CONNECTING DRUG DELIVERY

ON drugDELIVERY

DECEMBER 10TH 2018 • ISSUE Nº 93

Aptar pharma
BD
BIOCORP
COGNITA Labs
H&T PRESSPART
MERCK
Nemera
Phillips Medisize a molex company
Portal Instruments
SENSIRION THE SENSOR COMPANY
YPSOMED SELFCARE SOLUTIONS

ADVANCING MEDICAL CARE THROUGH THE SCIENCE OF

PRECISION METAL COMPONENTS

ISO 13485 - FDA Facilities - Clean Room

MW® INDUSTRIES inc.

Medical Solutions

Medical contract manufacturers rely on our speed and quality for these applications:

- Auto-injectors
- Dispensing Tips
- Surgical Devices
- Drug Delivery
- Life support
- Powered Surgical Components
- Implants
- Heart Pumps

ECONOMY SPRING & STAMPING
MW Industries, Inc.

LAVEZZI PRECISION
MW Industries, Inc.

Servometer®
MW Industries, Inc.

BellowsTech
MW Industries, Inc.

HELI-CAL PRODUCTS COMPANY
MW Industries, Inc.

mwmedicalsolutions.com

Together, we can tackle patient adherence. Let's connect.

Aptar Pharma – delivering connected, intuitive devices to improve patient health outcomes

As the leader in respiratory drug delivery systems, Aptar Pharma is focused on supporting customers and patients to effectively treat respiratory diseases including asthma & COPD.

Today, 60% of patients fail to comply with their medication regimen. At Aptar Pharma, we strongly believe that patient behavior can be changed through connected and intuitive, user-friendly devices. This can significantly increase dose adherence and improve patient health outcomes. That's why we are partnering with digital health solution providers to develop a portfolio of connected devices such as MDIs and DPIs.

To find out more about how we can help you deliver better patient health outcomes via connectivity, call **Sai Shankar**, Director, Business Development – Connected Devices, at Aptar Pharma on **+1 847-800-6058** or email **sai.shankar@aptar.com**

Delivering solutions, shaping the future.

Aptar pharma

Contents

ONdrugDelivery Issue N° 93, December 10th, 2018

CONNECTING DRUG DELIVERY

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

EDITORIAL CALENDAR

Jan 2019	Ophthalmic Delivery
Feb	Prefilled Syringes & Injection Devices
Mar	Skin Drug Delivery: Dermal, Transdermal & Microneedles
Apr	Pulmonary & Nasal Drug Delivery
May	Injectable Drug Delivery
Jun	Connecting Drug Delivery
Jul	Novel Oral Delivery Systems
Aug	Industrialising Drug Delivery Systems
Sep	Wearable Injectors
Oct	Prefilled Syringes & Injection Devices
Nov	Pulmonary & Nasal Drug Delivery
Dec	Connecting Drug Delivery

EDITORIAL:

Guy Furness, Proprietor & Publisher
T: +44 1273 47 28 28
E: guy.furness@ondrugdelivery.com

James Arnold, Assistant Editor
T: +44 1273 47 28 28
E: james.arnold@ondrugdelivery.com

SUBSCRIPTIONS:

Audrey Furness, Subscriptions Manager
E: subscriptions@ondrugdelivery.com
11-12 issues of ONdrugDelivery Magazine published per year, in print, PDF & online.
Electronic subscription is always completely **free**.
Print subscription costs **£99/year + postage**.

ADVERTISING:

Guy Furness, Proprietor & Publisher
T: +44 1273 47 28 28
E: guy.furness@ondrugdelivery.com

MAILING ADDRESS:

Frederick Furness Publishing Ltd
The Candlemakers, West Street, Lewes
East Sussex, BN7 2NZ, United Kingdom

ONdrugDelivery Magazine is published by Frederick Furness Publishing Ltd

Registered in England: No 8348388
VAT Registration No: GB 153 0432 49
ISSN 2049-145X print / ISSN 2049-1468 pdf

ONdrugDELIVERY

YDS SmartPilot™ YpsoMate

Go for smart guidance.

swissmade

10130479-MSTR-en/V02

Reusable add-on transforms YpsoMate® into a fully connected smart autoinjector.

