabetes in particular, the software market is both well established and crowded, so we're focusing development of our own assets on other therapeutic areas where partners are less likely to have their own system already set and decided upon.

Figure 2: With its successful commercial launch, Mallya is now in the hands of patients as part of their day-to-day lives.

As for which stakeholders have the most influence, it really depends on the system. Sometimes you'll have a pharma company that has invested a lot in its own internal platforms and wants to leverage these assets, and so they ask us to integrate with their assets specifically. This is usually as part of their own business strategy priorities – control of the data and the value chain – which means Mallya needs to be integrated into their system. Most of the time, however, in the diabetes space in particular but also more generally, it's really driven by the patients and the users, which means working with the solution best positioned in the specific market you're looking at. Health management software is most widely used by patients and HCPs, so the solution they prefer is the best one to pick.

A perfect example is Taiwan. Taiwan's best solution is, by far, Health2Sync. It's well connected with both clinics and patients, so we leveraged that and it's proven to be successful for the three parties involved: Sanofi, Biocorp and Health2Sync itself.

Q Ultimately, drug delivery device development is about patients, and adding connectivity is no exception to this. Can you share any feedback from patients on Mallya, or from studies that have illustrated how patients respond to and engage with Mallya?

A We're actually at a really good point to assess this because, now that Mallya's been launched, it's in the hands of patients out there in the real world (Figure 2). Before launch, all we had were results from our human factors studies that we collected as part of our typical development process, but those had already given us some interesting information regarding the absence of risk in using the device together with the pen and how well patients were able to understand how to install it, pair it, use it and understand the feedback it generated. That was very positive information for us, it was something we really focused on with Mallya. However, when we reached the market, we weren't dealing with clinical or supervised environments, instead we're dealing with thousands of patients in a whole host of settings.

So, with Mallya now out there in the world, we've received a lot of very valuable feedback, including testimony from patients and beta testers, also influencers have posted reviews of Mallya on the internet, including on social networks and YouTube (Figure 3). We've been very positively surprised by what we've been getting back, because Mallya is fairly new in terms of what it does and how it's used, but what we're getting back is that this was something that patients have been looking for and they specifically appreciate the fact that Mallya is interoperable with other devices. For example, a key point has been the ability for patients to combine their glucose data with insulin readings, enabling them to have meaningful conversations with their HCP. It's always a concern when you market an add-on device whether it's going to be an issue for patients to put on, take off and put back on, but the feedback we're seeing from patients really confirms the fact that we're creating value for them (Box 1).

"We've been very positively surprised by what we've been getting back, because Mallya is fairly new in terms of what it does and how it's used, but what we're getting back is that this was something that patients have been looking for and they specifically appreciate the fact that Mallya is interoperable with other devices."

Figure 3: The diabetic community has embraced Mallya, with influencers such as Ines Nerina (pictured) discussing Mallya and posting reviews online.

BOX 1: FEEDBACK FROM PATIENTS

Quotes from Mallya users, as posted on Biocorp's website:

"I almost regret not using an insulin pen anymore."
– Virginie, 29 (Type 1)

"I am far less stressed since I've been using Mallya."
– Serge, 62 (Type 2)

"I really like the device." – Laura, 24 (Type 1)

"This new medical device does most of the work for me."
– Mélanie, 35 (Gestational)

And testimony from lifestyle blogger Ines Nerina:

"I have been living with Type 1 diabetes for five years and I have tested many medical devices designed and developed for the management of diabetes. Today, I can say that Mallya is by far a revelation – everything is easier with Mallya! Indeed, one of the most difficult tasks in the routine of a patient living with diabetes is to remember what time the injection has been made, how many units were selected for injection and sometimes whether you have already done your insulin injection or not. This smart device is totally changing the lives of patients with diabetes and my only regret is that I didn't discover Mallya sooner."

There's one specific example I really love – we did a clinical study in the UK with Dr Edward Holloway from the Croydon Health Institute, and he made a presentation about the solution. He said that Mallya enabled him to spot specific gaps in the treatment of a patient that he was following, whose diabetes wasn't well controlled and they couldn't figure out why. So they equipped Mallya, and Dr Holloway could see the patterns and he found some issue with this patient's behaviour related to specific issues, which he was able to discuss with them and improve the management of their diabetes.

That study was first conducted in the context of covid-19, so you can imagine how hard it was, but getting that kind of feedback was a really great motivator for us. In terms of direct feedback to us, with the exception of business-to-business distribution, the customer support is all handled by our distributor, but it's been very quiet in terms of complaints. I would say that wherever we have had issues, we've had a good solution and good troubleshooting to identify them, so we've be able to then solve these issues very quickly. Overall, we are very positive, although we need to be careful, as it's only the first 1,000 patients, and the more patients we have, the more challenges we face, but still it's very encouraging I would say.

Q We've discussed 2021, so now let's turn to the future. What's next for Mallya in 2022 and beyond?

A That's a great question. Let's focus on Mallya first, when it was first launched it convinced us that we've got the right approach, it got a really positive response, but now it's a matter of increasing general awareness of smart pens, including with respect to getting reimbursements. I think this is really the roadmap for mass adoption because the value of smart pens wasn't obvious a few years ago, but now there are more and more publications around this value and there's more and more need to hear directly from patients and HCPs about it. We need to actively support these efforts, but I think this awareness is out there, and growing. Overall, it's a really positive place to be.

The second part to building a strong roadmap for mass adoption is reimbursements. As such, we are already working with our partners – our distributors, pharma companies and software partners – to build the relevant ecosystem to optimise the user experience, and therefore the value of the product, demonstrating clinical benefits in collaboration with HCPs. Reimbursement options for digital health solutions are maturing in various markets, such as with new current procedural terminology (CPT) codes in the US, digital health applications (DiGA) framework in Germany and the *ETAPES* programme in France, opening new possibilities for Mallya.

Q Thinking about potential markets, currently the nature of connected technology tends to restrict connected devices to wealthier and more developed countries. So, taking Mallya as the example, do you think that, as time goes on, production factors might mean that the price point can drop to the point that other markets, such as China and India, open up?

A That's a very good question. In China, we're also dealing with specific cultural aspects. Sticking with diabetes as the example, there's a lot of education and awareness you need to put in place with patients first, such as on the importance of adjusting your dose based on your glucose. Then we need to adapt to the specifics of the local digital ecosystem. For instance, in China, everything goes through WeChat, so connectivity with that system will be a key factor, plus you need to integrate with local hospitals and clinics. That's a challenge. On top of that, there's a lot of pressure on the price of insulin in China right now. That being said, the needs generated by diabetes don't change with geography, plus China is a big market with a very digital-friendly population, so it's not all negative, we just need to go steadily, step by step.

> "I think the first thing we need to do now is prepare for mass production of Mallya. We have the right products and are well positioned with strong partners, so we've got a really strong footing for true mass production of Mallya."

Thinking about price points, as I mentioned, the price of insulin in China is an issue so, we need to leverage everything that we can to decrease this price point and optimise it, as well as doing the same for the device itself. This is also required in India, and potentially even more so. It's something we're currently studying.

Q Lastly, let's broaden the scope a little. Thinking about Biocorp as a whole, and connected drug delivery in general, what do you see coming up on the horizon?

A For Biocorp, I think the first thing we need to do now is prepare for mass production of Mallya. We have the right products and are well positioned with strong partners, so we've got a really strong footing for true mass production of Mallya. I would say that's the big industrial challenge ahead of us.

Talking more broadly, what we want is to transition Biocorp a bit more from being seen as just a device provider to a full solution provider, meaning device plus digital ecosystem. That doesn't mean we're pivoting to saying you have to use our system, we're still committed to integration, however, our pharma partners expect us to bring a solution to the table. It's about being able to deliver on our partners' requirements, sometimes they have their own digital solution, sometimes they don't and sometimes they're somewhere in the middle and have some local things that they want to leverage at a global level, and they want us to bring an understanding of end-to-end systems and how to take a project from A to Z in the digital space. It is very important to us to be able to cater to all of these. We already have a good position with device players where we work with them from design to manufacturing. I think we should have the same approach and mindset for connected solutions, going from the device design to when the data touches the digital ecosystem, mobile app or web client. That's what we're aiming for, and we have the expertise and the ability to achieve it. There's also potential in some markets for us to go agnostic and go business-to-business-to-consumer or directly business-to-consumer.

As for connectivity in the industry overall? I think it's very interesting what's happening right now. I think that covid-19 has really changed the game because there are a lot of patients who, under normal circumstances, were never going to use any kind of

telemedicine service, connected device or mobile app to monitor their disease. However, as covid-19 forced the issue, they've tried out this sort of device and, in most cases, judging by the data that we collect, they actually enjoy it and find it a reliable benefit.

For chronic disease management, there are many valuable connected solutions out there, it's just a question now of scaling up, by demonstrating clinical benefits and obtaining reimbursements.

> "The challenge for the industry is really to educate payers and market access people so that they can understand the real value of these digital solutions and how we should evaluate them, the digital ecosystem as a whole and its specific components."

I think that the challenge for the industry is really to educate payers and market access people so that they can understand the real value of these digital solutions and how we should evaluate them, the digital ecosystem as a whole and its specific components. There are a number of questions that need answers in this area; for example, what's an appropriate reimbursement for the digital ecosystem? What's the reimbursement for the Mallya components? There are programmes in the pilot phase in some countries that are now going full speed. For example, in France there is the *ETAPES* programme that I mentioned earlier, which is set to be transferred to a permanent initiative. So it's definitely going there. Earlier, I mentioned the US CPT codes, which are very exciting for the industry. I think we're at a moment where things are really starting to take shape and that will open new doors.

Diabetes has definitely been a driver, and will continue to be, because of all the context in this field. But the whole injector field, I believe, will follow behind because of various factors. If you think about it, we have very expensive drugs combined with adherence issues, so payers want to look into what is taken, or not in some cases, and how effective these drugs are in real-life settings. I'm sure this will also come up in respiratory and nasal delivery. There are a lot of areas where I think the theoretical benefits are there, sometimes having been demonstrated in trials, but now we need to do the hard work of building a body of real-world empirical data.

