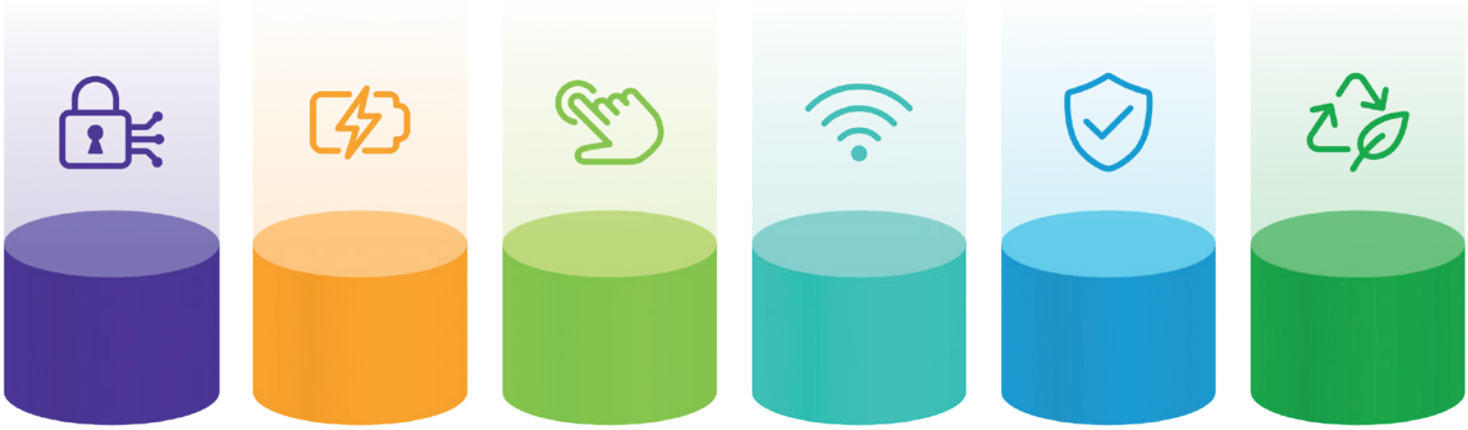
CONNECTING DRUG DELIVERY

ON drugDELIVERY



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ONdrugDelivery Issue N° 155, December 13th, 2023

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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Feb	Skin Drug Delivery: Dermal, Transdermal & Microneedles
Mar	Ophthalmic Drug Delivery
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Sep	Wearable Injectors
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Nov	Pulmonary & Nasal Drug Delivery
Dec	Connecting Drug Delivery

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Symbioze™

Smart and sustainable on-body injector platform

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HOW TO NAVIGATE A COMPLEX CONNECTIVITY ENVIRONMENT

In this article, Pascal Dugand, Technology Product Manager, Cécile Gross, Global Category Manager, Parenteral, and Mark Tunkel, Global Services Director, all at Nemera, consider the complexity of the landscape for connected devices and demonstrate how a balance can be achieved between patient needs, technology and the cost of integrating this technology into a device.

The methods available to pharmaceutical companies and device suppliers to support the patient journey and experience offer more possibilities than ever before. Traditionally, the focus of the patient experience was on optimising the "administration task" as outlined in the instructions for use, with an emphasis on the reduction of use error risk. However, as clinical outcomes are increasingly driving payer decision making, developers are expanding their efforts to support the patient journey more broadly.

> "Nemera helps to ensure that developed technologies are not only meeting market needs but that they are doing so in an optimal way."

Nemera achieves this through mapping the patient journey to develop an intimate understanding, which should be considered at the earliest stages of development. This starts from when a patient is diagnosed, to receiving their device, onboarding, acclimation, through the entire process of preparing, administering and disposal, and the times in between treatment to understand how the process changes over time and how frequency of administration may impact the patient experience.

This enables Nemera to determine how those needs can be most effectively addressed, whether through the device, the integration of connectivity, instructions or packaging materials (paper or digital), training, onboarding or other means of longitudinal engagement. Nemera helps to ensure that developed technologies are not only meeting market needs but that they are doing so in an optimal way.

This can support the trend of virtually every developer in the branded and generic space formulating some variation of a digital health approach. This often includes add-ons or accessories that are compatible with a commercially available device and provide users with device performance feedback. They can also provide error correction and other means of feedback to help eliminate use errors.

There has also been convergence within the drug delivery ecosystem, where all aspects of managing a disease state are integrated through connectivity that often requires partnerships to address broader steps in the patient journey to leverage complementary technologies (Figure 1).

BENEFITS OF PARTNERING WITH AN INTEGRATED PRODUCT AND SERVICE PROVIDER

Successful navigation of these challenges often requires a partner with a broad set of capabilities, products and services. Nemera's integrated development, consulting and manufacturing services allow customers to achieve successful regulatory submission and commercial launch of safe, effective and

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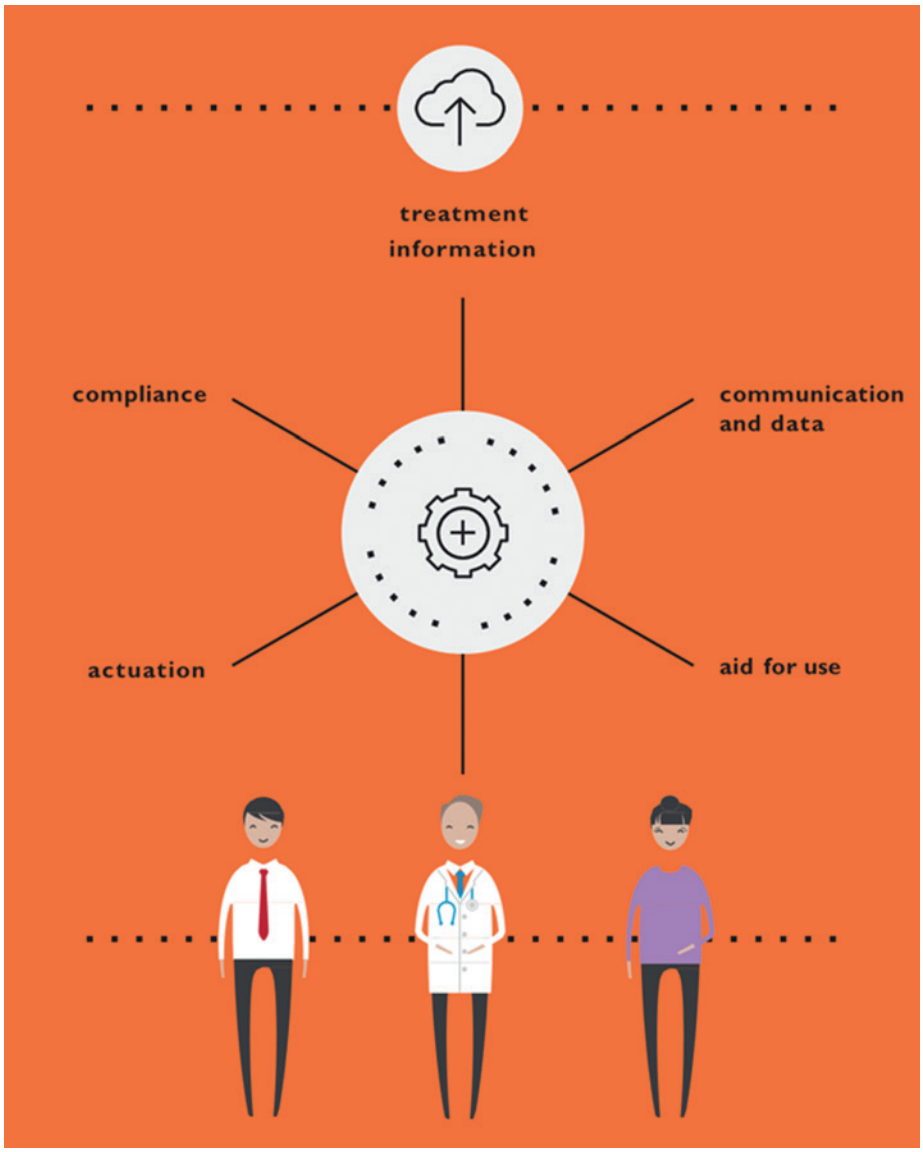

Figure 1: Connected devices.

differentiated combination products, with a single partner applying an agile process across the device and combination product value chain. Nemera supports every device strategy that a customer may consider, from organic development to the use of the company's intellectual property (IP) platforms, and a wide range of services to support the customer's journey towards a combination product.

Nemera's services include front-end innovation and device development, clinical and commercial device manufacturing, and combination product services. Ultimately, the benefits of this approach will drive:

Flexibility to Focus on the Core

The value of Nemera's integrated services lies in the flexibility it offers, allowing its customers to focus on the core business of drug discovery and development. Nemera can act as a partner and extension of customer teams and provide best-in-class solutions for devices and combination products, ensuring that no compromises are made when collaborating with the company.

Patient-Centricity and Engagement

The needs of patients and clinical stakeholders are central from the outset of the programme to develop a customised patient engagement strategy, which is consistently at the heart of the process to maximise effectiveness when launched into the market to drive stakeholder loyalty.

Innovation Across the Journey

Nemera's world-class design, development and consulting capability ensures the deployment of innovative development strategies as unique as its customers' applications for both the company's IP products and custom development services, regardless of the point of engagement.

Reduction of Risk and Increased Speed of Market Access

A single partner working across the journey limits transitions between suppliers and ensures consistent execution of strategy. Nemera offers a wide range of options for developing and realising a device to accelerate the time to registration and market, spanning from small-series to large-scale manufacturing, with the flexibility to provide interim supply as needed. When combined with Nemera's service offering, this can significantly reduce the time to market.

Nemera also offers an array of connected devices, ranging from embedded solutions with best-in-class partners operating in the field, to the customisation of an existing platform and extending an add-on solution.

"A single partner working across the journey limits transitions between suppliers and ensures consistent execution of strategy."

SYMBIOZE™, A SMART AND SUSTAINABLE ON-BODY INJECTOR PLATFORM

Targeting mid- to long-term medication in therapeutic areas such as oncology or immunology, the Symbioze™ drug delivery system is a connected and reusable on-body injector suitable for large-volume injections. The use of such devices is more than likely to expand, as many drugs in these fields are transferred from intravenous to subcutaneous delivery, which makes the disease burden even more cumbersome for patients.

To alleviate part of this burden, the focus has been – when designing the product – on an automated and safe injection process totally invisible to the user, as well as the secure administration of the prescribed drug. Combining electronics and "proximity card" technology is Nemera's choice to address these issues.

In the same way, a Bluetooth connectivity feature has been built in to allow functionality such as data recording and sharing, notifications and reminders. Although such a feature is common and well accepted in diabetes care, it remains innovative in cancer treatment and inflammatory pathologies.

Oncology patients need, on top of a seamless device, to achieve treatment adherence outside the hospital setting successfully, and to keep a link with remote healthcare professionals. Symbioze™ can be easily integrated into the patient journey.