- Bluetooth®-based wireless tracking of injection date, time and success
- Advanced patient guidance throughout the injection process
- NFC-based identification of combination product label to increase patient safety
- YpsoMate® autoinjector compatibility with SmartPilot™ without further changes
- No need to charge SmartPilot™ during its entire lifetime

For more information visit www.ypsomed.com/yds

Ypsomed AG // Brunnmattstrasse 6 // 3401 Burgdorf // Switzerland
T +41 34 424 41 11 // info@ypsomed.com

YPSOMED SELFCARE SOLUTIONS

INNOVATIVE SOLUTIONS: DIGITAL DEVICES, DRUG DELIVERY AND SERVICES IN HEALTHCARE

In this article, the Medical Devices & Services team of Merck Group based in Coinsins, Switzerland, discuss the value of capturing "life data" using a connected device for improving patient adherence and therapeutic outcomes, using Merck's easypod™ device as an example of how digital technology can be successfully employed in a healthcare environment.

INTRODUCTION

Over the past 20 years, the healthcare landscape has changed significantly. While major advances in many therapeutic areas have been made, new challenges have arisen. For example, while life expectancy is increasing in many countries, the prevalence of chronic disease is also rising, which is coupled with the use of biological medicines. In 2015, EU member states' healthcare costs were >€1 trillion (£926 billion), equivalent to 7.2% of the EU's gross domestic product (GDP).[1] Healthcare has the potential to drive towards unsustainable higher speciality care costs. As such, there is an increasing need to go beyond the molecule and look at innovative ways to demonstrate and offer value to healthcare professionals and patients.

In parallel with the changing healthcare landscape, recent years have seen the advent of the digital age, with widespread use of the internet, smartphones and wearable technology in many markets. This has led to new and innovative ways to connect people with information and each other, and also offers opportunities to capture data at a patient population and individual patient level that can help inform current and future management approaches.

"While in 2007 only 9% of hospitals used eHealth records, a decade later 90% of hospitals employ and use them routinely."

CURRENT PICTURE OF DIGITAL SOLUTIONS IN HEALTHCARE

The digital era has brought both advances in medical understanding and new technologies that have revolutionised healthcare. The use of eHealth records across medical services and centres, for example, can offer rapid access to patient information across different specialities supporting holistic care. While in 2007 only 9% of hospitals used eHealth records, a decade later 90% of hospitals employ and use them routinely.[2]

The digital revolution in healthcare shows no signs of stopping and presents many opportunities for patients to explore their health. The internet is often a source of health information, with one in five people in a UK survey reporting that they self-diagnose online.[3] More than 165,000 apps currently available for the Apple iPhone and Android phones are health-related. They offer medical information on conditions, symptoms and treatments, monitoring of health factors related to the user's condition, advanced medical consultation and appointment booking.[4-6] But how accurate are these apps in reality?

Whilst these tools may be useful for people who can't decide whether or not they ought to see a doctor, this method of obtaining information does not replace a

Merck Group
Frankfurter Straße 250
Darmstadt, 64293
Germany

E: MDSCommunications@merckgroup.com

www.merckgroup.com

"The ability to capture "life data" beyond the clinic has evolved rapidly, but its use in healthcare is limited and under-utilised, leading patient insight between clinic visits to be lost."

face-to-face medical consultation and users should exercise caution when receiving the information.[7] In a study, funded by the US National Institutes of Health, software algorithms identified the correct diagnosis first only 34% of the time and symptom checkers tended to be overly cautious, encouraging users to seek medical attention when it was not needed – actions which could have serious implications for healthcare spending.[7] Despite their poor level of accuracy, digital medical apps continue to be used by patients and practitioners for a range of healthcare tasks and their use is not predicted to decline.[7]

WHAT DOES THE FUTURE HOLD?