ABOUT THE COMPANY

Recognised for its expertise in the development and manufacture of medical devices and delivery systems, Biocorp has acquired a leading position in the connected medical device market, thanks to Mallya. This intelligent sensor for insulin injection pens allows reliable monitoring of injected doses and thus offers better compliance in the treatment of diabetics. Available for sale since 2020, Mallya spearheads Biocorp's product portfolio of innovative connected solutions.

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Mallya
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YPSOMED
SELFCARE SOLUTIONS

YPSOMATE ON – GO FOR SIMPLY CONNECTED

In this article, Philippe Müller, Innovation & Business Development Manager, and Silas Mächler, Technical Leader Frontend-Innovation, both of Ypsomed, discuss the benefits of integrated digital therapy management systems and the role of YpsoMate On – the newest addition to Ypsomed's connected device portfolio.

Medication non-adherence is one of the principal reasons why patients do not achieve expected treatment outcomes. Solving this challenge is a major goal for healthcare organisations. However, studies indicate that 50–60% of chronically treated patients still miss doses, take the wrong dose or discontinue treatment in the first year.[1]

Medication non-adherence is the result of a complex interaction of five sets of factors, as illustrated in Figure 1:

1. Disease-related factors
2. Socio-economic factors
3. Health-system-related factors
4. Therapy-related factors
5. Patient-related factors.

Accordingly, any intervention to improve adherence needs to target the relevant adherence barrier and be tailored to the specific needs of the individual and therapy context.[2]

Connected injection devices, in combination with digital health interventions, enable new forms of integrated device-and-digital solutions to address the challenge of medication non-adherence and non-persistence, thereby aiming to improve treatment outcomes.

VALUE ADD OF CONNECTED INJECTION DEVICES FOR THERAPY MANAGEMENT

The benefits of connected injection devices fall into three categories: advanced user guidance, treatment evaluation and intervention design, as illustrated in Figure 2.

First, connected devices provide additional visible and/or audible feedback directly on the device to guide the user through the injection process. Specific sensors can detect use errors, and smart labelling enables the connected device to check drug expiry date and potential

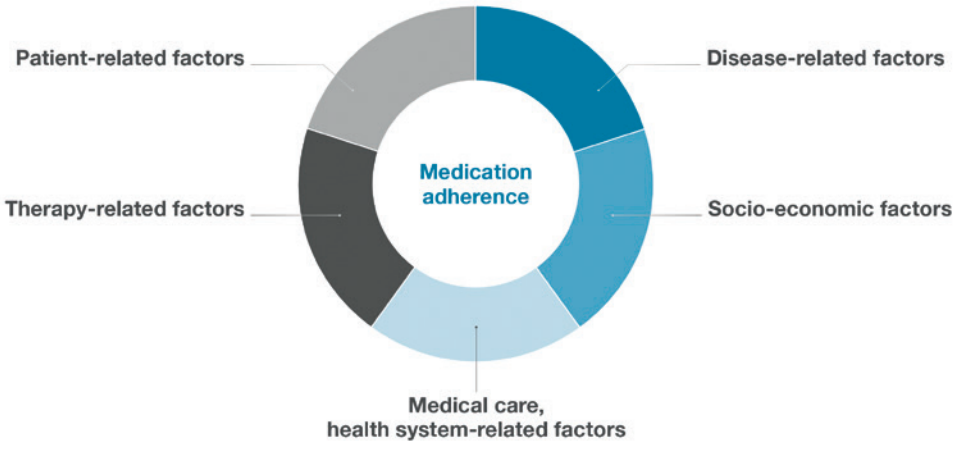

Figure 1: Five dimensions of medication adherence.

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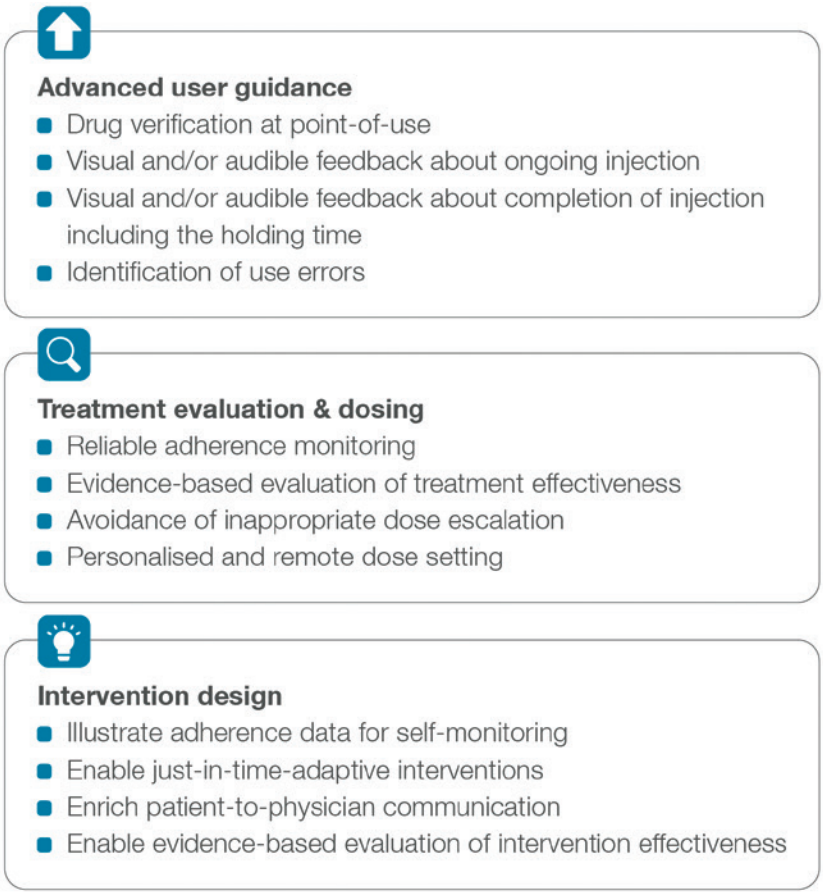

Figure 2: Value of connected devices for therapy management.

recall. Second, injection data provide important information to healthcare professionals for treatment effectiveness evaluation. Several studies have shown that self-reported adherence data is upward biased as patients overestimate their adherence, leading to inappropriate dose escalation by the healthcare professional.[3] Having precise electronic adherence data is key to personalising the treatment schedule and dosage.[4,5]

Third, injection data can be used for intervention design, such as self-monitoring, prompts and rewards to reinforce adherent behaviour. Interestingly, studies indicate that just capturing and displaying adherence data for self-monitoring has a positive effect on medication adherence, for example in growth hormone treatment.[6] Further, feeding injection data into digital therapeutics solutions allows for timely and targeted interventions.

These just-in-time adaptive interventions aim to provide the right type and amount of support, at the right time, by adapting to an individual's changing internal and contextual state.[7] The contextual state, for example, includes the detection of use errors by the connected device that then triggers a push notification adapted to the type of use error and the specific user profile. Another example is providing positive feedback or a reward directly after a successful injection. Accordingly, ongoing data collection is required to decide whether the individual requires support, what type of support and whether there is potential to change behaviour.[7]

"Connected device data can serve as a key input for digital therapy management applications."

"Ongoing data collection is required to decide whether the individual requires support, what type of support and whether there is potential to change behaviour."

As illustrated in Figure 3, connected injection devices may play a key role for just-in-time adaptive interventions as they report an individual's state in terms of therapy adherence and correct use of the device, and serve as an interface to directly communicate with the user via visual or audible feedback. As such, connected device data can serve as a key input for digital therapy management applications. In addition, the injection data points allow for an evidence-based evaluation of intervention effectiveness in terms of improved medication adherence and persistence.

Looking ahead, new connected device technologies are emerging that focus even more on user-centric design to ensure they are easy and intuitive to use. To achieve this aim, Ypsomed has been working on the development of YpsoMate On, the first prefilled connected autoinjector.

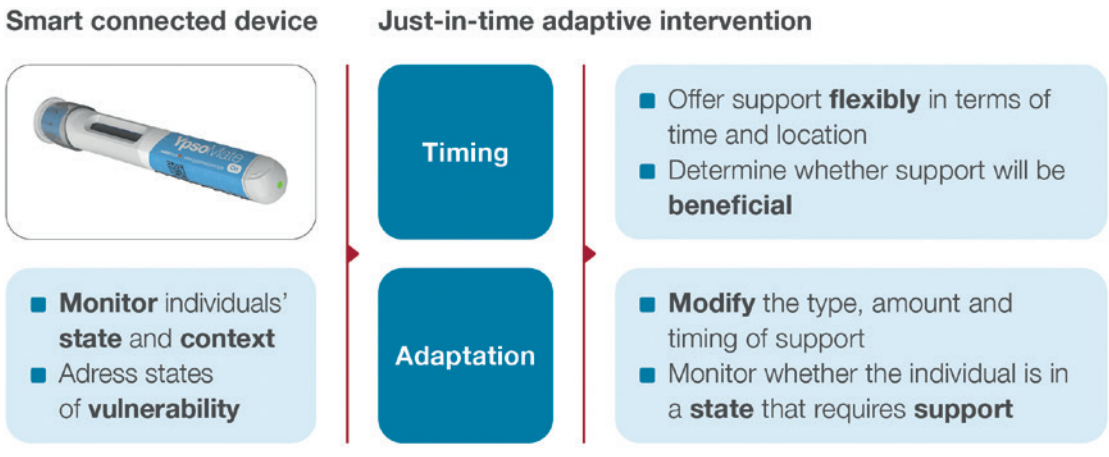

Figure 3: Leveraging injection data for just-in-time adaptive interventions.