To fine-tune the development of the electronics and software parts of the platform, Nemera has entered into a partnership with Zollner Elektronik (Zandt, Germany), one of the largest electronic manufacturing service providers. Zollner specialises in advanced mechatronics for healthcare and life sciences, railway technology, aerospace and defence, automotive technology and many other sectors.

As a partner of choice, it will support the design, development and manufacturing of electronic drug delivery systems for both Nemera's proprietary and customer-owned products. This collaboration will begin with the Symbioze™ platform (Figure 2).

Erwin Stöckinger, Senior Vice-President Business Division Electronics at Zollner, explained that from the start, Nemera and Zollner have been an excellent match, on both technological and human levels for the mutual development of groundbreaking solutions towards a sustainable society. The partnership will enable entry into new growth markets.

Figure 2: The Symbioze™ smart and sustainable on-body injector platform.

In the same way, Nemera is expanding its view of the patient journey beyond the treatment journey to embrace the patient's perspective more holistically; adding sustainability is a means for Nemera to show its commitment as a company to the climate, as well as being consistent with its motto, "We put patients first".

LOOKING INTO THE FUTURE: CUSTOMISED AND ADD-ON CONNECTIVITY

Keeping in mind patient adherence and looking for an innovative means to alleviate the burden of regular self-injections, it seemed natural to Nemera's technical teams to review the customisation possibilities on its safety system platform Safe'n'Sound®. The selected solution was to incorporate a near-field communication (NFC) connectivity tag into the device mechanism. Given its extremely large capabilities of data retrieval and transmission, the first prototype has been built upon data related to injection completion and injection history. The NFC tag has been customised to allow two device configurations: before and after injection (Figure 3).

The initial phase prior to injection aims to reassure patients that the device has never been used and to check the authenticity and expiration date of the drug. Once the device has been activated and the injection performed, this information is integrated into the patient's injection history, confirming a full injected dose. No specific application has to be downloaded to store the data as, by simply placing the device near the phone, all data are easily accessible through a web browser.

With high traceability features, this technology holds significant value, including for clinical trials. On the topic of clinical trials, an integrated connected pen is also available. Customised from Nemera's reusable pen platform Pendura AD, the device features a Bluetooth module integrated into the pen itself, which can help transfer data to an app. Before transferring it, the data related to the injected dose are displayed on

Figure 3: Customised Safe'n'Sound® with NFC tag.

Figure 4: Integrated reusable connected pen injector, ideal for tracking injected doses during clinical trials.

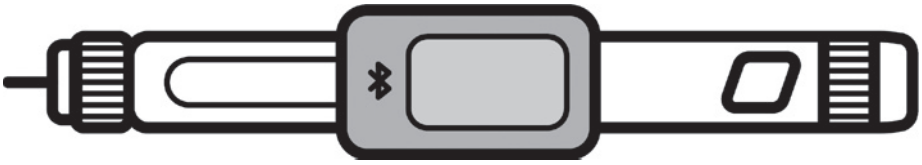

Figure 5: Specialised add-on for disposable pen injector, enabling key parameters detection to count administered doses accurately.

the screen, together with the date and time of injection. Complete data are available in the history on the application (Figure 4).

Another area of interest is to record the number of doses injected. When the treatment becomes regular, sometimes even daily, patients have difficulty following up their regimen. Within the ageing population, many individuals often undergo multiple treatments, making it challenging for them to remember whether they have taken their prescribed doses. To avoid underdosing or overdosing, Nemera's pen injectors can be customised with a specialised add-on. Designed to assist patients in monitoring their injections, it collects details of injected doses and adds them into the history. The main point is to accurately count the number of administered doses by recognising key parameters such as typical pen use sequences, pen position and the distinctive injection dose signature while detecting each specific step of priming and injection (Figure 5).

Finding the right balance between patient needs, technology and the cost of integrating this technology into a device as smoothly as possible is no easy task. Nemera strongly believes in its experience, its internal capabilities and its renowned partners to offer tailored solutions to patients worldwide.

> "To avoid underdosing or overdosing, Nemera's pen injectors can be customised with a specialised add-on."

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ABOUT THE COMPANY

As a world-leading drug delivery device solutions provider, Nemera's purpose of putting patients first enables it to design and manufacture devices that maximise treatment efficacy. Nemera is a holistic partner and helps its customers succeed in the sprint to market with its combination products. From early device strategy to state-of-the-art manufacturing, Nemera is committed to the highest quality standards. Agile and open-minded, Nemera works with its customers as colleagues. Together, it goes the extra mile to fulfil its mission.

ABOUT THE AUTHORS

Pascal Dugand graduated as a Polymer Engineer from the European Association of Hospital Pharmacists in Strasbourg, France. He holds a master's degree in Polymer Mechanics and joined Plastic Omnium in 1990 where he started to work in development and innovation. In 2004, the medical division of Plastic Omnium was acquired by Rexam and more recently the four drug delivery devices plants, including the Innovation Centre, became Nemera. Mr Dugand is an experienced medical device developer engineer specialising in the development of parenteral drug delivery devices. He has developed several of Nemera's own IP products, including the Safe'n'Sound safety device as well as working on early-stage projects and several customer injectable product developments.

Mark Tunkel is Global Category Director, Services at Nemera. He was previously a partner at Insight Product Development, which was acquired by Nemera in 2019 and became the Insight Innovation Center. With more than 20 years of global business development experience and a deep understanding of the marketplace challenges and trends impacting the pharma industry, Mr Tunkel has advised many of the world's leading companies on their product development and innovation strategies, with an emphasis on driving realisation and the most favourable business outcomes.

Cécile Gross is Marketing Global Category Manager at Nemera, focusing on parenteral devices. She oversees the product portfolio strategy, development and lifecycle for safety system, pen injector and on-body injector platforms. She has more than two decades of experience in the medical device industry, marketing business-to-business technological products and implementing product lifecycle management for various kinds of devices. Ms Gross holds a degree in International Business and completed her initial training with a master's degree in Marketing and Management in the Healthcare Industry at IMIS Institute, Lyon, France.

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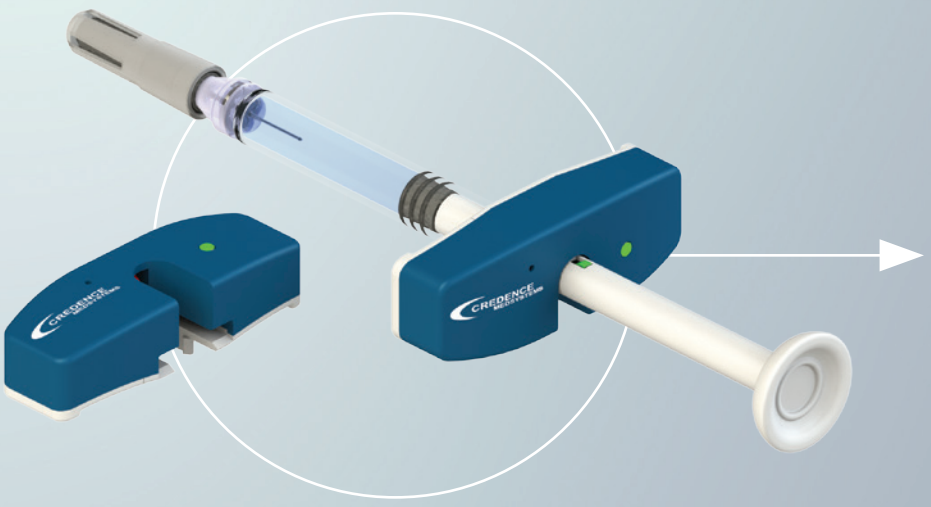

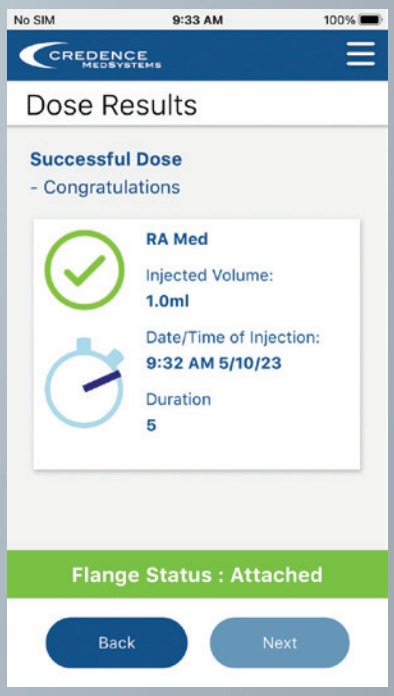

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UNLOCKING THE POTENTIAL OF CONNECTED DRUG DELIVERY DEVICES FOR DIABETES

In this article, Paul Draper, Senior Sector Manager – Medical and Scientific at DCA, discusses the current state of connected injection pens and devices in the diabetes space, exploring the benefits that connectivity can bring to drug delivery devices and considering how to exemplify good design in a connected injection device for diabetes drug therapies.

Diabetes is a chronic condition in which the body does not produce sufficient insulin, or use it properly, potentially leading to severe health implications. To help prevent these problems, many people rely on insulin therapy, which can require administration of multiple doses of different insulins every day. Frequent adjustments to insulin dosage are commonly needed to accommodate variations in diet or lifestyle. Keeping track of all these factors and adjustments can be challenging, particularly when trying to manage diabetes alongside the other complexities of daily life.

A chronic condition with a patient-adjusted treatment regimen will carry clear and significant challenges to patient adherence. Notwithstanding the challenge in accurately determining real-world adherence rates, studies have indicated that adherence rates for insulin therapy could be as low as 44.3% in Type 2 diabetes patients.[1] Furthermore, studies have shown that only 20% of people starting a basal insulin treatment plan continued beyond the first year.[2] What's more, these figures are unlikely to fully capture those patients who miss doses or take incorrect dosage values. Whatever the true figures are, there is, undoubtedly, a clear problem with patients lacking the control they need to avoid the secondary health complications that inevitably arise from inadequately managed diabetes.

The majority of patients deliver insulin therapy with pen injector devices (59% in the US and 93.6% in Europe) rather than syringe and vial systems.[3] Through continual optimisation, the design of these pens has matured over the last 20 years but, today, these classical mechanical pen injectors and advances in pharmaceutical molecules may well be reaching the top of their respective developmental 'S-curves', leaving only modest opportunity to improve outcomes without a change in the model. This is where connected insulin delivery devices can now make the difference.

> "The aim of connected devices in diabetes is simple – to empower patients and healthcare professionals with accurate data to improve their ability to achieve better glycaemic control, through increased adherence and persistence with insulin therapies."

The aim of connected devices in diabetes is simple – to empower patients and healthcare professionals with accurate data to improve their ability to achieve better glycaemic control, through increased adherence and persistence with insulin therapies. Indeed, implementing connectivity has long been a target of pharmaceutical and drug delivery device companies more broadly. However, to date, relatively few connected devices have been commercialised, and those that have been have often added significant usability burdens for patients, which limits their appeal and means that uptake is unlikely to be widespread.