Despite advances, there remains a significant need in chronic diseases for healthcare professionals (HCPs) and patients to be connected, by harnessing wider data points the quality of conversations between patient and HCP can be significantly improved. Currently, healthcare insights are primarily driven by clinic appointments and evaluations performed in association with healthcare visits. This provides very limited knowledge as to the treatment behaviour on a day-to-day basis. It is during these "non-connected" periods that a patient can face challenges that impact their medication adherence and ultimately their clinical outcome.

The ability to capture "life data" beyond the clinic (e.g. patient attitudes and preferences, diet, exercise, sleep patterns and adherence) has evolved rapidly, but its use in healthcare is limited and under-utilised, leading patient insight between clinic visits to be lost. Adherence, for example, is a major consideration in patients with chronic diseases. Approximately 50% of patients do not take medications for chronic illnesses as prescribed and only a quarter of ongoing medication users are completely adherent, which can have a major impact on outcomes. For individuals with growth hormone disorder (GHD), for example, high adherence (≥78%) in the first two years was associated with significantly increased height gains compared with low/medium adherence (<78%), with a mean height standard deviation score (HSDS) gain of +1.16 in high adherence groups versus +0.88 in low/medium adherence groups (p= 0.01).[8]

With limited ongoing monitoring in most diseases, information about an individual's disease progression and treatment behaviour is missed and their appointments may only provide a snapshot in time. As a result, the patient's care team use an incomplete picture to inform treatment management decisions.

Digital solutions, including smart devices, can help complete the picture of the patient beyond the clinic and provide additional support to healthcare professionals. Data about an individual's condition, disease perception and adherence to medication can help enhance disease and treatment understanding, thereby informing and optimising medical practices. By leveraging digital technology and this "life data", a more complete picture of the patient journey can be achieved, giving a more holistic view to the HCP (Figure 1).

Merck has significant experience in the development and commercialisation of smart injection devices. The easypod™ electromechanical autoinjector administers a pre-set dose of Saizen®, a growth hormone for individuals with GHD. Over 40,000 of these devices were used worldwide in 2017 alone. easypod™ stores the date, time and status (complete, partial, missed) of each injection. easypod™ also has an eHealth component called easypod Connect, which uploads data wirelessly from the patient's home to a cloud-based platform and allows different stakeholders (healthcare