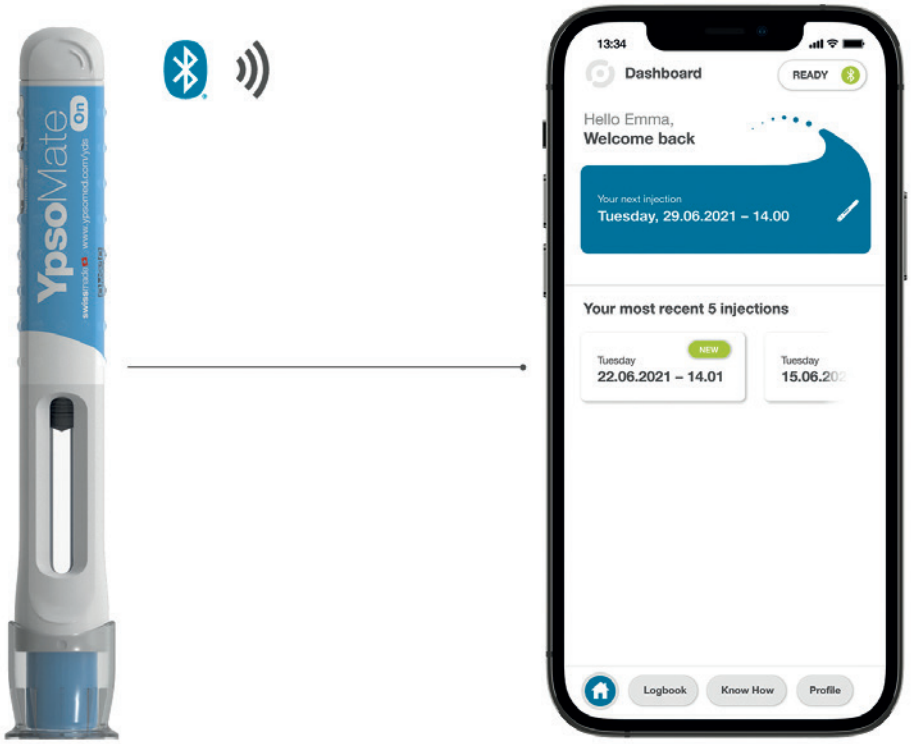

Figure 4: YpsoMate On – the prefilled connected autoinjector.

> "YpsoMate On is the world's first prefilled autoinjector with integrated connectivity that automatically logs injections on the user's therapy management app."

YPSOMATE ON – GO FOR SIMPLY CONNECTED

YpsoMate On is the newest addition to Ypsomed's connected device portfolio. It is the world's first prefilled autoinjector with integrated connectivity that automatically logs injections on the user's therapy management app (Figure 4). This new autoinjector adds connectivity and retains the market-proven two-step handling of the YpsoMate platform. As such, YpsoMate On provides connectivity without compromising ease of use. The key features of YpsoMate On are described below in more detail.

Automated Data Capture and Injection Guidance

YpsoMate On consists of a sensor and electronic module that is built into the top end of the device. The sensor captures the start and end of injection and transfers this data via Bluetooth to the user's smartphone. Furthermore, the LED-based visual feedback allows the user to track the injection progress, including the holding time.

Innovative Device-to-Smartphone Connection Without Pairing

The device-to-smartphone connection is automatically established by Bluetooth proximity measurement, similar to the working principle of covid-19 contact tracing apps. This form of Bluetooth protocol enables secure data transfer without active pairing of the injection device and the smartphone. The device transmits an encrypted report, and the system decides on the validity of the report in the background. If the report is valid, the user receives a new entry in the injection logbook with information about drug product and dosage, as well as time and date of the injection. The injection logbook can then be shared with the healthcare professional and/or caregivers for therapy management and treatment evaluation.

Sustainable Design

YpsoMate On is designed with a focus on separation of the electronics and battery for re-use or recycling. The electronics and battery can be easily detached from the autoinjector, as they are compactly integrated into the top end of the device and do not directly interfere with the inner autoinjector mechanics. The separation process may be performed directly by the user or by a dedicated recycler. Furthermore, YpsoMate On uses sustainable materials and optimisations along the supply chain to minimise the environmental footprint of the device, for example, by using chemically identical bio-based plastics for the majority of the plastic device parts.[8]

Leverage the YpsoMate Platform

YpsoMate On builds on the market-proven YpsoMate platform. It includes the same spring-driven drug delivery mechanism for reliable and effortless injection. The newly added connectivity module includes a sensor to capture the start and end of the injection without requiring any modification to the core drug delivery mechanics. YpsoMate On is therefore compatible with existing YpsoMate manufacturing and end-assembly lines. This allows for rapid scale-up and short time to market. This also allows existing YpsoMate customers to move to a connected autoinjector without significant new investments in final assembly and packaging infrastructure.

YPSOMED'S CONNECTED DEVICE PORTFOLIO TO SERVE DIFFERENT USE CASES

To serve different market needs and use cases, Ypsomed has developed a portfolio of connected injection devices. The portfolio can be divided into two broad device categories:

1. Connected add-ons, such as SmartPilot for YpsoMate
2. Injectors with integrated connectivity, such as YpsoDose and YpsoMate On.

Comparing SmartPilot for YpsoMate with YpsoMate On, there are similarities as well as key differences between the two device categories (Figure 5). SmartPilot is the re-usable connected add-on for YpsoMate. SmartPilot captures injection events, detects use errors and provides comprehensive real-time injection support, including drug authentication at point of use and step-by-step guidance. YpsoMate On provides a narrower feature set, retains the proven two-step device handling and enables automated data capture. Moreover, the device includes LED-based visual feedback signalling ongoing injection and completion of the injection, including the holding time.

SmartPilot and YpsoMate On represent two different device categories and feature sets that target different user needs.

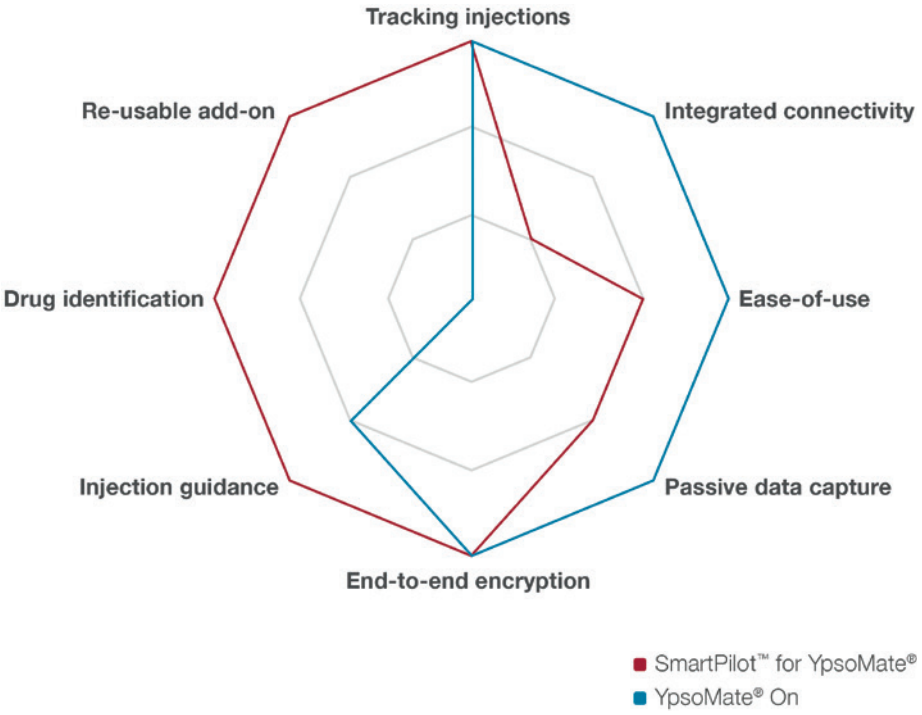

Figure 5: Complementary feature set to serve different patient needs and use cases.

Ultimately, the device choice depends on the intended use of the overall system as well as on the specific user population, injection frequency and other indication-specific factors.

CONCLUSIONS

Integrated digital therapy management systems that consist of connected injection devices, a digital therapeutics app and biomarkers offer great potential to improve medication adherence and, ultimately, therapy outcomes. As such, close collaboration between device manufacturers and digital therapy management providers is needed to design effective just-in-time interventions adapted to the specific needs of the individual.

With YpsoMate On, Ypsomed extends its connected device portfolio with a prefilled autoinjector with integrated connectivity. The key differentiating factor is ease of use as YpsoMate On maintains the two-step handling process. Ypsomed offers a growing portfolio of connected device technologies, including SmartPilot for YpsoMate and the YpsoDose connected patch injector. The optimal device choice depends on the drug product, the intended use and the specific user population. Looking ahead, Ypsomed continues to focus strongly on the user-centric development of next-generation drug delivery devices and services to fulfil the needs of evidence-based digital therapy management systems.

ABOUT THE COMPANY

Ypsomed's comprehensive drug delivery device platforms consist of autoinjectors for prefilled syringes in 1 and 2.25 mL formats, disposable pens for 3 and 1.5 mL cartridges, re-usable pen injectors, ready-to-use prefilled wearable patch injectors and injection devices for drugs in dual-chamber cartridges. Unique click-on needles and infusion sets complement the broad self-injection systems product portfolio.

With over 30 years of experience in the development and manufacture of innovative injection systems, Ypsomed is well equipped to tackle digital healthcare challenges and has strategically invested in the development of connected solutions and therapy-agnostic digital device management services. Anticipating the future needs of patients, pharmaceutical customers, payers and healthcare professionals, Ypsomed moves beyond manufacturing connected sensors. Ypsomed's smart device solutions strive to transform patients' lives by capturing therapy-relevant parameters, processing them to facilitate self-management of chronic diseases, and integrating these insights with third-party digital ecosystems.

The company leverages its in-house capabilities in electronics, software and connectivity for the development of new devices and digital product systems. Ypsomed is ISO 13485 certified and all processes comply with design control and cGMP guidelines with operational QA/QC experts on-site at each location. Ypsomed's US FDA-registered manufacturing facilities are regularly inspected by pharma customers and regulatory agencies to supply devices for global markets including the US, Europe, Japan, China and India.