For diabetes specifically, the advantages for patients, payers and insurance companies alike can be shown by examining the total cost associated with related treatments. Data from UK expenditure published in a 2011 study is illustrated in Figure 1, showing that, in total, £13 billion was spent on diabetes treatment. Of this, only £1 billion was on the cost of

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drugs for direct treatment.[4] The majority of the rest of the costs are associated with the treatment of complications. As such, it can be argued that the opportunity already exists to reduce the burden on the healthcare and insurance systems using connected devices.

The upside for pharmaceutical companies can be expressed relatively simply as well. If patient adherence and persistence is low, then less insulin is being purchased. This is magnified if one considers that prescribers may be more likely to switch to an alternative insulin product that has a compliance-aiding connected device if a patient is not achieving good control of their condition.

Therefore, it is arguable that the potential value of connected insulin delivery devices to patients, healthcare providers, payers and pharmaceutical companies is compelling. Hence, the challenge remains to develop devices that are capable of taking maximum advantage of this value by addressing the needs of patients within a framework that also considers the overall cost to healthcare systems.

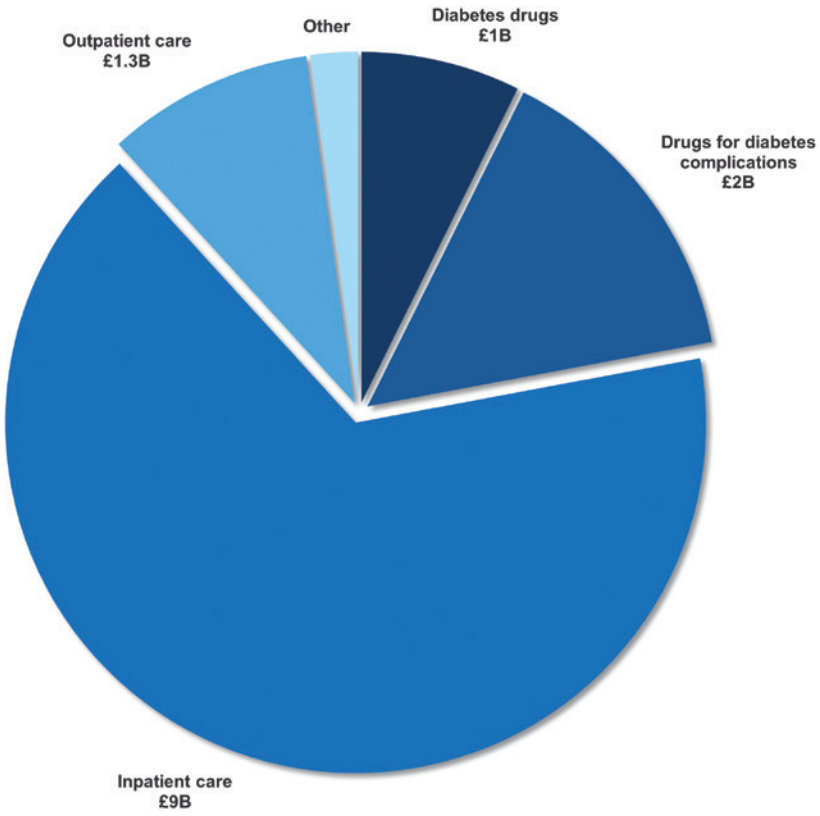

Figure 1: UK healthcare cost for treatment of diabetes and complications.[4]

A CONNECTED ECOSYSTEM

The increasing rates of adoption of continuous glucose monitors (CGMs) could be considered to be paving the way for highly effective diabetes management with connected insulin injection devices.[5] CGMs illustrate why usability is a critical factor for patient adoption. One of the key reasons why CGMs are popular is the reduction from one finger "stick" per reading to one "stick" every 14 days. Note also that the latest generation of CGMs seems to be tending towards fully seamless data synchronisation via Bluetooth, also demonstrating the importance of simplified user interaction.

For the most part, the benefit of connecting pen injectors themselves comes down to management of information. The right information, well-presented, can inform decision making and more timely interventions, ultimately leading to better outcomes (Figure 2). For some people, it could be said that the ideal for diabetes treatment would be a fully closed-loop system, with a body-worn insulin pump working in conjunction with a CGM to form a pseudo "artificial pancreas".

However, algorithm-controlled dosing may not be the perfect fit for everyone, and losing control of therapeutic decisions may be of particular concern for some physicians. A fully wirelessly controlled delivery device, such as a pump, also carries the downsides of a likely higher upfront product cost and cybersecurity vulnerabilities. As a balanced option for growing patient populations, connected injection pens are a compelling alternative – indeed, studies have been published with some of the latest connected injection devices demonstrating clinically measurable benefits.[6]

Figure 2: The information-to-outcome pathway.

THE ADOPTION EQUATION

The level of interest, and ultimately adoption, can be said to follow a relatively simple equation (Figure 3). The primary consideration is the value to the individual patient, which will differ from person to person. However, it should also include metrics such as convenience and peace of mind, as well as the health outcomes that provide value to the patient as well as the healthcare providers and payers.

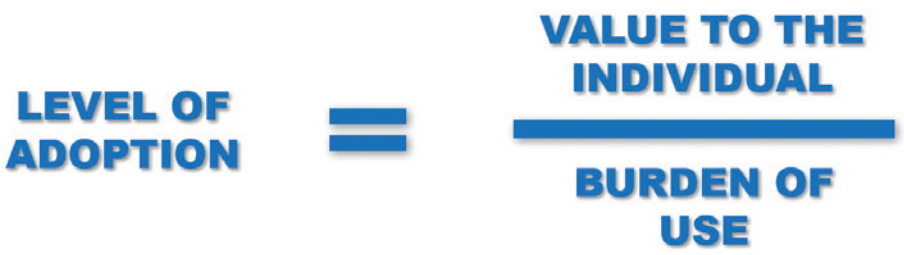

Figure 3: The adoption equation.

Figure 4: The seven pillars of connected drug delivery development.

> "It is important to make usability the central factor when considering the level of adoption, and ultimately the success, of an injection device."

Similarly, the "burden" will also change from person to person and is likely to include aspects such as the full-life fiscal cost to the patient or payer, environmental impact, number of task steps required, the complexity of those tasks and the time overhead per patient for the healthcare professional, among others. For connected, or smart, devices to succeed, the equation must be balanced such that the value proposition outweighs the overall burden.

THE SEVEN PILLARS OF CONNECTED DRUG DELIVERY DEVELOPMENT

It can be helpful to categorise the aspects of device development into seven topics to illustrate the key things that need to be considered both to maximise the value and reduce the burden (Figure 4). This article will reference just a few of the key topics from the seven, in order to highlight some important considerations.

It is important to make usability the central factor when considering the level of adoption, and ultimately the success, of an injection device. It is often all too easy to make compromises to usability when seeking to design connected injection devices or device accessories. A few examples of the problems associated with these compromises are discussed below.

Insulin pen injectors are often optimised during design to balance the thumb extension, for single-handed operation, with the dispense force (note that increased mechanical advantage brings lower dispense forces but longer travel distances). It is often simplest to integrate the connectivity hardware into the button of the insulin pen, conveniently encoding the mechanism for dispensing recording, for example. Figure 5 illustrates how this can be detrimental to the device's ergonomics and can start to exclude some user groups from dispensing how they want to and have been able to historically.

Further to considering the impact on existing steps or user actions, there is the consideration of additional use steps. The clear best-case scenario here is a seamless user experience, meaning a solution that can be implemented in a way that adds virtually no additional user steps. This will likely require greater innovation and engineering expertise during development but may, ultimately, be a key factor in driving the success of the product.

When considering adding electronics to an injection device, it will, realistically,

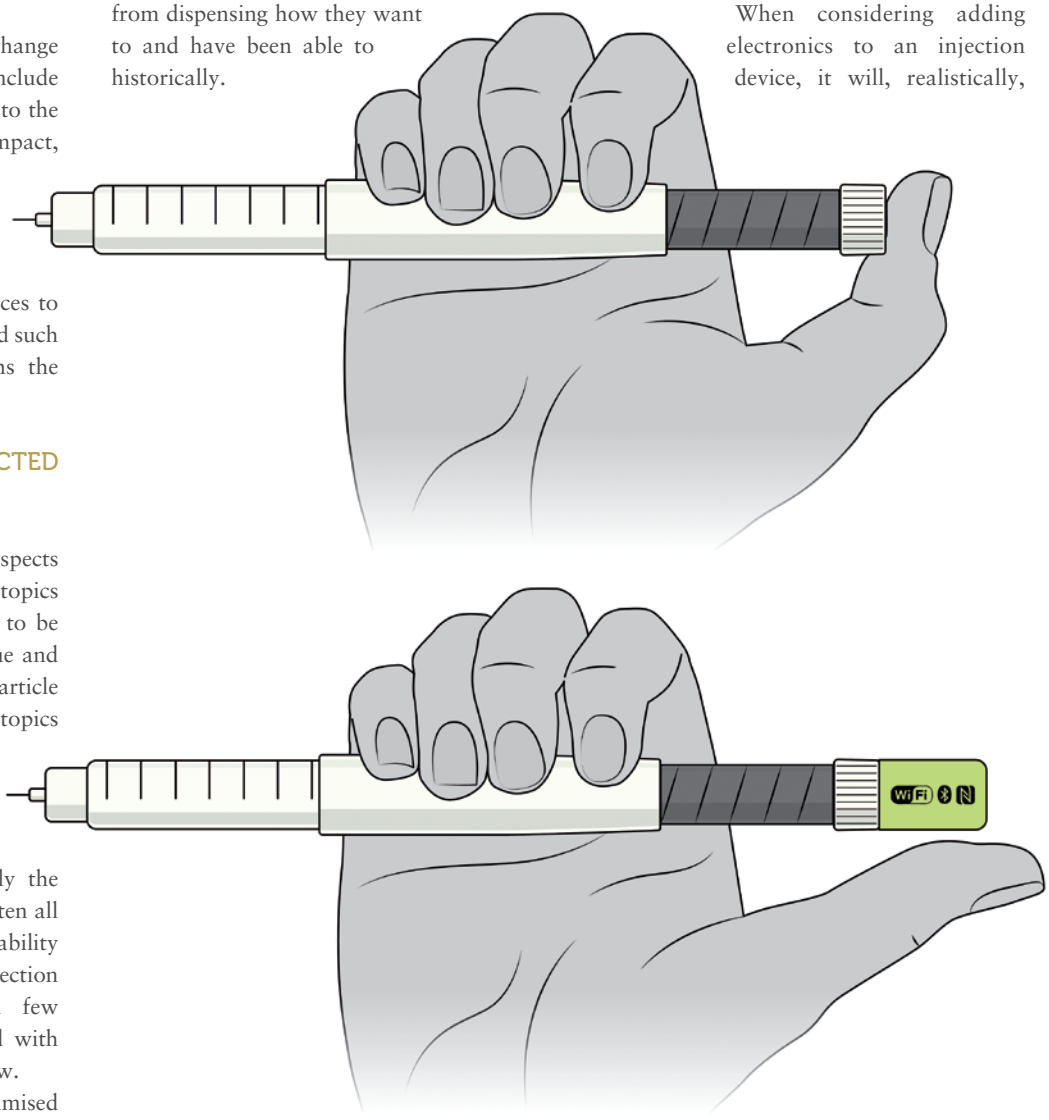

Figure 5: Illustration of the potential impact of integrated electronics.

require the incorporation of a battery and, therefore, it is necessary to make choices concerning what battery technology to use, as well as battery charging and replaceability. There is significant user overhead associated with charging, in both the physical action of connecting cables or docks and the cognitive aspects of interpreting signals from the device and remembering to charge at the appropriate times.