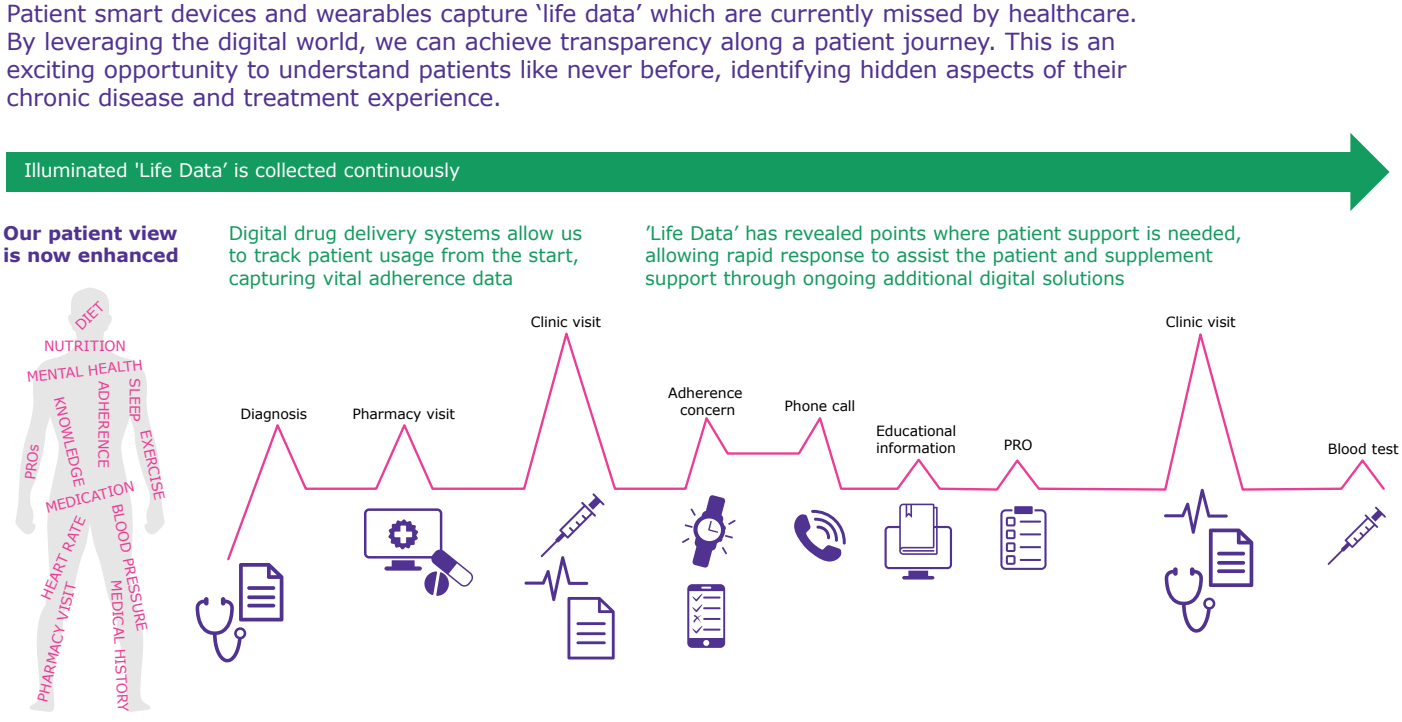


Figure 1: An enhanced patient view.