REFERENCES

1. *Hichborn J et al, "Improving patient adherence through data-driven insights". McKinsey, Dec 14, 2018.*
2. *Sabaté E, "Adherence to long-term therapies: evidence for action". World Health Organization, 2003.*
3. *Guedes VG et al, "Comparing objective and self-reported measures of adherence in haemophilia." Haemophilia, 2019, Vol 25(5), pp 821–830.*
4. *Bittner B et al, (2019). "Connected drug delivery devices to complement drug treatments: potential to facilitate disease management in home setting." Med Devices, 2019, Vol 12, pp 101–127.*
5. *Vrijens B, "Strategy to Monitor Adherence" in Feldman SR et al, "Treatment Adherence in Dermatology" (Feldman SR et al). Springer International Publishing, 2020, pp 13–19.*
6. *Koledova E, Tornincasa V, van Dommelen P, "Analysis of real-world data on growth hormone therapy adherence using a connected injection device". BMC Medical Informatics and Decision Making, 2020, Vol 20(1), pp 1–7.*
7. *Nahum-Shani I et al, "Just-in-Time Adaptive Interventions (JITAIs) in Mobile Health: Key Components and Design Principles for Ongoing Health Behavior Support". Ann Behav Med, 2018, Vol 52(6), pp 446–462.*
8. *Gerner S, Schneider A, "Paving the Way to Zero Carbon Emission Combination Products: Insights From the Ypsomate Zero Case Study". ONdrugDelivery, Issue 112 (Sep/Oct 2020), pp 56–59.*

ABOUT THE AUTHORS

Philippe Müller is Innovation and Business Development Manager at Ypsomed Delivery Systems. His responsibilities include the definition and development of new platform devices and business models, with a particular emphasis on connected device systems. As such, he has been actively involved in the design and development of YpsoMate On – the prefilled connected autoinjector. Mr Müller holds an MSc in Applied Economic Analysis from the University of Bern, Switzerland.

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SELFCARE SOLUTIONS

TRIALS WITHOUT TRIBULATIONS: A PATIENT-CENTRIC, CONNECTED INJECTION DEVICE FOR DECENTRALISED AND HYBRID CLINICAL TRIALS

Here, Rebecca Beck, PhD, Connected Health Innovation Leader for Advanced Drug Delivery Solutions, and Hervé Monchoix, Strategic Innovation Leader, both at BD Medical – Pharmaceutical Systems, Strategic Innovation Group, discuss how stakeholder needs are driving the development of a new, connected injection device from BD, to support decentralised and hybrid clinical trials.

The challenges of clinical trials are well documented. These include growing trial costs and complexity,[1] increased cycle time to database lock,[2] non-adherence to protocol[3] and data quality issues due to labour-intensive data transcription and complex integration processes.[4] Clinical trials also face mounting challenges in recruiting and retaining study participants,[5–7] in part due to the travel and time burdens placed on participants required to get to and from the trial site.

> "The adversity and challenges of the pandemic have catalysed movement towards decentralised clinical trials and their potential to overcome many of the restrictions imposed by covid-19."

These issues were being addressed prior to the advent of the covid-19 pandemic. However, the adversity and challenges of the pandemic have catalysed movement towards decentralised clinical trials (DCTs) and their potential to overcome many of the restrictions imposed by covid-19.[8] Indeed, the impact of the current pandemic on clinical trials has been significant – more than 1,200 clinical trials worldwide were disrupted due to covid-19.[9] Significant decreases in new patients entering trials were observed globally, with decreases as severe as 87–98% in the most affected regions in April 2020, relative to figures from April 2019.[9] However new patient recruitment improved thereafter.[10]

The covid-19 pandemic is considered to have greatly accelerated the move towards DCTs or hybrid decentralised/in-person clinical trials, with many of these gains expected to remain once the pandemic recedes.[8]

While the trend towards DCTs brings many advantages in terms of flexibility for participants, it does heighten the need for high-quality remote data collection – in particular, data related to the timing of drug administration.

To support the successful transition to decentralised clinical trials, BD is developing a new, connected injection device designed to meet the needs of each stakeholder group (participants, trial sponsors and contract research organisations (CROs)) undertaking DCTs or hybrid clinical trials.

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DEVELOPING A CONNECTED INJECTION DEVICE FOR CLINICAL TRIALS

BD is a world leader in injection devices, with billions of products produced each year. Working on connected injection solutions is part of a larger focus at BD on patient-centric solutions. With this in mind, BD is presently developing a connected product capable of capturing and transmitting injection-related data. The device will be an optional upgrade of the BD Ultrasafe Plus™ Passive Needle Guard subcutaneous injection device, and it is intended to support clinical trials. The product under development intends to address the needs of patients, CROs and study sponsors for a safe, easy-to-use self-injection device that automatically captures reliable, high-quality and time-stamped data about the injection event from the patient (who may be self-injecting remotely) to the trial's selected electronic platforms.

> "To inform the development and component definition of a new, connected device for the clinical market, and to increase confidence in stakeholder acceptance, BD undertook both qualitative and quantitative research, including industrial design and field research."

To inform the development and component definition of a new, connected device for the clinical market, and to increase confidence in stakeholder acceptance, BD undertook both qualitative and quantitative research, including industrial design and field research. This research is the result of collaboration between teams at BD, including BD Medical – Pharmaceutical Systems (BDM-PS) and BD Technology and Innovation (BDTI). The goals of this research were divided into the following areas:

- **Product Journey** – Establish the typical clinical product journey relative to the workflow of selected clinical stakeholders (researchers and patients).
- **Concept Acceptance** – Determine stakeholder acceptance of two conceptual workflow impacts.
- **Preferred Workflow** – Determine stakeholder preference of a conceptual connected workflow.

The result of the research-informed design is a connected injection solution comprised of four components: a Bluetooth-enabled injector, a data gateway, a BD Cloud solution application programming interface (API) and access to third-party platforms used for clinical trial data management (Figure 1).

CONTOURS OF THE BD CONNECTED SOLUTION

Connected Injection Device

The connected device will be available as an optional upgrade of the BD UltraSafe Plus™ Passive Needle Guard subcutaneous injection device. Wireless connectivity (Bluetooth Low Energy (BLE)) is assured by a module that is integrated into the plunger rod. This module provides the device ID and injection start and stop event capture. The BD connected plunger rod does not modify device operation and closely aligns with the form factor and ergonomics of the base device. The device requires minimal user intervention and incorporates a reliable, switch-based event capture mechanism. Injection-related data are transmitted directly to a background app on a smartphone, which transfers the data to the BD cloud. Depending on the application, these data can then flow via the gateway device (smartphone, tablet, etc) to the BD cloud and on to another relevant platform used by pharma or CROs.

BD Mobile Application

The app functions on a Bluetooth-enabled mobile device, typically a smartphone or smartphone-like device. The mobile app is being developed to serve as a gateway between the device and the cloud and to timestamp injection-related events received from the connected injection device. It will operate as a background app and require no user interaction (other than to ensure the phone is powered on and in range and BLE is enabled) and has no user-facing screens. It therefore will relieve the user from any additional steps.

BD Cloud

The BD cloud database will automatically receive the uploaded data from the app/mobile device. Data include the device ID, a timestamp of injection start and a timestamp of injection completion.

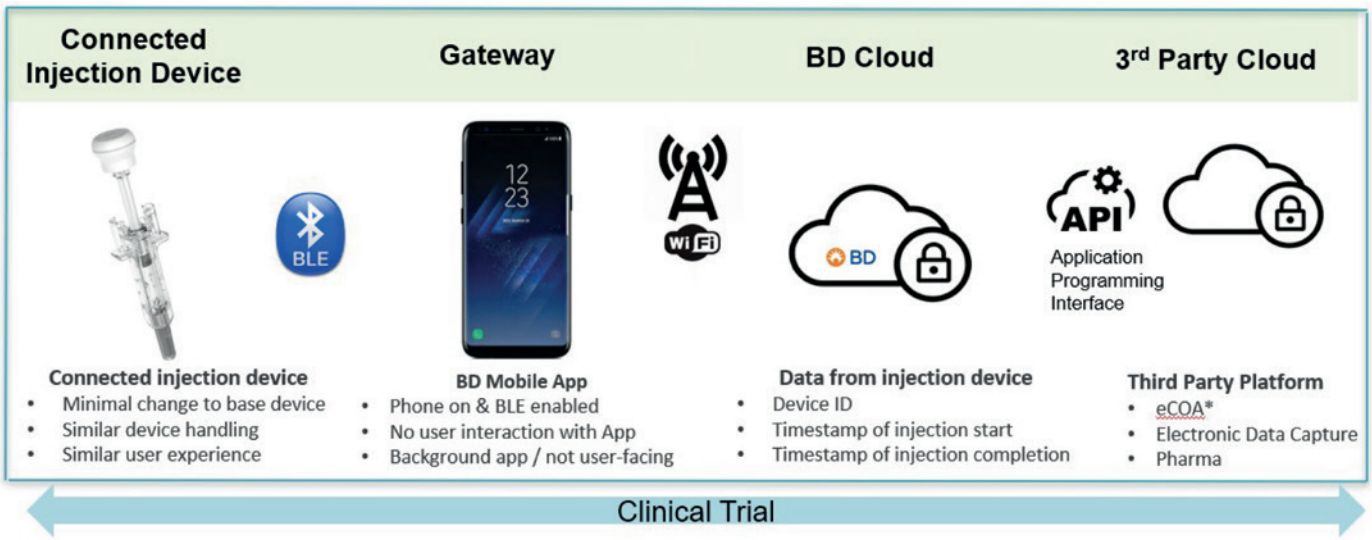

Figure 1: Contours of the BD Connected Solution. Informed by the research output, BD developed the solution architecture to match the needs of key stakeholders involved in clinical trials. eCOA: electronic Clinical Outcome Assessment tool.

Data Collection and Third-Party Platforms

The three data points will flow from the device to the background mobile app and on to the cloud-based database. From there, the data can transfer to a third-party platform, be it an electronic clinical outcome assessment (eCOA) tool, an electronic data capture system or directly to a pharma platform, via APIs.