The alternative approach of making the battery replaceable by the user leads to all sorts of usability challenges for accessing and handling small batteries and casework covers. However, with leading-edge engineering development and innovation in low-power solutions, it is possible to implement a battery that lasts the lifetime of the injection device, thereby requiring no specific intervention from the user above and beyond the normal use of the device.

Another key topic is data communication technology. It is a fundamental fact that, to make a connected solution, data connectivity is required. Again, seamlessness is incredibly powerful here. However, communication is heavily linked to power usage, as well as usability, and cannot be considered in isolation.

The lowest power and easiest technologies to implement inherently carry additional user burdens. A wired or optical data download will require the user to take steps to connect cables or docks and to initiate the data transfer from either side, or both sides, of the communication link. Similarly, the use of near-field communication (NFC) technology may require slightly fewer user steps, but still requires a deliberate and conscious action to be taken. On the other hand, a longer-range wireless technology, such as Bluetooth, can be made to operate seamlessly in the background. However, this comes with a greater power requirement and therefore adds to the development challenge. That said, the ultimate reward for overcoming this challenge is likely to be measurable in the adoption rates for the product in market.

> "The lowest power and easiest technologies to implement inherently carry additional user burdens."

CONCLUSION

Designing connected drug delivery devices that can succeed is a complex and multifaceted challenge. It is a key strategic requirement to understand the business case for the device, as well as its value proposition to the patient. It is then even harder to design and develop a connected device that preserve these strategic goals without accepting compromises at some point in the process. Success requires a truly integrated approach, from strategy, human factors, mechanical engineering, electronic engineering, software engineering and industrial design, to manufacturing and industrialisation. All of these aspects need to be led by decision makers with the vision and experience to forge a path to success.

ABOUT THE COMPANY

Founded in 1960, DCA is a leading product design and development consultancy. Its multidisciplinary service offering includes systems engineering, mechanical engineering, industrial design, insight and strategy, user experience/interface, human factors, electronics, software and prototyping. With a range of global pharmaceutical, biotech and device companies amongst its long-standing clients, DCA has deep experience in the field of drug delivery devices. Work undertaken in this area includes design, development, analysis and industrialisation support for injection devices, inhalers, wearables and intranasal devices and applicators, including smart and connected devices. DCA has won multiple major industry awards and contributed to over 1,700 granted patents in the last 10 years. The company's development service is certified to ISO 9001 and ISO 13485 standards.

REFERENCES

1. *Perez-Nieves M et al, "Basal insulin persistence, associated factors, and outcomes after treatment initiation among people with type 2 diabetes mellitus in the US". Curr Med Res Opin, 2016, Vol 32(4), pp 669–680.*
2. *Yavuz DG, Ozcan S, Deyneli O, "Adherence to insulin treatment in insulin-naïve type 2 diabetic patients initiated on different insulin regimens". Patient Prefer Adherence, 2015, Vol 9, pp 1225–1231.*
3. *Masierek M et al, "The Review of Insulin Pens-Past, Present, and Look to the Future". Front Endocrinol (Lausanne), 2022, Article 827484.*
4. *Kanavos P, van den Aardweg S, Schurer W, "Diabetes expenditure, burden of disease and management in 5 EU countries". LSE Health, Jan 2012.*
5. *"2021 Annual Report". Abbott, Mar 2022.*
6. *Adolfsson P et el, "Increased Time in Range and Fewer Missed Bolus Injections After Introduction of a Smart Connected Insulin Pen". Diabetes Technol Ther, 2020, Vol 22(10)m pp 709–718.*

ABOUT THE AUTHOR

Paul Draper has 20 years of experience working on and leading medical device projects, including the leadership of complex multidisciplinary drug delivery device projects encompassing strategy, research, design, mechanical engineering, electronic engineering, software engineering and industrialisation. Mr Draper has experience of low-part-count mechanical devices through to advanced electromechanical devices, including IEC 62304 software development for embedded software and supporting mobile applications.

Aptar digital health

IMPROVING MEDICATION ADHERENCE AND CLINICAL OUTCOMES THROUGH CONNECTED DRUG DELIVERY DEVICES

In this article, Joachim Koerner, Director of R&D Connected Devices, and Marcus Bates, Vice-President of Business Development, both at Aptar Digital Health, discuss the challenge that medication non-adherence presents to the healthcare sector, and the potential value of connected digital health solutions as a way of overcoming this challenge.

Medication non-adherence and its many complications have posed a significant challenge to healthcare and the life sciences for decades. However, because many factors contribute to non-adherence, which can vary significantly based on the conditions a patient is managing, there is no one-size-fits-all solution to the non-adherence problem.

That said, the growing field of connected drug delivery solutions highlights the potential of purpose-built products to support patients managing chronic health conditions. Through education, engagement, communication, evidence-based recommendations and more, these solutions can guide patients through taking their medications, tracking their side effects and living their everyday lives.

To achieve these results – and to help shift the needle away from reactive disease management towards preventive care – organisations must consider how patients will use connected drug delivery solutions in tandem with their therapies. This may require a new approach to solution development, one that begins when the therapeutic itself enters the early stages of development.

> "Twenty years ago, a seminal report from the WHO found that average medication adherence rates for patients with chronic conditions were around just 50%."

THE CHALLENGE OF MEDICATION NON-ADHERENCE

Twenty years ago, a seminal report from the WHO found that average medication adherence rates for patients with chronic conditions were around just 50%. These rates were significantly lower in developing countries and for certain conditions, particularly asthma and high blood pressure.[1] Additional research has shown that adherence rates have increased in the years since, but remain at less than 60%.[2] The American Medical Association considers patients non-adherent if they take less than 80% of their prescribed medications.[3]

While a multitude of factors contribute to non-adherence, they tend to fall into five general categories:

1. **Individual patient motivation:** There are many personal reasons that patients may choose not to take medication – denial of diagnosis, cognitive impairment, religious or cultural aversion, history of substance use, fear of side effects or preference to allow health to decline without treatment.

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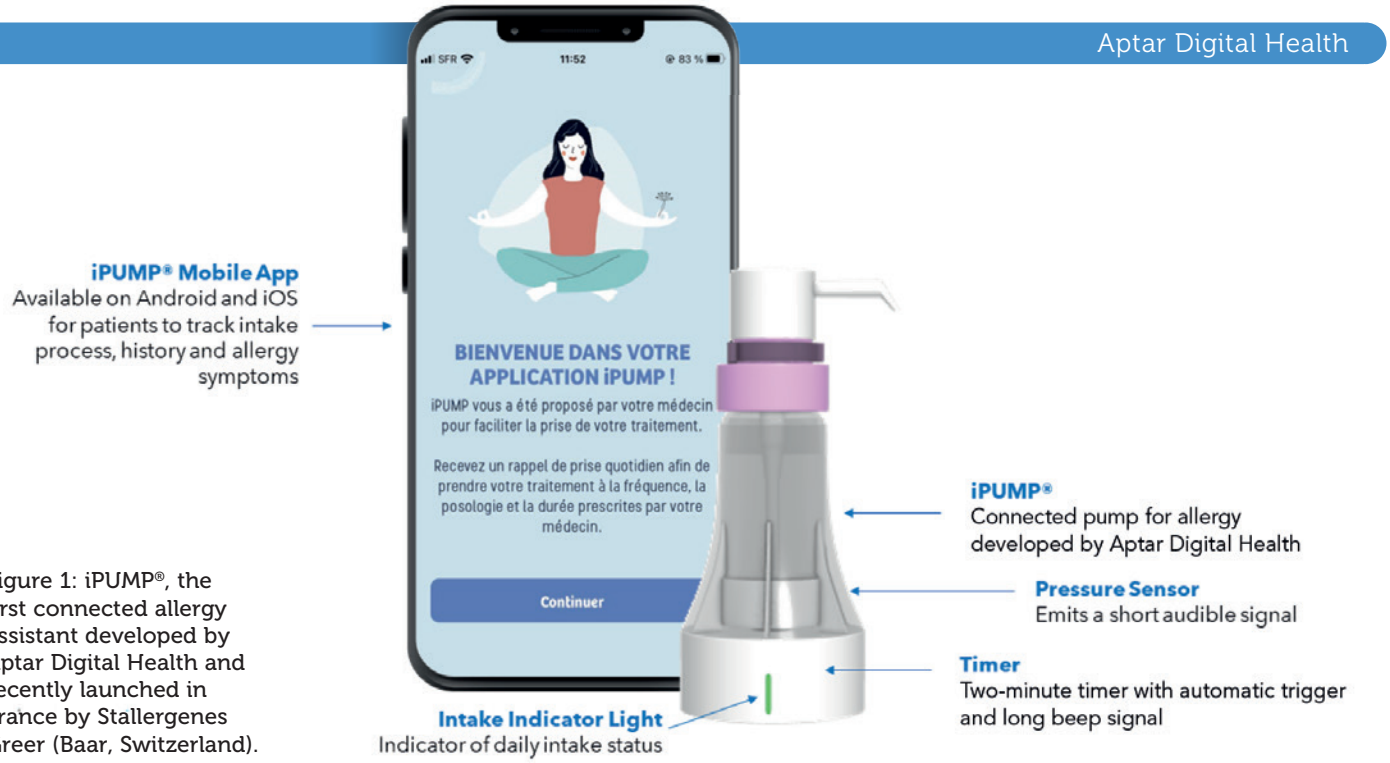

Figure 1: iPUMP®, the first connected allergy assistant developed by Aptar Digital Health and recently launched in France by Stallergenes Greer (Baar, Switzerland).

2. **Social determinants of health:** Limited access to reliable and convenient care, including the means to travel to in-person appointments or participate in telehealth appointments, may make it difficult for patients to renew prescriptions or speak to healthcare providers.
3. **Insurance coverage:** Cost is a common barrier to adherence. This is especially the case for biologics or other highly targeted therapies, as well as for patients taking medications to manage multiple chronic conditions.
4. **The condition being treated:** If a chronic condition is asymptomatic, as is common with autoimmune diseases, patients may not realise that they need to continue taking their medication. Additionally, non-adherence rates are shown to be higher for patients with psychiatric conditions.[2]
5. **The treatment prescribed:** Patients often skip treatments that are difficult to take, such as pills that are hard to swallow or injectables that require self-administration. It is also common for patients to skip, or stop altogether, treatments with negative side effects.

The consequences of poor medication adherence are significant. In the US alone, non-adherence has been linked to an estimated 125,000 preventable deaths and up to US$300 billion (£240 billion) in direct and indirect healthcare costs.[4] Non-adherence also contributes to poor clinical outcomes, as patients are likely to see a condition worsen if they are unable to treat it with the medication they have been prescribed.