DESIGN INFORMED BY RESEARCH

BD conducted both quantitative and qualitative research studies.[3,11] The quantitative study comprised an online, double-blind survey with responses from 43 professionals working in the pharmaceutical and biotech industries, as well as those in CROs and eCOA providers. The qualitative study comprised one-on-one, in-depth interviews with clinical researchers and patients with experience in clinical trials involving subcutaneous drug delivery. These interviews were conducted via video link and lasted about 90 minutes each. Six clinical researchers and four patients were interviewed.

Study participants perceived several benefits of the proposed connected injection device solution for clinical trials, such as the elimination of manual data entry, avoidance of transcription errors, enhanced data quality and automatic data transfer. However, timely detection of deviation from protocol was perceived to be the most valuable benefit, addressing the biggest pain point recorded by respondents.

Study participants were asked to identify the most important data to be captured. The start time of the injection, device ID and the time of injection completion were cited as the most important data to be captured by a connected injection device within the context of clinical trials. Concerning device handling, participants emphasised that the connected solution should not bring with it any burdensome additional steps, that the form factor and function of the connected solution should closely align with that of the base device, and that the user should not be required to handle or interact with the phone at the time of injection.

PLUNGER ACTIVATION FORCE EQUIVALENCY

BD undertook a series of lab-based tests[12] to confirm that the connected solution was fully compatible with the base device. Preliminary results of the mechanical testing indicate comparable performance of the BD Ultrasafe Plus™ Passive Needle Guard with the connected and standard plunger rods. The evaluation confirmed complete dose delivery, successful triggering of the safety mechanism and equivalence in plunger activation force. The success of event capture and data transfer were also tested and found to be functioning as expected (Figure 2).

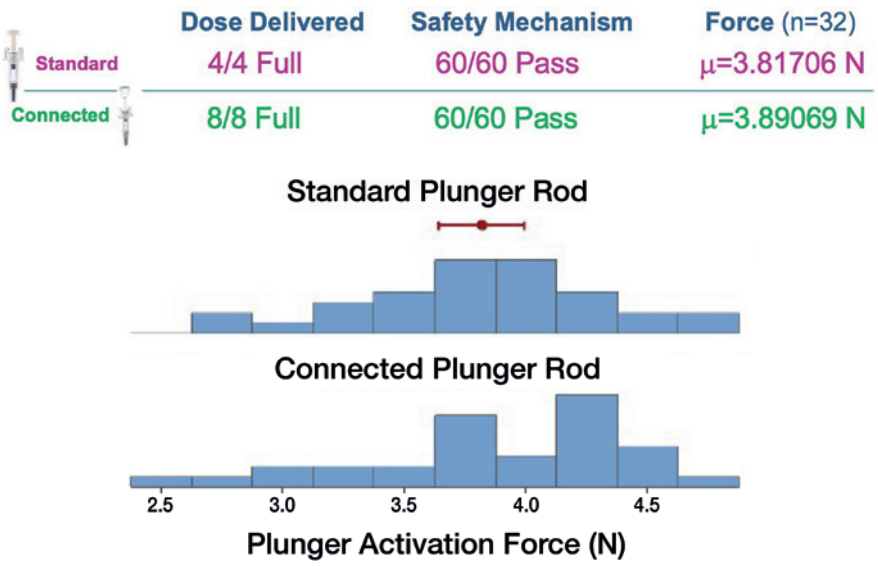

Figure 2: Preliminary results of mechanical testing indicate comparable performance of the BD Ultrasafe Plus™ Passive Needle Guard with standard (top) and connected (bottom) plunger rods.[12]

HUMAN FACTORS EVALUATION

BD is currently undertaking a human factors assessment to evaluate the usability and functionality of the connected solution. Outputs from this study will support and inform future development. The study includes both on-site and home-based simulated injections. This proof-of-concept study will provide an opportunity to gather detailed observations and user feedback on the handling and use of the device, and to assess the automatically captured injection data.

FINDINGS OF BD RESEARCH ALIGN WITH A LARGE, INDUSTRY STUDY

In a study undertaken by Informa Pharma Intelligence (London, UK) on behalf of Oracle Health Sciences (Austin, TX, US),[13] participants were asked to identify what they consider to be the main challenges in adopting decentralised trials in their organisations. A total of 252 professionals involved in clinical trials at biopharmaceutical companies, medical device companies and CROs responded to the online survey. The top three challenges identified by the study were:

- Patient monitoring and engagement
- Ensuring data reliability and quality
- Data collection.

The connected injection device solution that BD proposes would address these fundamental challenges identified in this independent study. By providing reliable, automatic and real-time data capture, clinical researchers could remotely monitor compliance and engagement, and quickly detect and respond to any deviation from protocol. This valuable and timely insight into patient behaviour could be employed to strengthen engagement. The challenge of collecting high quality drug-administration data would also be addressed as the injection-related data would automatically be captured, time-stamped and securely transferred and stored.

> "BD is currently undertaking a human factors assessment to evaluate the usability and functionality of the connected solution. Outputs from this study will support and inform future development."

LOOKING AHEAD

BD is actively responding to the challenges and needs surrounding connected solutions for injection devices, and is working to facilitate digitally enabled clinical trials. BD is presently identifying partnerships with pharma to run pilot studies.

ABOUT THE COMPANY

BD is a large, diverse, global medical technology company. Its Medical Pharmaceutical Systems division is the world's largest syringe manufacturer. It offers prefilled syringes, self-injection systems, safety and shielding solutions, needle technologies and associated pharma services.

REFERENCES

1. *Getz KA, Campo RA, "Trial watch: Trends in clinical trial design complexity". Nat Rev Drug Discov, 2017, Vol 16(5), p 307.*
2. *"Industry Survey Reveals Clinical Data Management Delays Are Slowing Trial Completion". PDF, Veeva, Sep 21, 2017.*
3. *Delmas I, "Final Report: Value assessment of a subcutaneous connected device". Internal Study, 2020, GLG Projects.*
4. *Kondo H et al, "Evaluation of Data Errors and Monitoring Activities in a Trial in Japan Using a Risk-Based Approach Including Central Monitoring and Site Risk Assessment". Ther Innov Regul Sci, 2021, Vol 55, pp 841–849.*
5. *Chaudhari N et al, "Recruitment and retention of the participants in clinical trials: Challenges and solutions", Perspect Clin Res, 2020, Vol 11(2), pp 64–69.*
6. *Ross S et al, (1999), "Barriers to Participation in Randomised Controlled Trials: A Systematic Review", J Clin Epidemiol, 1999, Vol 52(12), pp 1143–1156.*
7. *Tudur Smith C et al, "The Trials Methodological Research Agenda: Results from a Priority Setting Exercise", Trials, 2014, Vol 15, Article 32.*
8. *"No place like home? Stepping up the decentralization of clinical trials". McKinsey & Company, June 10, 2021.*
9. *"Covid-19 Pandemic Disrupted More Than 1,200 Clinical Trials: Global Data", Pharmaceutical Technology, March 2, 2021. Accessed August 23, 2021.*
10. *"COVID-19 and Clinical Trials – The Medidata Perspective – Release 9.0". PDF, Medidata, September 21, 2020.*
11. *"Connected Syringe - Research Report". Internal study, 2020, BD.*
12. *Internal BD lab report.*
13. *"The Accelerated Evolution of Clinical Trials in a Pandemic Environment". Research Report by Pharma Intelligence Informa, on behalf of Oracle Health Sciences, Nov, 2020.*

ABOUT THE AUTHORS

Rebecca Beck, PhD, is the Connected Health Innovation Leader for Advanced Drug Delivery Solutions for BD Medical – Pharmaceutical Systems. She is responsible for driving the digital programme for connected drug delivery solutions, identifying and developing future innovative value offerings and leading research and development activities. Prior to joining BD, Dr Beck successfully delivered a wide range of multidisciplinary projects in clinical and neuro-rehabilitation settings, in academia and in business. She holds a PhD in Biomedical Engineering, a degree in Electronic Engineering, and has published 47 peer-reviewed scientific journal articles and conference proceedings in biomedical engineering and medicine.

Hervé Monchoix is a Strategic Innovation Leader for BD Medical – Pharmaceutical Systems, Strategic Innovation Group, where he is tasked with identifying opportunities and leading projects aimed at developing distinct and novel products, technologies and solutions for the global injectable drug delivery market. Prior to joining BD in 2010, Mr Monchoix spent more than 15 years in the semiconductor equipment industry, ranging from start-ups to large companies, in a variety of roles from new product development to commercialisation. Mr Monchoix holds an MS in Electrical Engineering from Arizona State University (US) and a BS in Applied Physics from Institut National Polytechnique de Grenoble (Grenoble, France). He holds seven US and several international patents, and is the author of more than ten peer-reviewed publications.

SENSIRION

HOW MINIATURISED LIQUID FLOW SENSORS ARE REVOLUTIONISING SUBCUTANEOUS DRUG DELIVERY

In this article, Andreas Alt, PhD, Sales Director Medical, and Susanne Pianezzi, Business Development Manager, both at Sensirion, describe the drivers accelerating industry trends towards both wearable subcutaneous injection devices and connecting such devices to monitor patient dosing, providing a number of benefits. They go on to explain how Sensirion's miniaturised disposable liquid flow sensors can confirm and track subcutaneous drug delivery in real time, enable precise dosing in terms of flow-rate as well as administered volume, and enable automatic failure detection, adding substantial value at low cost.

Whether smart injectors, infusion pumps or digital pills – digital drug delivery is revolutionising the medical and pharmaceutical industry and accelerating the emergence of self-care. As demographic change leads to an increase in patients with chronic diseases, the need for a larger number of digitalised home care therapies grows.

The increasing demand for self-treatment at home, as well as the rise of biotechnology-based therapeutics and precision medicine, have prompted the rise of wearable subcutaneous injectors. The trend for connecting these and other drug delivery devices to the Internet of Medical Things (IoMT) had already grown strong through the 2010s. With the covid-19 pandemic accelerating the push towards digitalisation across the board, and patient-centric solutions in healthcare further, smart delivery systems for monitoring how, when and where patients use their therapeutics have really come to the fore.

> "With the covid-19 pandemic accelerating the push towards digitalisation... smart delivery systems for monitoring how, when and where patients use their therapeutics have really come to the fore."