> "Connected drug delivery solutions are designed to help patients take their treatments as effectively and efficiently as possible."

THE VALUE PROPOSITION FOR CONNECTED DRUG DELIVERY DEVICES

Given the diverse challenges associated with improving medication adherence, it comes as no surprise that there is growing interest across the healthcare ecosystem for digital tools that help patients not only take their medications but also manage their chronic conditions. Connected drug delivery solutions are designed to help patients take their treatments as effectively and efficiently as possible (Figure 1).

Some connected solutions use sensors to gather vital signs or other important information, whereas others rely on patient-reported outcomes (PROs), such as symptoms or side effects. Instructions for administration are also a common feature. From there, they aggregate and analyse data for multiple use cases, such as providing next-best action recommendations to patients, offering additional educational materials, assessing patient progress over the course of their treatment and providing updates to clinical care teams.

These solutions empower patients in three important ways. The first is providing them with a better understanding of their condition, as well as the importance of their therapy as part of their overall condition management plan. The second is a more personalised approach to treatment, as recommendations are based on their own data coupled with evidence-based treatment pathways. The third is an ability to receive feedback and communicate with care teams far more frequently than in the past, when patients were often limited to in-person appointments with specialists a few times each year.

The market for connected drug delivery solutions is growing. Grand View Research (CA, US) estimated the global market at more than $4.8 billion in 2022 and projected the market would exceed $25 billion by the end of the decade.[5] The industry's effort to improve medication adherence is one key factor driving this growth. Another is the increased prevalence of asthma, diabetes and other chronic conditions that require lifelong monitoring, management and engagement from patients.

> "As part of their goal of improving medication adherence and enhance chronic condition management beyond the clinical setting, there are 10 main ways that connected drug delivery solutions support patients."

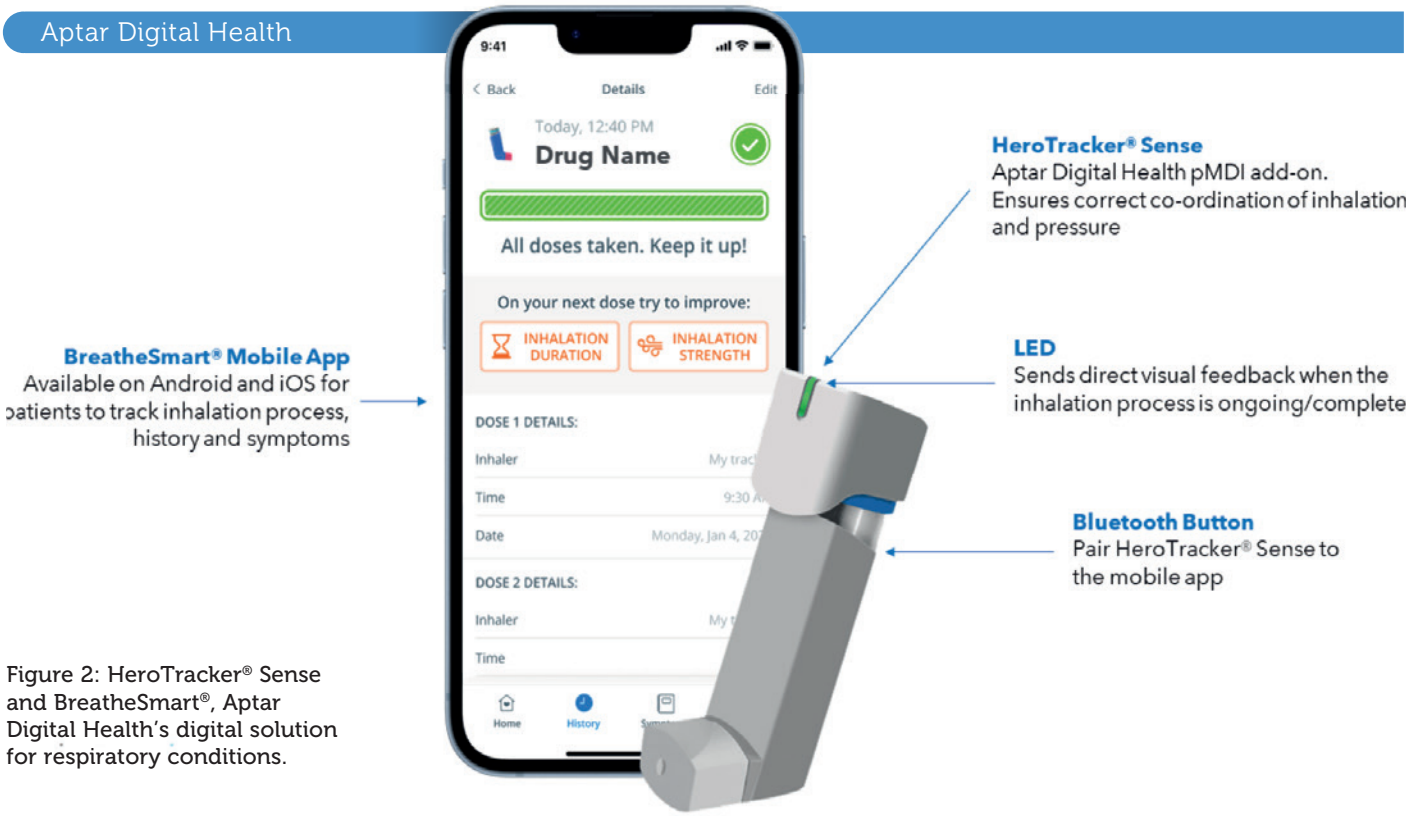

Figure 2: HeroTracker® Sense and BreatheSmart®, Aptar Digital Health's digital solution for respiratory conditions.

10 USE CASES FOR CONNECTED DRUG DELIVERY DEVICES

As part of their goal of improving medication adherence and enhance chronic condition management beyond the clinical setting, there are 10 main ways that connected drug delivery solutions support patients. Critically, these use cases support development, commercialisation and real-world monitoring of therapeutics.

Decentralised Clinical Trials

Connected devices let patients participate in clinical trials without the need for frequent in-person visits to the trial site. Trial sponsors can enrol patients from traditionally under-represented patient populations and geographies, giving them additional evidence of how a therapy works in practice.

Supporting Self-Administration

Tutorials can remind patients to shake an inhaler prior to actuation to get the correct dosage (Figure 2). They can also show patients the proper angle and demonstrate the correct pressure for injectables, which is a critical consideration for therapies that are administered on an infrequent basis and/or come with a high out-of-pocket cost (Figure 3).

> "Along with logging side effects, connected devices can provide insight into which side effects are normal and which may require medical attention."

Providing Education

Patients can learn how a treatment works in their body, along with why it is important to take it even if they do not present symptoms. For certain conditions, patients can learn to identify which symptoms should prompt administration of a treatment and, in doing so, potentially prevent an acute care episode.

Meaningfully Communicating PROs

Instead of writing symptoms in a physical notebook or note-taking app, connected devices let patients log PROs as structured data and, if they choose, send that information to their clinical care team. These curated summaries keep healthcare providers informed of a patient's condition without the need for a thorough review of their records.

Managing Side Effects

Along with logging side effects, connected devices can provide insight into which side effects are normal and which may require medical attention. Evidence-based, non-clinical recommendations for managing discomfort may help as well, and they can reduce the volume of non-urgent communication with a clinical care team.

A Platform for Supplemental Products

Giving patients a place to access their prescriptions, as well as other products approved by their physicians, from blood pressure cuffs to dietary supplements to diagnostic tests, provides a more integrated care experience and makes it easier for patients to obtain the products they need to manage their health and wellness.

Patient Support Programmes

Whether patients manage common chronic conditions or rare diseases, they benefit from connecting to others who can provide guidance and support. This is especially true for aspects of everyday life that are often not covered in conversations with their care team.

Motivation and Encouragement

Especially with life-long chronic conditions, patients face setbacks and have bad days. Providing encouragement tailored to a patient's specific treatment plan and condition can help get them back on track.

Recommendations for Preventive Care

Connected devices can help determine the right course of action based on a patient's current symptoms or predicted future risk through features such as screening questionnaires and virtual care triage tools. This enables care teams to provide preventive services instead of waiting for a patient to be admitted to hospital.

A Single Platform for Data Access

Market-leading connected devices sync to single, open platforms where, with their consent, patients can make data available to healthcare providers, insurers

Figure 3: AdhereIT®, Aptar Digital Health's autoinjector add-on.

and life science organisations. This gives all stakeholders a longitudinal view of a patient's progress towards clinical goals and metrics associated with outcomes-based arrangements they may be enrolled in.

ENSURING THAT SOLUTIONS MEET PATIENTS' NEEDS

For all their benefits, getting patients to consistently use connected drug delivery solutions and other digital health products remains an uphill battle. Only 40% of patients use the portals connected to their electronic health record systems[6] and an estimated 70% of patients abandon remote monitoring devices and other assistive technologies.[7] Numerous factors contribute to this disinterest, including, but not limited to, difficult set-up, low-quality feedback, poor usability, low reliability and unnecessary features.[8]

Making sure that connected drug delivery solutions can meet the diverse needs of patients across a multitude of use cases will require an iterative approach to design, development and commercialisation. While this process may vary from one organisation to the next, there are generally six steps involved:

1. Identify patients' barriers to managing their condition and taking their therapeutic as prescribed
2. Look holistically at patients' needs and determine the user experience elements and solution workflows that can address them
3. Create a solution prototype for stakeholders, including patients, to react to
4. Incorporate feedback and make necessary adjustments before beginning full-scale development
5. Ensure that solution development is tightly aligned with clinical development of the corresponding therapeutic
6. Approach solution development and approval like a clinical trial, conducting summative studies and human factors studies; address all problems before the next phase of development begins.

Approaching the development of a connected drug delivery solution in this manner requires a significant up-front investment in time, energy and resources. It is also in stark contrast to the typical process of creating a standalone digital health application, especially one not regulated by authorised bodies.

The payoff is that a solution goes through the same rigorous development and testing process as the therapeutic it will support. As a result, the therapeutic and the solution are ready to go to market at the same time, helping to ensure that patients can get the support they need as soon as they begin a new treatment plan.

> "The payoff is that a solution goes through the same rigorous development and testing process as the therapeutic it will support."

LOOKING TO THE FUTURE OF CONNECTED DRUG DELIVERY DEVICES

As valuable as today's use cases for connected drug delivery solutions are, it is exciting to think about what the future may hold. For example, data aggregated onto a single platform makes it possible for industry stakeholders to better understand how individual therapies work across a patient population. This could allow healthcare providers to modify and improve treatment pathways, help payers determine which therapies have the greatest impact on clinical and financial outcomes and empower life science organisations to identify additional indications or other new development opportunities.

Additionally, connected solutions will further enable the industry to push preventive care upstream. Real-time insight into how patients experience symptoms and respond to therapies will allow for more informed and evidence-based decision support. The potential to provide recommendations for new treatments, including over-the-counter products or digital health solutions, is poised to change the way healthcare providers approach chronic condition management – a positive outcome that all healthcare stakeholders can agree on.

ABOUT THE COMPANY

Aptar Pharma's Digital Health division is part of AptarGroup, a global leader in the design and manufacture of a broad range of drug delivery, consumer product dispensing and active material science solutions and services. Aptar Digital Health creates end-to-end solutions to enhance patient experiences, leveraging a holistic ecosystem of digital interventions. Amplified by an industry-leading portfolio of products and solutions, Aptar Digital Health's offering combines mobile and web apps, connected drug delivery systems, onboarding, training and advanced data analytics services to empower patients and create a positive treatment journey.

REFERENCES

1. *"Failure to take prescribed medicine for chronic diseases is a massive, world-wide problem". WHO, Jul 2003.*
2. *Foley L et al, "Prevalence and predictors of medication non-adherence among people living with multimorbidity: a systematic review and meta-analysis". BMJ Open, 2021, Vol 11(9), Article e044987.*
3. *Brown M, Sinsky CA, "Medication Adherence: Improve Patient Outcomes and Reduce Costs". AMA STEPS Forward, Jun 2015.*
4. *Benjamin RM, "Medication Adherence: Helping Patients Take Their Medicines As Directed". Public Health Rep, 2012, Vol 127(1), pp 2–3.*
5. *"Connected Drug Delivery Devices Market Size, Share & Trends Analysis Report By Product, By Route Of Administration (Parenteral, Inhalational), By Application (Asthma, COPD, Diabetes Management, Others), By Region, And Segment Forecasts, 2023–2030". Market Report, Grand View Research, 2023.*
6. *Johnson C, Richwine C, Patel V, "Individuals' Access and Use of Patient Portals and Smartphone Health Apps, 2020". ONC Data Brief No 57, Sep 2021.*
7. *Howard J et al, "Exploring the barriers to using assistive technology for individuals with chronic conditions: a meta-synthesis review". Disabil Rehabil Assist Technol, 2022, Vol 17(4), pp 390–408.*
8. *Park JI et al, "Lack of Acceptance of Digital Healthcare in the Medical Market: Addressing Old Problems Raised by Various Clinical Professionals and Developing Possible Solutions". J Korean Med Sci, 2021, Vol 36(37), Article e253.*

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Joachim Koerner is the Director of R&D Connected Devices at Aptar Digital Health. He has spent more than 25 years in highly regulated industries, including space technology and the medical device industry, across several R&D positions. Mr Koerner led the team that achieved the first EMA approval for an electronic lockout system and developed the first connected assistant for allergy management. He is currently responsible for electronic device development, scale-up and production worldwide. Additionally, Mr Koerner also manages intellectual property for Aptar Digital Health.

Marcus Bates is Vice-President of Business Development at Aptar Digital Health. He has more than 20 years of experience working in the pharmaceutical industry. Mr Bates has worked in several positions, mainly focused on the commercial and business aspects, including being responsible for supply chain activities, such as the identification of and contracting with key long-term partners. At Aptar Digital Health, Mr Bates is responsible for the development of the company's digital health offering across different therapeutic areas, including immunology and respiratory.

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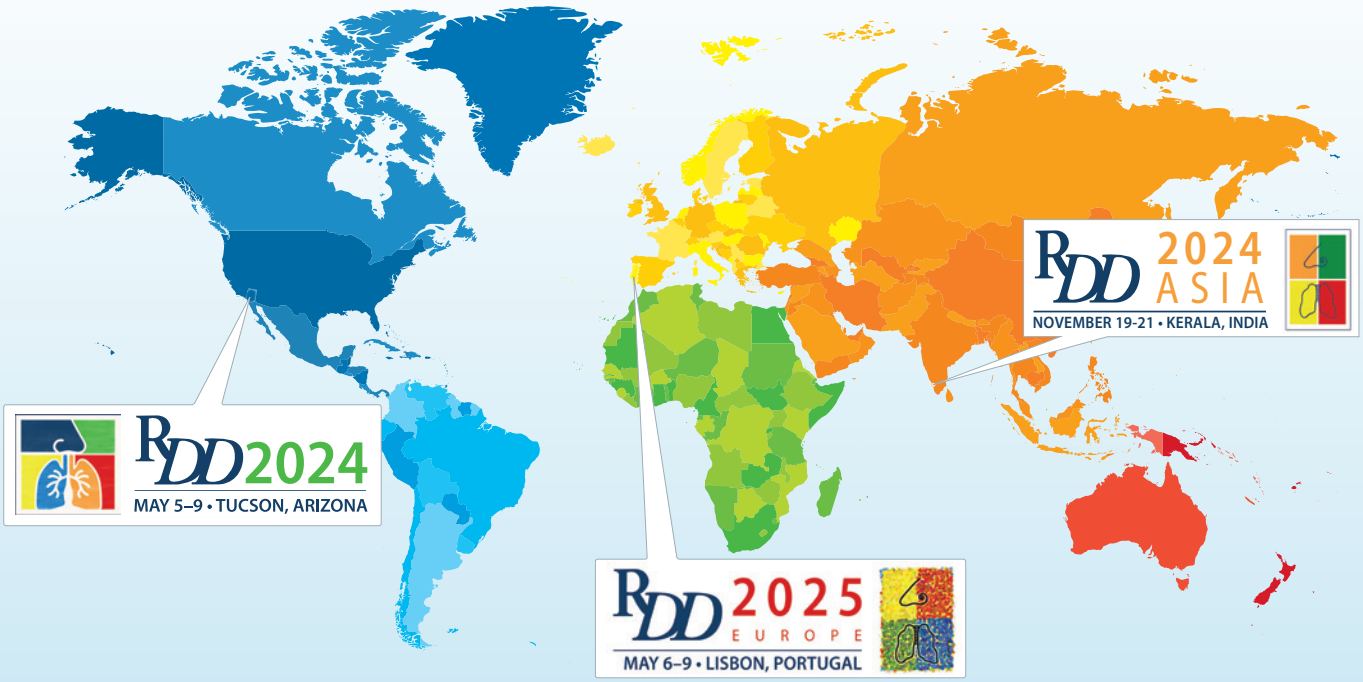

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CUSTOMISABLE NEBULISER PLATFORM TO MONITOR ADHERENCE

Here, Edgar Hernan Cuevas Brun, Business Development Manager & Scientist, Aerosol Drug Delivery, and Yuan-Ming Hsu, PhD, Research and Development Director, both at HCmed Innovations, discuss the value that customisable nebuliser platforms bring to patient adherence.

Innovative approaches in inhaled drug delivery systems have contributed to improvements in delivery performance and overall user needs. These approaches aim to address some longstanding shortcomings, which have remained unsolved for several decades. One such shortcoming has been widely described as the challenge of accurate adherence monitoring. Adherence monitoring plays a crucial role in understanding how effectively patients follow their prescribed treatments and how that relates to the subsequent outcomes.

Deterioration of a patient's health is the primary consequence of poor treatment adherence. Simultaneously, the lack of effective adherence to chronic disease management is often associated with an extensive economic burden on healthcare systems. Patients may experience more severe symptoms when not following the treatment prescribed to them by health professionals. In many cases, these scenarios can lead to more frequent emergency hospital visits, further increasing the financial stress on healthcare systems.

Among the respiratory diseases that are often treated by the use of inhaled devices, asthma in particular is associated with recurrent hospital visits due to a higher number of exacerbations.[1,2] Inconsistent intake of medications can also impact the treatment of other conditions, such as chronic obstructive pulmonary disease, cystic fibrosis and pulmonary arterial hypertension.

Over the past few years, the incorporation of adherence monitoring solutions has gradually been implemented in new inhalers and nebuliser systems in increasing numbers, either as add-ons or integrated forms. A large number of these solutions rely on Bluetooth connectivity for this purpose. The goal has been to provide patients, healthcare professionals and healthcare systems with a tool that can alleviate some of the burdens caused by lower adherence levels.

> "Deterioration of a patient's health condition is the primary consequence of poor treatment adherence."

The focus is on monitoring approaches that could eventually result in higher adherence levels. Although, initially, studies did not show significant improvements in adherence or were inconclusive to some extent, more recent studies are beginning to shed light on this matter. This has ignited a sense of contribution to the development of connected devices, cementing a space for their future adoption, thanks to constant advances in the internet of things (IoT).[3,4]

A NEBULISER SOLUTION, ADHERESP = ADHERENCE + RESPIRATORY

Pharmaceutical companies developing new inhaled therapies are showing increasing interest in incorporating more advanced nebulising systems. These include mesh nebulisers, which are characterised by their portability and high delivery

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Figure 1: AdheResp – a smart, breath-actuated mesh nebuliser.

performance, especially when used with specific medications as drug-nebuliser combination products. With these effective solutions, attention is also being paid to to the inclusion of higher-end products that not only focus on performance efficiency, but also aim to integrate new features. Connectivity is at the top of this list of features.

Driven by the demand for adherence monitoring and the potential of connectivity to fulfil this requirement, the smart, breath-actuated mesh nebuliser, AdheResp, was designed to record data that could effectively support these needs (Figure 1). The AdheResp nebuliser was developed with the latest Bluetooth technology to transmit data from the handheld device to a mobile application, which can, in turn, be linked to a medical cloud service platform. The primary goal is to support adherence monitoring and provide pharmaceutical partners with the option of including connected features in their new combination products, while also benefiting from other functions, including breath-actuation and activation.

The standard version of the AdheResp nebuliser can transmit three major sets of data to a mobile device. These data sets include time information, battery status and pressure changes recorded as part of the breath-actuation. These data sets were selected based on their identification as key parameters for supporting adherence monitoring and usability during extensive product research. Additionally, supported by the customisable nature of the AdheResp platform, the optimised versions of the AdheResp nebuliser offer expanded possibilities for connectivity beyond these aspects. This includes other usability and traceability options, such as inhalation feedback, guidance on successful inhalation and tracking of medication batches.

> "Driven by the demand for adherence monitoring and the potential of connectivity to fulfil this requirement, the smart, breath-actuated mesh nebuliser, AdheResp, was designed to record data that could effectively support these needs."

As new demands in adherence monitoring are identified, it can be expected that newer functions could be made available thanks to the close collaboration between software or mobile app developers, medical cloud service providers and smart mesh nebulisers, such as HCmed Innovations's customisable AdheResp platform.

STANDARD AND CUSTOMISABLE FEATURES OF THE ADHERESP NEBULISER PLATFORM

During the development process of the AdheResp nebuliser, some key functions were identified to monitor adherence, with the aim of meeting the needs of the different stakeholders involved in a patient's treatment. Pharmaceutical companies, healthcare professionals and patients themselves are part of this intertwined system, each with unique needs but all sharing a common goal – supporting adherence for the benefit of patients.

While batch traceability and tracking treatment efficiency may be more valuable for pharmaceutical companies, patients would perceive greater benefits from real-time data transmission and data recording, which is also indispensable for healthcare professionals. Some of the

existing and customisable functions that could be captured within the AdheResp platform (in some cases in combination with a customisable mobile app and medical cloud service) are discussed here.