Implementing miniaturised liquid flow sensors in wearable devices allows subcutaneous drug delivery to reach the next level, benefitting patients, doctors, nursing staff, pharmaceutical companies and healthcare systems.

ACCELERATING PATIENT-CENTRICITY

The covid-19 pandemic challenged hospitals all over the world. Scheduled surgeries and therapies were put on hold due to a shortage of beds, over-burdened personnel and fear of infection. Patients became wary about visiting doctors' offices and hospitals, and in some countries were even encouraged by the government to stay away, and so they resorted to telemedicine appointments where possible.

The pandemic shone a light both on shortcomings and areas where smart technology can make a real positive impact, both in terms of being prepared to deal with future healthcare crises such as covid-19 but also more generally. Reducing hospital visits for routine checks and treatments of chronically ill patients is a key part of the required transformation, likewise improving efficiency of medical staff to help reduce overall treatment costs.

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"Another group of stakeholders driving the adoption of smart delivery systems is payors such as health insurers."

Connected digital technology can play an important role by improving collaboration between nurses, doctors, management and patients, providing additional safety by monitoring drug delivery and treatment and allowing more data-driven interpretation of treatment plans and a faster response to changing patient conditions. New portable or wearable designs enable patients to manage their conditions safely at home, with more individualised, flexible treatment options supported by remote monitoring.

From a macro-economic viewpoint, the trend towards digitalisation is associated with decreasing prices of electronic components. This not only justifies more competitive equipment pricing, but also enables medical device manufacturers to innovate and develop new designs incorporating digital elements that truly add value. For example, the direct documentation of ongoing treatments and the accurate logging of the amount and timing of successfully delivered drugs in hospital electronic health records (EHR), could also easily be extended to treatments taken at home.

Another group of stakeholders driving the adoption of smart delivery systems is payors such as health insurers. Pharmaceutical and insurance companies have been moving towards models that incorporate proof of use or even proof of effectiveness.

Smart inhalers that measure the inhaled flow profile and dose actuation, for example, are already able to prove that the dose was taken correctly.

BIOPHARMACEUTICALS AS A DRIVING FORCE

Whether for personalised or participatory patient care, precision medicine and advancements in biotechnology also have an impact on self-care trends. Compared with conventional medicines, the use of high-value drugs enables diseases to be treated in a more targeted way with fewer side-effects.

Unlike chemically synthesised drugs, biopharmaceuticals are made of complex structures derived from micro-organisms, mammalian cells or plant extracts. For example, they include proteins that stimulate blood cell formation, insulin, or antibodies that inhibit the growth of cancer cells. These high-value drugs also improve the opportunities to cure other previously untreatable diseases like autoimmune disorders, cardiovascular diseases, diabetes or neurological disorders.

However, because they must be administered parenterally, biopharmaceuticals are still not universally accepted. Due to the large size of the molecules, the most prevalent mode has traditionally been intravenous infusion, which requires professional clinical support, adding clinical costs to already high production costs.

The specialised handling that high-volume and viscous formulations require means that conventional drug delivery devices are not compatible or suitable. Furthermore, some new drugs require specific dose timing, concerning flow rate for example, while others are in a lyophilised state and require reconstitution prior to administration. To overcome these administration-related challenges, new drug delivery mechanisms have been developed, with wearable subcutaneous large-volume injectors (LVIs) being a notable category.

LVIs designed for existing products have strong commercial benefit, creating new revenue streams. For example, the patent for Amgen's Neulasta (pegfilgrastim) expired in 2015. The new on-body injector version of the product, Onpro, led to an extension of the drug's product lifecycle.

CONNECTED LARGE-VOLUME INJECTORS

For a few years now, LVIs – also called on-body delivery systems, patch pumps or wearable drug-delivery devices – have been enabling pharma companies to move products from intravenous infusion presentations to subcutaneous injection and with it the opportunity for self-administration at home. In particular, prefilled and preloaded drug-device combinations, as well as those with simple and intuitive patient filling steps, are providing a more convenient yet safe and reliable alternative to outpatient treatment. The patient-filled systems allow lyophilised drugs, that need be delivered by the user shortly after reconstitution, to be filled at the point of use.

Connecting these devices to the IoMT means that they not only enable patients to receive therapeutics at home, but they also enable therapy to be monitored in real time and remotely, increasing adherence, and reducing both effort and cost for patients, healthcare providers and insurers.

Because of the high volumes and viscosities, delivery of the biopharmaceutical dose from the device must be controlled, confirmed and tracked. This requires accurate and reliable sensor technology to be incorporated into the device.

Challenging Device Design

The market for LVIs for non-insulin drugs is expected to grow at a fast pace during the current decade. Over 50 such wearable products and more than 10 drug-device combinations with high storage capacities are already either commercialised or in development. Whether selling devices including a medication or not, the drug-delivery industry is facing many design challenges: improving the handling of viscous formulations and optimising usability, as well as keeping devices small and costs low. Consequently, most LVIs are made of a combination of both disposable and re-usable parts, which makes sense in terms of environmental sustainability.

The battery, motor, readout electronics, connectivity module and display are re-usable, the needle, drug compartment, patch and wetted sensors are disposable.

Miniaturised, Cost-Effective, Disposable Sensors

Since there are various biopharmaceuticals with different properties, LVI designers must individually guarantee reliable, precise function

"Sensirion's sensor solutions allow miniaturised, disposable liquid flow sensors to be integrated into LVIs to control, confirm and track subcutaneous drug delivery in real time. They enable precise dosing in terms of flow-rate as well as administered volume, and enable automatic failure detection."

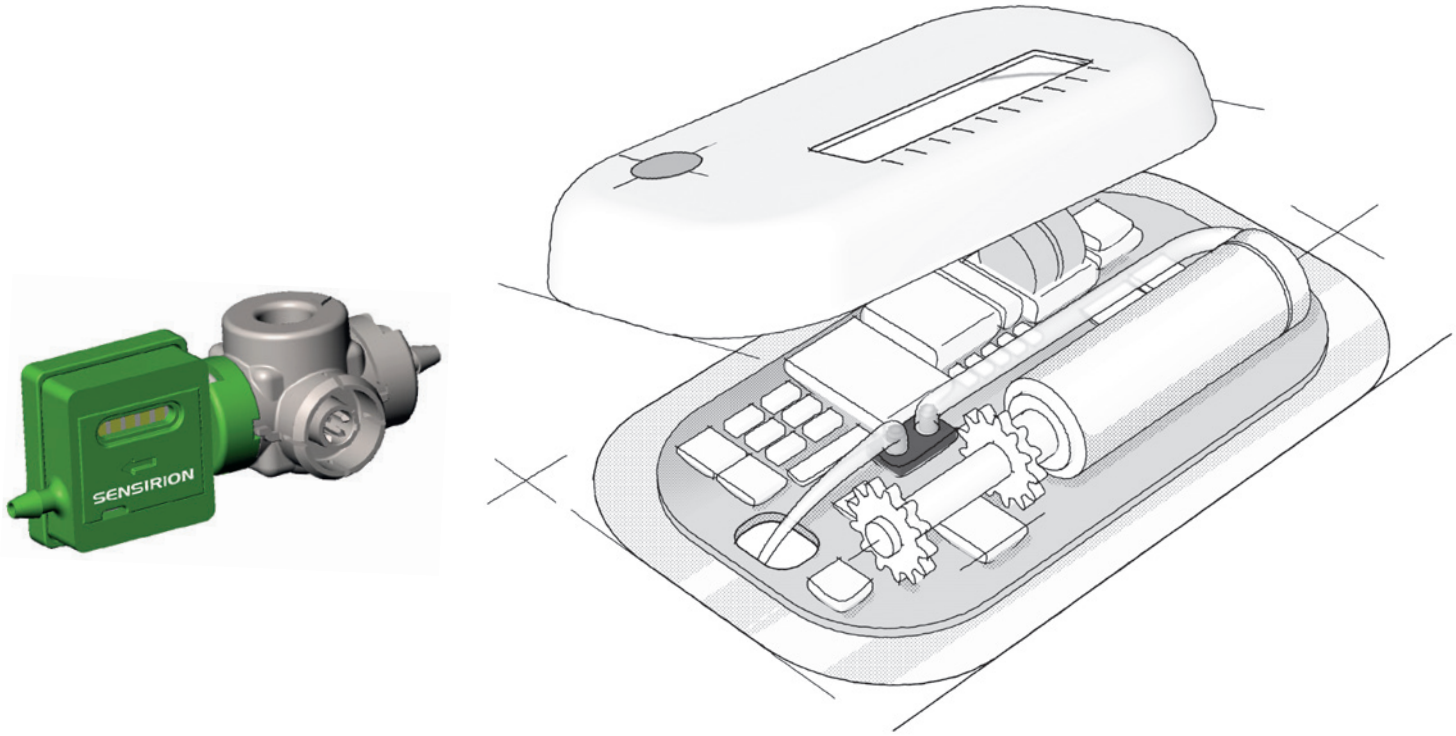

Figure 1: Sensirion's sensor solutions allow miniaturised, disposable liquid flow sensors (left) to be integrated into large-volume injectors (right). Images not to scale.

as well as ease of use. Up to now, they equipped devices with visual, audio or tactile indicators for needle positioning and on-body attachment. Even failures like occlusions can be detected to some degree, but currently only in an indirect way, leaving the possibility of false positives.

Even more important is the ability to incorporate direct flow measurement and measure delivered volumes accurately, as well as bidirectional measurement capability, which conventional sensors are not capable of. Sensirion's sensor solutions allow miniaturised, disposable liquid flow sensors to be integrated into LVIs (Figure 1) to control, confirm and track subcutaneous drug delivery in real time. They enable precise dosing in terms of flow-rate as well as administered volume, and enable automatic failure detection, such as occlusion or air-in-line, in a cost-effective and direct manner.