Treatment Data Recording

Data recording is an essential tool that benefits all parties during adherence monitoring. The AdheResp nebuliser can transmit data, including the time of treatment, length of individual treatment period, changes in pressure during treatment (associated with the breathing profile) and feedback on the expected inhalation period, which can be interpreted as a successful/unsuccessful inhalation. These records can be shared between patients, healthcare professionals, healthcare systems and even pharmaceutical companies via the incorporation of medical cloud services that enable the uploading of the transmitted data to a mobile app. Furthermore, and also supported by a mobile app, recorded data could be exported to files, which could then display selected data based on specific dates or timeframes.

Drug Traceability

This tool is associated with the transmission of batch information from a vial or ampoule at the time of treatment. The AdheResp nebuliser features an activation mechanism that uses near-field technology (NFC) to activate the nebuliser before each treatment. It is possible to integrate the NFC tag into the label of a vial or ampoule to activate the nebuliser and, at the same time, transmit the information of the nebulised drug. The information, which is initially stored in the device, can then be transmitted to the mobile app for data recording. Drug traceability is another major option that benefits all parties in monitoring patient adherence to the prescribed treatment, enabling follow-up during subsequent appointments.

Tuneable Delivery Platform

For certain indications, a specific triggering span during inhalation or output rate may be required. To address this need, the AdheResp nebuliser can be activated using different NFC tags, which contain customised algorithms to enable the appropriate operation during activation. This activation configuration can be transmitted to the mobile app, providing further information for periodic review within the treatment scope, as well as space for adjustments during the overall treatment. This function could be particularly beneficial for healthcare professionals and patients to identify an optimal and/or personalised course of treatment.

Real-time Guidance

For treatments in which a specific breathing pattern has been identified as optimal for enhancing the delivery and deposition of medication in the respiratory airways, the connectivity function, supported via a mobile app, could provide guiding instructions on when to inhale and exhale using graphics. By relying on pressure change readings transmitted from the AdheResp nebuliser, the data can be combined with the app's algorithm to understand how best to synchronise breathing with the optimal profile. This would provide feedback to the patient during the treatment for self-adjusting to the expected breathing profile.

> "To support adherence in younger users, the implementation of games in a mobile app could serve as the means to engage with the use of the nebuliser."

Gamification Elements

To support adherence in younger users, the implementation of games in a mobile app could serve as the means to engage with the use of the nebuliser. Pressure changes could be used as a guiding tool in a customised mobile app.

Reminders for Cleaning and Consumable Replacement

Maintenance of the device is an important factor to ensure that patients receive their medication under the optimal delivery conditions. By using the data recorded in the AdheResp nebuliser, it is possible to display reminders in a mobile app for when the medication reservoir should be cleaned, disinfected or when the consumables should be replaced. This patient tool also provides useful information to healthcare

professionals and pharmaceutical companies seeking to understand how the patient adheres to the suggested maintenance procedure. Similarly, the effects associated with cases where patients do not adhere to the standard cleaning procedure can also be identified.

Treatment Reminders

Primarily focused on patients, treatment reminders are intended to assist adherence through notifications, which can be configured on the mobile app and linked to the time information transmitted by the AdheResp nebuliser.

Prescriptions and Appointments

While not directly linked to the AdheResp nebuliser, features such as facilitating the issuance of prescriptions and arrangement of appointments for future hospital visits are important tools that benefit patients and healthcare professionals during the course of treatment. These features could indirectly contribute to improved adherence.

CONNECTIVITY AND COLLABORATION OPPORTUNITIES

As the delivery of connected solutions can extend beyond the medical device features, the collaboration of multiple companies in the development of these products becomes crucial. Smart nebulisers possess integrated Bluetooth modules and other components, enabling the collection and transmission of data. However, translating these data into a quantifiable and visual format is necessary for presenting it in a way that patients and healthcare providers can fully benefit from. To achieve this, mobile app developers who are experienced in creating secure and easy-to-comprehend app platforms have an indispensable role to play.

This type of collaboration requires device manufacturers to share data transmission formats that can be received in mobile apps. Once received, the algorithms created by app developers can process these data to display the desired information. Depending on the function and scope of a mobile app, it may be classified as medical device and require regulatory filing in certain countries and regions.

Similarly, cloud service providers contribute to the exchange of data between all parties that could benefit from it in the process of monitoring adherence. For medical devices, several cloud services providers can ensure the secure transmission and storage of data to protect private information. Although prioritised during development, data privacy remains one of the most controversial issues surrounding the medical IoT, especially in respect to the safety of transmitting data between devices and data ownership once collected. Nonetheless, as new guidelines are being drafted and released more frequently, targeting harmonisation of the overall connectivity environment, the goal is to reduce concerns regarding this aspect as much as is feasibly possible.

Companies such as HCmed Innovations are open to creating collaboration opportunities with app developers and medical cloud service providers to implement the connectivity functions supported by the AdheResp nebuliser. HCmed Innovations' objective is to establish a network of solutions for future development with pharmaceutical companies, aiming to include connectivity as an effective mechanism to monitor adherence and further improve patients' treatment outcomes.

OTHER APPLICATIONS AND THE FUTURE OF CONNECTIVITY

Besides the implementation of connectivity in a commercial product, connectivity solutions can also be implemented during clinical trials. Data collection in clinical trials could add value to the outcome of the study, which may not be accurately and effectively recorded without connectivity functions.

Pharmaceutical companies intending to include connectivity in the scope of their trials could benefit from this process, although cybersecurity and the lack of a clearly standardised procedure for the implementation of connectivity in trials remain points to be addressed. Currently, a large number of clinical trials using connectivity have mostly focused on the data aspect or existing therapies, rather the development of a new therapy.

Nevertheless, as technological advancements continue to cement their position in the medical field and new guidelines are released, the future of connectivity is increasingly promising for future treatments, including those in the respiratory field. The AdheResp nebuliser offers an accessible platform for the use of connectivity from early development to commercialisation. Standard and customisable functions comprise options for different indications and target populations, while also incorporating other smart functions, such as breath actuation and device activation, to add value to adherence monitoring.

In the nebuliser space, HCmed Innovations is committed to creating more value by actively collaborating with pharmaceutical companies that aim to incorporate adherence monitoring solutions in new therapies in the push for connectivity implementation, thus assisting patients in their treatment.

> "Translating these data into a quantifiable and visual format is necessary for presenting it in a way that patients and healthcare providers can fully benefit from."

ABOUT THE COMPANY

Founded in 2014, HCmed Innovations is a contract development and manufacturing organisation that provides high-quality and cost-effective vibrating mesh nebuliser technology and services to support global pharmaceutical partners in the development of drug nebuliser combination products for inhalation therapies. HCmed offers mature customisable mesh nebuliser platforms to enhance drug delivery. The company's technology enables efficient and reliable nebulisation of different types of medication, ranging from small-molecule synthetics to large molecule biologics, as either solutions, suspensions or even difficult-to-deliver high-viscosity drugs. Its latest platform includes the incorporation of breath actuation and connectivity features to enhance drug delivery and monitor patience adherence.

REFERENCES

1. *Makhecha S et al, "Novel electronic adherence monitoring devices in children with asthma: A mixed-methods study". BMJ Open Respir Res, 2020, Vol 7(1), Article e000589.*
2. *Mosnaim G et al, "Digital Health Technology in Asthma: A Comprehensive Scoping Review". J Allergy Clin Immunol Pract, 2021, Vol 9(6), pp 2377-2398.*
3. *Zabczyk C, Blakey JD, "The Effect of Connected "Smart" Inhalers on Medication Adherence". Front Med Technol, 2021, Vol 3, Article 657321.*
4. *Moore A et al, "A randomised controlled trial of the effect of a connected inhaler system on medication adherence in uncontrolled asthmatic patients". Eur Respir J, 2021, Vol 57(6), Article 2003103.*

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Edgar Hernan Cuevas Brun is Business Development Manager at HCmed Innovations. He has over nine years of experience in the drug delivery field and holds a BS in Biomedical Engineering from National Tsing Hua University (Taiwan) and a Master's in Business Administration. He is responsible for expanding and co-ordinating the establishment of new partnerships with global pharmaceutical companies, while also supporting the development of drug-nebuliser combination products. Furthermore, he is involved in the development of connected devices, assisting in the company's programmes and establishing alliances with new partners to expand into digital health.

Yuan-Ming Hsu, PhD, is R&D Director at HCmed Innovations, leading the R&D department. He is responsible for new product development and product customisation for drug-nebuliser combination products. He holds a PhD in Biomedical Engineering from National Yang-Ming University (Taiwan). Additionally, he has worked as a researcher at a medical centre in the field of regenerative medicine and controlled-release drug delivery systems. Dr Hsu also gained experience in animal and clinical studies while he was the R&D supervisor in a pharmaceutical company. In the medical device field, he has more than eight years of experience in developing Class II and III products and clinical trials, including for drug-device combination products.

OWEN MUMFORD
Pharmaceutical Services

CONQUERING THE CHALLENGES OF CONNECTED DRUG DELIVERY DEVICE DEVELOPMENT

In this article, Michael Earl, Director, Pharmaceutical Services, at Owen Mumford, discusses the factors that need to be taken into account for successful connected drug delivery device development.

The connected devices trend shows no signs of stopping, with the market for connected drug delivery devices expected to grow from US$0.87 billion (£0.69 billion) this year to $3.92 billion by 2028 – a compound annual growth rate of 35.13% over the five-year forecast period.[1] The increasing prevalence of chronic diseases, such as asthma, chronic obstructive pulmonary disease and diabetes, is one of the major factors driving the growth of the market, along with the ageing population. Increased patient connectivity and engagement is also a significant factor.

VALUE PROPOSITION

In this growing market, it is tempting to think that the more connectivity is included in new drug delivery devices, the better. But, without a clear value proposition at the start of the design and development process, the result could be a variety of new features offering little real benefit to patients or healthcare professionals (Figure 1).

For consumer products, trial and error can often be used to fine-tune device development – with amendments to the design over time once a clear picture emerges

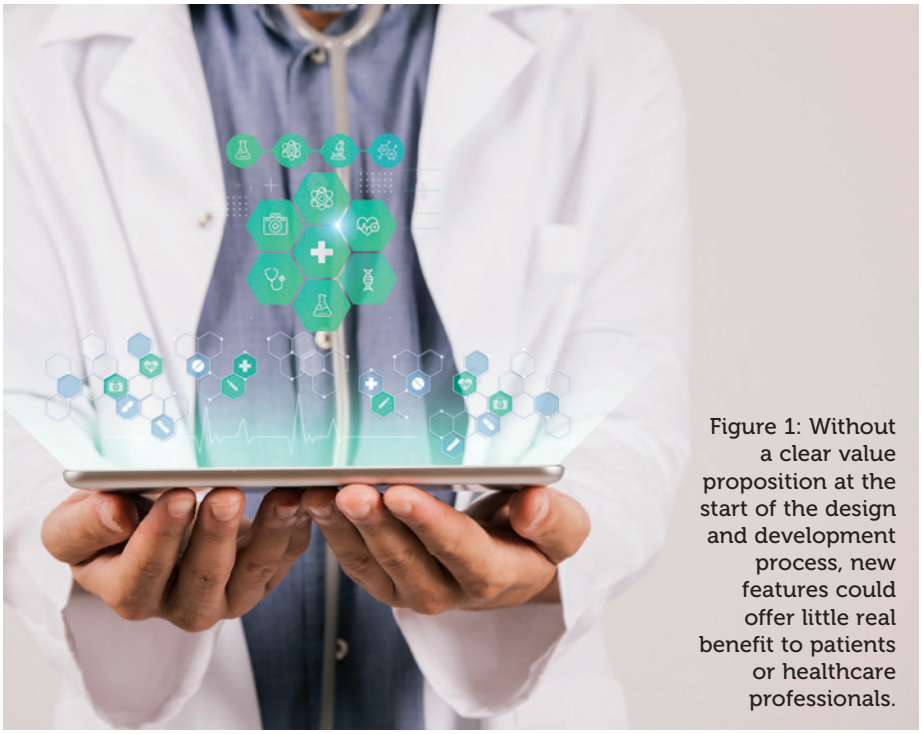

Figure 1: Without a clear value proposition at the start of the design and development process, new features could offer little real benefit to patients or healthcare professionals.

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> "There is no point in collecting data just for the sake of it – the data have to be relevant, useful and accessible to everyone who needs it."

of which features consumers are keen to adopt. But this kind of "fail fast" approach is not available in the highly regulated world of drug delivery device development, where new products need to be demonstrably safe and effective from the word go. Add in fears around data security and privacy – and the rapid evolution of connectivity technologies – and it is clear that the pressure is on to get things right first time.

So, a good place to start is consideration of why the drug delivery device needs to be connected. There is no point in collecting data just for the sake of it – the data have to be relevant, useful and accessible to everyone who needs it, otherwise it is not going to add value to a device. If there is a legacy non-connected version of the device, for example, analysing how patients use it can give valuable insights into how a certain new feature or information could help with a particular task.

DEVICE CONCEPT

Device manufacturers have a useful role to play when it comes to translating user research into a successful design concept. They can help match the appropriate technology and functionality with patients' needs and requirements. For example, they can demonstrate the full range of indicators and sensors that can be incorporated into a device – and highlight the different options and combinations that are available to suit the specific drug and therapy area.

It is also crucial not to lose sight of the fact that a connected drug delivery device will only be as good as a patient's experience of interacting with it (Figure 2). A seamless user experience is vital to avoid widening the gap between human and machine. Understanding how a patient or carer currently manages a particular disease will yield valuable information to help break down any barriers that could interfere with how a new connected device is used in real life – rather than in a computer simulation.

TESTING TIME

Once relevant and valuable new features have been identified and incorporated into the device concept, it is time to put them to the test. The addition of connectivity increases complexity and the number of components in a device, and they all need to be tested, validated and verified – so this has to be factored into the development process. Additional testing is also required for batteries and other electronic components – with consideration given to the different environmental conditions that the device will be exposed to during its lifetime and the potential impact on the shelf life of the batteries. Biologics, for example, will use cold-chain distribution, which could affect device components and electronics.

There also needs to be stringent quality control during manufacturing, transportation and storage to ensure that the device is reliable throughout its lifetime. Battery life is becoming increasingly important, so the algorithms that determine and optimise sensors, indicators and battery use need to be a particular focus.

REGULATORY PATHWAY

As with any medical product, connected drug delivery devices face stringent regulatory hurdles along the road to commercialisation. It is critical to understand all the regulatory requirements thoroughly right from the start of product development so that the process can be de-risked through well-designed and meticulous steps to avoid problems further down the line during regulatory submissions. From mechanical, hardware and software requirements through human factors considerations and ultimately to cybersecurity factors, the regulatory pathway has to be clear.

Developing a connected add-on to an existing device can be an easier regulatory option. The drug-device combination product will have already been validated and approved, so a regulatory filing can be submitted solely for the accessory – which may not be defined as a medical device. But fully integrated connectivity requires specific additional human factors testing and user studies to evaluate the connectivity and functionality – and its impact on the performance of the combination product.

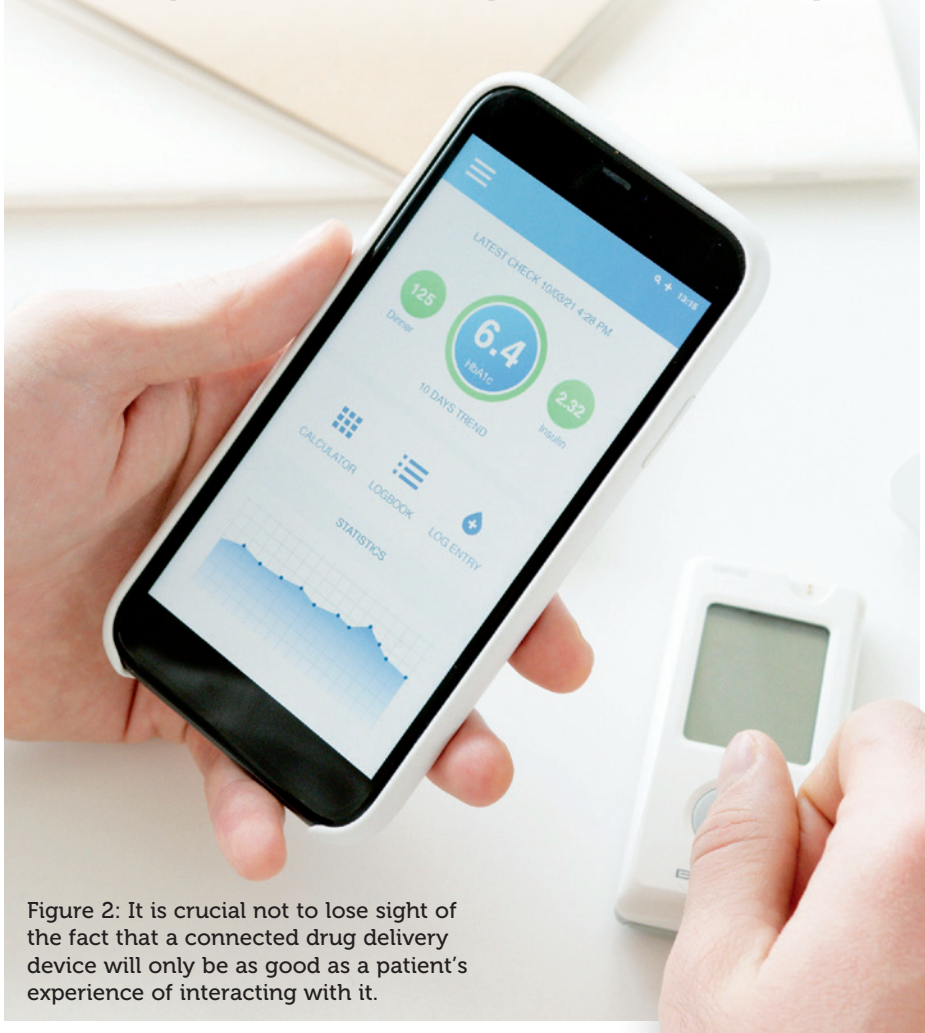

Figure 2: It is crucial not to lose sight of the fact that a connected drug delivery device will only be as good as a patient's experience of interacting with it.

"Selecting a sustainable design is more important than ever in the development of a new connected device."

ENVIRONMENTAL CONSIDERATIONS

The increasing pressure on drug delivery device designers to create environmentally friendly products means selecting a sustainable design is more important than ever in the development of a new connected device. Integrating electronics into single-use devices to enable connectivity generates electronic waste, for example, and disposal may be controlled by regulations such as that covering Waste Electrical and Electronic Equipment recycling.

Reusable connected devices avoid the complications of disposing of electronic components after each use – the drug cartridge or prefilled syringe is simply replaced. But it is important not to make assumptions about the difference in environmental impact between single-use and reusable systems. A thorough analysis is required, with a holistic approach using tools such as lifecycle assessment, which includes an assessment of everything from the raw materials to the manufacturing processes and complete supply chain.

Factors that need to be taken into account include the energy consumed in the manufacture, distribution and use of a product, the amount of material that is derived from renewable or recycled content, and the amount of material that can be recovered for reuse at the end of the product's life. But the choices are not straightforward as environmental considerations must be balanced with the many other requirements for safety-critical products, such as connected drug delivery devices.

"Environmental considerations must be balanced with the many other requirements for safety-critical products, such as connected drug delivery devices."

THE RIGHT CONNECTIONS

Developing a connected drug delivery device is a complex and often costly undertaking – adding risk and time to the process of device development, testing and regulatory approval. Harnessing valuable insights from the extensive experience of third-party experts can help to save time and resources during the digitalisation process. The right connections can make all the difference.

ABOUT THE COMPANY

Owen Mumford is a major healthcare company and device manufacturer that commercialises pioneering medical products in its own brand and custom device solutions for the world's major pharmaceutical and diagnostic companies. Owen Mumford's goal is to enhance access to diagnostics, encourage adherence to treatment and reduce healthcare costs, making a world of difference to a world of people.

REFERENCES

1. *"Connected Drug Delivery Devices Market Size & Share Analysis – Growth Trends & Forecasts (2023-2028)". Mordor Intelligence, 2023.*

ABOUT THE AUTHOR

Michael Earl joined Owen Mumford as Director of Pharmaceutical Services in November 2020. He was previously the Commercial Vice-President at Bespak (now part of Recipharm), leading the commercial team there to drive growth in its substantial medical devices business. Prior to that, he worked for a number of pharma, biotech and device companies. In a career spanning more than 35 years, Mr Earl has been responsible for all aspects and stages of drug and device development and commercialisation. He has also completed a substantial number of commercial, licensing, and mergers and acquisitions transactions.

ON drugDELIVERY

2024 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
January	Prefilled Syringes & Injection Devices	Deadline Passed
February	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Jan 11, 2024
March	Ophthalmic Drug Delivery	Feb 1, 2024
April	Pulmonary & Nasal Drug Delivery	Mar 7, 2024
Apr/May	Drug Delivery & Environmental Sustainability	Mar 21, 2024
May	Delivering Injectables: Devices & Formulations	Apr 4, 2024
May/Jun	Oral Drug Delivery	Apr 18, 2024
June	Connecting Drug Delivery	May 9, 2024
Jun/Jul	Industrialising Drug Delivery	May 23, 2024
September	Wearable Injectors	Aug 1, 2024
October	Prefilled Syringes & Injection Devices	Sep 5, 2024
Oct/Nov	Drug Delivery & Environmental Sustainability	Sep 19, 2024
November	Pulmonary & Nasal Drug Delivery	Oct 3, 2024
December	Connecting Drug Delivery	Nov 7, 2024

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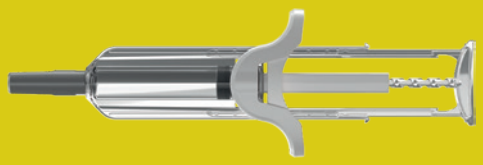

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