Integrated into a connected LVI, these next-generation sensors not only allow the administration to be monitored by the patient via a smartphone app, but additionally enable communication such as telemetry with stakeholders involved in the patient's care, like family members, parents or relatives. Nursing staff, doctors, pharmaceutical companies (for research) and health insurers (for verification) receive updates as well as metrics about the administration and the device status. Programmable features could also adapt or optimise the subcutaneous drug delivery process.

If an injection device shows issues, a flow sensor can provide peace of mind to patients as well as their relatives. Put simply: implementing a tiny smart sensor improves therapy outcome, patient adherence and quality of life.

Miniaturised liquid flow sensors enable LVIs to:

- measure the flow rate directly and bidirectionally to confirm the administered fluid volume in real time
- monitor system performance and guarantee reliable failure detection
- enable connected solutions for therapy monitoring and tracking by all stakeholders.

Sensor, Pump and Beyond

When designing LVIs, it is recommended to view the liquid flow sensor and the pumping mechanism from a holistic point of view. To identify the ideal design of the flow control system in terms of size, performance, ease of integration, manufacturability and cost, medical device manufacturers should aim for the best possible combination.

Conventionally, pump technology is selected first and often independently of the flow sensor, especially when unique requirements and related intellectual property of the device manufacturer are involved. Combining a previously selected pump with a liquid flow sensor can be challenging, especially when the pump performance requires further improvement, failure detection and resilience, all to be provided by the sensor. The pump's specific working principle, flow profile, mechanical design and fluidic connectors might further complicate the task.

CONCEPT STUDY: INTEGRATION WITH THIRD-PARTY DEVICE

Sensirion has put its extensive flow sensing experience to the test in a design study, assembling a small-footprint liquid flow sensor with a single-use micropump from Quantex Arc (London, UK).

Taking up only 0.5 cm3 of space (1.2 x 0.6 x 0.69 cm), Sensirion's liquid flow sensor stands out due to its millisecond-fast response times and direct as well as bidirectional flow rate measurement. The lightweight in-line pump used in the study was the Quantex Arc CS-3, which has a barbed inlet and outlet connectors for easy fitting to tubing, and is ideal for precise microdosing at flow rates of up to 100 mL/hr.

Being merely a concept study, there was surely space for further improvements and customisations, also considering different device requirements. However, the result here was a highly compact flow controller providing a steady flow with different flow regimes, and consuming very little energy.

CONCLUSION

When applied in subcutaneous LVI devices, miniaturised liquid flow sensors address the strong and accelerating market trends outlined in this article, and they do it at great value-to-cost ratio. Sensirion's technology is compatible with pumps from numerous manufacturers, and we are at the beginning of an exciting journey.

ABOUT THE COMPANY

Sensirion is a leading manufacturer of digital microsensors and systems. The company's product range includes gas and liquid sensors as well as differential pressure and environmental sensors for measuring temperature and humidity, volatile organic compounds, CO_2 and particulate matter (PM2.5). An international network, with sales offices in the US, Europe, China, Taiwan, Japan and Korea, supplies international customers with standard and custom-made sensor system solutions for a vast range of applications. Sensirion sensors can commonly be found in the medical, industrial and automotive sectors, analytical instruments, consumer goods and HVAC products. One of the hallmark features of Sensirion products is the use of its patented CMOSens® technology, which permits intelligent system integration of the sensor element, logic, calibration data and a digital interface on a single chip. Sensirion's credentials as a reliable supplier are underscored by its loyal customers, quality reputation (ISO/TS 16949) and top customer pedigree.

ABOUT THE AUTHORS

Andreas Alt, PhD, is Sales Director Medical at Sensirion. Dr Alt leads Sensirion's medical business and oversees the worldwide expansion of sensors and sensor solutions for the measurement and control of flow and environmental parameters into medical devices. Furthermore, he is responsible for medical OEM projects. He has a PhD in electrical engineering and experience in strategic market development and international project management

Susanne Pianezzi is Business Development Manager at Sensirion and is responsible for identifying and recognising trends in the field of sensor technology. Together with her team, she works on new sensor solutions for the measurement and control of flow and environmental parameters in diverse markets and applications. Ms Pianezzi has a degree in physics and many years of experience in international project management and business development. Her focus in the recent years has been on the medical market and the usage of single-use liquid flow sensors.

USING BLOCKCHAIN AND DATA ANALYTICS FOR IMPROVED MEDICAL CANNABIS EFFICACY

In this article, Brad Moore, Chief Executive Officer of Global Cannabis Applications Corp, and Tim Morch, Freelance Content Writer, describe GCAC's technology offering, a blockchain-based software system that is able to transparently track the progress of medical cannabis from cultivation through to consumption.

The history of legal medical cannabis is a brief one – it is only in the last decade or so that cannabis has been legalised, and only in some regions. However, with restrictive regulations and harsh penalties eliminated in many jurisdictions, medical cannabis is gaining traction for treating several ailments.

> "GCAC's core technologies include machine learning and Ethereum blockchain that interface with easy-to-use mobile and web applications for professional and personal use."

The lack of scientific knowledge about cannabis limits our understanding of the plant and its medical benefits. Growing safe medical cannabis repeatably is a challenge. And on top of this, legalisation has resulted in complex regulations that vary in every jurisdiction.

Global Cannabis Applications Corp (GCAC) is a leader in designing and developing innovative software-as-a-service (SaaS) data technologies specifically for the medical cannabis industry. Its technologies benefit the ecosystem by helping the cultivator control and optimise their product lifecycle to enhance the consumer experience, understand how different strains of the plant work and, ultimately, improve patient outcomes.

GCAC's core technologies include machine learning and Ethereum blockchain that interface with easy-to-use mobile and web applications for professional and personal use. These technologies transparently disclose cannabis chain-of-custody events and enable patients to crowd-source medical cannabis efficacy data. The use of a decentralised ledger helps establish medical cannabis efficacy.

Citizen Green Efixii is the world's first blockchain-powered medical cannabis platform that connects the cultivator and consumer by providing tools for every stage in the process. With Efixii, cultivators who already meet stringent cannabis cultivation requirements are rewarded by connecting these steps to a patient experience on a per-gram basis. The result is a revolutionary approach to using big data to determine cannabis efficacy.

Prescriptii Patient Experience is a personal cannabis guide to help users make better choices and optimise their journey. Patients can learn which strains are best rated for a condition, view efficacy comments from other verified consumers and provide personalised feedback. Additionally, for cannabis businesses, the extensive database provides detailed chemical analysis of active ingredients and helps find strains related to those they currently use.

GCAC's blockchain-based software empowers a community of medical professionals, cultivators, regulators and consumers to understand product efficacy better and deliver improved patient outcomes.

HOW BLOCKCHAIN DELIVERS TRANSPARENCY AND SECURITY

Blockchain technology offers numerous advantages for the medical cannabis industry. Using a decentralised ledger can establish medical cannabis efficacy. Transparency ensures that all data is visible to everyone. A blockchain is immutable and cannot be changed, certifying data integrity for all stakeholders – cultivator, manufacturer, regulator, consumer and medical professional.

By recording every step in the lifecycle of a plant, cultivators can analyse the

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data to improve productivity, efficiency and consistency. Manufacturers can trust suppliers and add valuable data to the chain. Regulators can audit the process with ease and confidence. Medical professionals can see every step for improved prescriptions. Everyone can review the entire chain of events by simply scanning a QR code.

Transparency enables stakeholders to see corporate statements turned into actions. Without traceability, consumers cannot use their collective purchasing power to drive and reward more responsible production.

THE LACK OF CANNABIS DATA IMPACTS CONSUMER SAFETY

Historically, the illegal status of cannabis left researchers unable to study the plant thoroughly. The result is a glaring lack of meaningful information about cannabis – its effects and benefits – impacting product safety and consumer guidelines.

Industry experts, medical and pharmaceutical professionals and, most importantly, patients agree that developing safer, more effective products is crucial. A core issue is the lack of guidance on how to use the product effectively. For patients, it is often a prolonged process of trial and error, further complicated by the variable potency of the products they consume. The requirement for labels that list tetrahydrocannabinol (THC) and cannabidiol (CBD) levels does not account for variations in plant strains and manufacturing processes. To date, there is an absence of data evaluating efficacy and dosage guidelines.

In the recreational cannabis market, consumers are starting to demand more information about how the cannabis they consume was grown. They want to ensure the authenticity of test labs and THC/CBD levels and guarantee product consistency.

EFIXII – DATA SOLUTIONS FOR THE MEDICAL CANNABIS INDUSTRY

Citizen Green Efixii is an end-to-end blockchain-based mobile app that provides solutions for every stakeholder in the medical cannabis ecosystem. For example, it helps medical cannabis cultivators optimise the growing process for better yields and improved product consistency. Efixii securely records and tracks each step in the product lifecycle using artificial intelligence (AI) and deep learning algorithms to reduce compliance costs and stimulate more profitable cultivation. Post-harvest data analyses the impact of different manufacturing processes and evaluates consumer preferences with the SeedtoSeed™ feedback loop, which establishes a strong cultivator-to-consumer relationship, analysing data from cultivation to consumption on a "one gram grown, one gram consumed" basis.

> "The downstream benefits of blockchain transparency are numerous, from easier regulatory compliance and secure tracking at every stage to improved product safety."

The downstream benefits of blockchain transparency are numerous, from easier regulatory compliance and secure tracking at every stage to improved product safety. Anyone can scan an Efixii QR code and see the complete life story of a product.

HOW EFIXII WORKS

Efixii is a blockchain-powered compliance solution, enabling fast, agile registration of regulated goods and their source on the public ledger. Robust "Know Your Customer" on sign-up prevents criminality, ensuring each user involved in the process is known. It includes background checks against anti-money-laundering and politically exposed persons databases. The software assigns individual roles to users based on their access-level requirements, meaning that users can only access information and process questions pertaining to their role. A user's ID is notarised within each step of the process, enabling detailed reporting.

The secure technology documents and notarises each step in the production, supply and shipping process. In this way, GCAC's technologies allow the entire product history, from seed to retail sale, to be fully tracked and traced down to the second, with every input stored on the blockchain and viewable to anyone.

Efixii is licensed to cultivators using a SaaS model and is a free-to-use app for cannabis consumers. Efixii's cannabis efficacy data is the intellectual property (IP) of GCAC. This IP creates an inherent difficulty in replicating or competing with GCAC's cannabis datasets. GCAC defined its protocols in a US Utility Patent Application "Tracking System For Cultivated Products And Associated Methods", serial number 17/456,385, filed November 24, 2021, Inventor Bradley Moore, ADDG file number 0132077.

THE SEEDTOSEED™ FEEDBACK LOOP

At the heart of Efixii is the patent-pending SeedtoSeed™ direct, real-time feedback loop. SeedtoSeed™ analyses every gram grown and consumed to generate transparent data for all stakeholders. Most importantly, it cements a consumer-to-cultivator relationship that yields better data for both. Consumers feed their experiences with a specific medical cannabis product into the loop, allowing cultivators to understand its effects, and cultivators learn which strains are more popular and why.

GCAC's proprietary technologies use a decentralised ledger to establish medical cannabis efficacy, layering and analysing thousands of patient journeys. This allows cultivators to provide patients with repeatable results and assure safe, approved, effective products (Figure 1). Citizen Green Efixii provides data-driven solutions for medical cannabis cultivators, manufacturers and resellers. The blockchain technology is visible to all stakeholders,

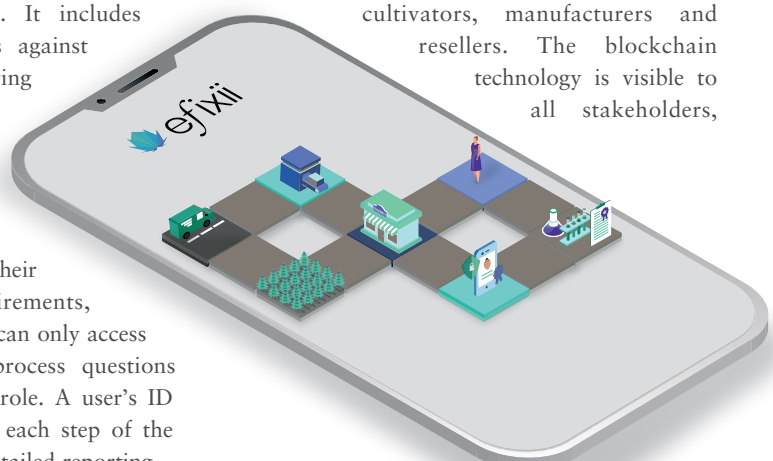
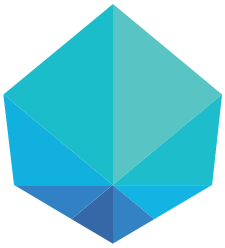


Figure 1: Illustration of how the Efixii SeedtoSeed™ feedback loop works.

including regulators, medical professionals and patients – this transparency breeds trust at every level:

- Manufacturers have increased trust in suppliers with best-in-class data
- Suppliers improve the value chain from grower to consumer and build strong relationships with patients
- Medical professionals can use the data for better prescriptions, improving patient outcomes
- Regulators can audit the entire process with ease and confidence, reducing compliance costs.

A pain point medical cannabis cultivators face is efficacy and dosing. Citizen Green solves this challenge by tracking and analysing every step in the product lifecycle. The goal is to understand what happens under certain, specific circumstances on a gram-by-gram basis. Thousands of personalised treatment journeys are analysed, letting cultivators accurately establish correct dosing levels and the average efficacy of product-ailment treatment.



Prescriptii

Patient-Care Solution

PRESCRIPTII – MAKE BETTER CHOICES AND OPTIMISE YOUR JOURNEY

The Prescriptii Patient Experience (PPE) website helps patients learn which strains are best rated for their condition and find related strains based on those they currently use. PPE is a Reddit-style web portal for medical cannabis consumers powered by an AI engine built by Curve Tech (Tel Aviv, Israel), creator of machine learning environments and prediction engines that are used by global e-commerce leaders like Shopify.

The advanced algorithm analyses over 600,000 verified data points from studies about cannabis, including questionnaires, user reviews and rankings of widely available strains, for more than 80 medical conditions. Machine learning establishes links between the conditions and strains to create a data-driven picture of medical cannabis. The proprietary heredity tree maps the origin and ancestry of over 9,000 strains and their chemical compound levels, including THC and CBD levels, indica and sativa ratios, and additional active compounds, such as cannabinol, cannabichromene, cannabigerol and tetrahydrocannabivarin.

The easy-to-use app features two search modes. The traditional mode will look familiar, and the neuro-linguistic programming (NLP) mode makes queries easy with an intuitive auto-suggest feature. Prescriptii helps find strains rated best for certain conditions using PAIN to STRAIN, analyses a strain to see which conditions it works best for with STRAIN to PAIN, and helps find other strains similar to a strain a user is familiar with or already uses with STRAIN to STRAIN. Prescriptii offers basic search results, and consumers can create an account for more comprehensive results, recommendations and preferred strains.

With the introduction of this free consumer service, GCAC is striving to improve customer knowledge and create confidence in this incredible plant. Additionally, for cultivators using Efixii, Prescriptii's powerful AI engine can evaluate new strains as the AI engine "learns" what the medical effect of existing strains is and can predict the behaviour of similar new strains.

REGULATORY VARIATIONS CHALLENGE THE MEDICAL CANNABIS INDUSTRY

Before legalisation, cultivators and consumers operated behind closed doors – with varying results. Potency fluctuations and inconsistent yields were common, compounded by an inability to test the product. Consumers had no advice on how to use the product safely. Legalisation has underscored the regulatory variations in every jurisdiction. Regulators require strict documentation, and the cost of compliance is high for cultivators, manufacturers and retailers.

> "With Citizen Green Efixii, regulators can inspect all information by scanning a secure QR code, which, because blockchain-based data is tamper-proof, makes their job easier, decreasing compliance costs and speeding approval times."

In the US, for example, every state with legal medical cannabis has different regulations that apply to the possession, consumption, cultivation, transportation, how to obtain a prescription and quantity limits. In contrast, Canada has fully legalised cannabis for medical or recreational consumption and medical cannabis is legal in many countries in the European Union, again with unique laws in each. With Citizen Green Efixii, regulators can inspect all information by scanning a secure QR code, which, because blockchain-based data is tamper-proof, makes their job easier, decreasing compliance costs and speeding approval times.

Efixii grows trust at every level. Manufacturers and retailers can get transparent, verifiable data and can add post-harvest events to the blockchain for compliance. An enhanced understanding of these processes creates solid relationships with all stakeholders and the decentralised ledger helps establish medical cannabis efficacy.

EFIXII ENHANCES MEDICAL CANNABIS CULTIVATION PROCESSES

The role of the cultivator has never been more critical. Cultivation requires meticulous attention to growing details, adherence to regulations and understanding every step post-harvest. It is a delicate balance of compliance with certification costs and optimising growing techniques to boost revenues. Every batch must be tested, certified and approved before it can move to the next stage. To develop better, more effective products, cultivators must make sense of the product lifecycle, especially the patient experience. The lack of valuable data often leaves them guessing.

Using the power of a blockchain to talk to connect cultivators and consumers, Efixii creates a unique relationship on a per-consumer basis, resulting in better cultivation and marketing decisions, as well as increased sales without customer acquisition costs. Attestations on the blockchain can be used as part of a cultivator's product marketing strategy.

BETTER EFFICACY FOR MEDICAL AND PHARMACEUTICAL PROFESSIONALS

Medical and pharmaceutical professionals depend on efficacy data to establish correct dosages. Efixii's decentralised ledger helps to establish a better understanding of what happens under specific circumstances on a gram-by-gram basis, accurately determining average product-ailment treatment efficacy and dosing recommendations. By making use of such data, medical professionals can properly prescribe cannabis and deliver better patient outcomes.

IMPROVED PATIENT EXPERIENCES WITH BLOCKCHAIN TECHNOLOGY

The consumer experience has never been more critical, and transparency is the new standard. Without traceability, consumers cannot use their collective purchasing power to drive and reward more responsible production. Visible, verifiable data improves the medical cannabis ecosystem and increases trust.

With Efixii, a simple QR code scan reveals the entire story of a product. Patients get trustworthy, tested and certified medical cannabis (Figure 2). They benefit from ratings and observations in the SeedtoSeed™ feedback loop and actively participate in the system. Tracking every gram grown and consumed for thousands of journeys supplies essential efficacy and dosing data, which, when fed back to cultivators, can help them to understand which products work, enhancing product efficacy and safety. GCAC's end-to-end data-driven solution for the medical cannabis industry transparently connects all stakeholders, resulting in better outcomes for medical cannabis patients.

Figure 2: Scan this QR code for sample product history and patient feedback.

ABOUT THE COMPANY

GCAC is a leader in designing and developing innovative software-as-a-service data technologies specifically for the medical cannabis industry. The company's technologies benefit the ecosystem by helping the cultivator control and optimise the product lifecycle to enhance the consumer experience, understand how different strains work, and improve patient outcomes. GCAC's core technologies include machine learning and Ethereum blockchain that interface with easy-to-use mobile and web applications for professional and personal use. These technologies transparently disclose cannabis chain-of-custody events and enable patients to crowd-source medical cannabis efficacy data. The decentralised ledger helps establish medical cannabis efficacy.

ABOUT THE AUTHORS

Brad Moore, Chief Executive Officer of Global Cannabis Applications Corp, has over 20 years of management experience working with Fortune 500 companies and tech start-ups. He is a military veteran, having served nine years with the Canadian Armed Forces and holds an MBA from Royal Roads University (Victoria, Canada). Mr Moore's focus is on creating better outcomes for medical cannabis patients using a decentralised ledger to establish medical cannabis efficacy.

Tim Morch is a seasoned freelance writer and communications strategist with over 30 years' experience developing content, strategies and analysis for a range of private and public sector clients. He helps brands create relevant, impactful messaging that both informs and entertains. Mr Morch is a veteran traveller with decades of international living, work and adventure. His heightened cultural awareness has shaped his ability to adapt to different situations and work with people of different backgrounds.

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