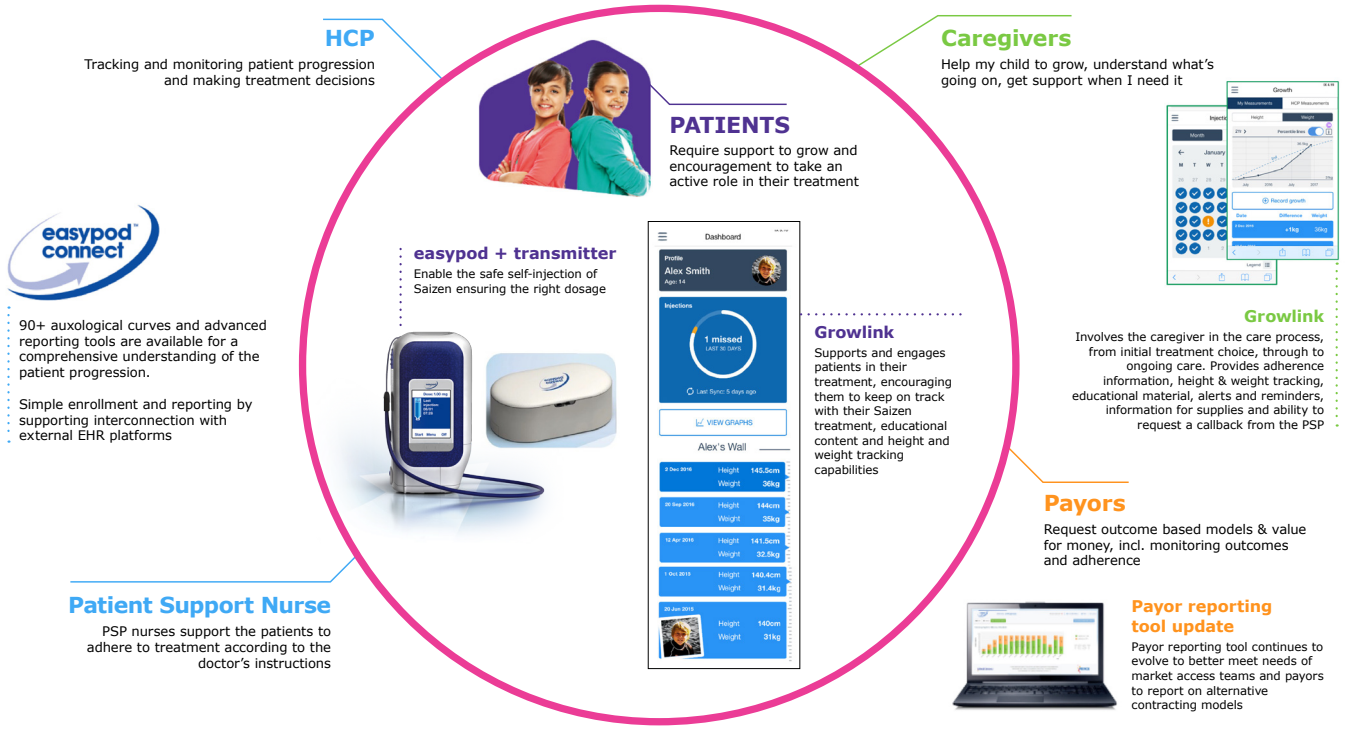


Figure 2: easypod™ eHealth approach to treatment management: the Saizen® ecosystem.

> "Merck is proud that this broad eHealth approach is now benefiting over 14,000 patients worldwide. Recent studies also show that this approach is resulting in clinically significant levels of adherence improvement in the real world."

professionals, payers and patient support nurses) to view this comprehensive data (Figure 2). This remote monitoring capability allows the care team to act in a timely manner in order to manage their patients more effectively and offer tailor-made interventions depending on the issue at hand. This data can also be anonymised and aggregated to offer payers the opportunity to look at the effective use of medication in specific geographical areas.

easypod™ also has a patient smartphone application called Growlink, which was developed alongside growth hormone deficient patients and their carers. Growlink gives the patient and/or their carer the opportunity to track their injection progress, monitor their height improvement, as well as order ancillaries for their easypod™ device. The combined view of both adherence performance and clinical outcome (in this case growth improvement) aims to engage the patient and/or their carer in their treatment. Merck is proud that this broad eHealth approach is now benefiting over 14,000 patients worldwide. Recent studies also show that this approach is resulting in clinically significant levels of adherence improvement in the real world.[9]

easypod™, in combination with the easypod Connect platform, was evaluated in a cohort of 9,314 patients across 33 countries, to assess adherence in real-world settings. The study reported that:

- The majority of patients using easypod™ had high adherence levels at each time point (1, 3, 6, 12, 24 and 36 months). This was defined as adherence at levels ≥85%, calculated as mg of growth hormone injected vs mg prescribed.
- At month 48, data were available for 665 patients, of which 67.8% of patients continued to achieve adherence levels ≥85%.
- Adherence was slightly better in girls than boys and showed a fall in levels with increasing age in both genders.
- These insights may help future inform strategies to target adherence in boys and older children.

easypod™ represents an important step in our ability to inform individual management and, by pooling data, disease-level interventions. With the opportunities available as technology advances, a future goal is to collect the full range of "life data" from patients, revealing further insights and points where support is needed and identifying unmet needs for future development focus.

PIONEERING EXPERTISE IN MEDICAL DEVICES AND SERVICES

The increasing digitisation of our lives is currently producing a radical change in business models across several industries and the opportunity presented by connected devices in healthcare has been recognised. However, regulatory hurdles, country-specific challenges, the need to design and develop a device that is intuitive for patients and HCPs alike and addresses future needs can impede success or prevent a device coming to market. Further to this, the ability to leverage such devices and digital solutions in a manner which truly adds value to multiple stakeholders can be a challenge.

Merck's Medical Devices & Services (MD&S) arm understands these challenges and has developed specific device and digital solutions that address many complex issues and opportunities across therapeutic areas such as endocrinology, fertility and neurology. Merck's unique blend of professionals ensures a global presence and offers 10+ years of experience in deploying

these solutions in more than 50 regulated healthcare markets.

Merck's MD&S arm is focused on developing connected solutions, like easypod™, that gather meaningful and actionable insights into the behaviour of the patient when they are away from their healthcare team. These solutions look to engage and empower patients with complex long-term diseases, gather data to drive insights into the disease and give a deeper, transparent understanding of patient activity and insights between visits. This holistic view may help inform efficiencies within clinics, help to identify patients requiring greater support and aim to improve the patient experience and, ultimately, outcomes.

CONCLUSION

With the digital revolution, there is an opportunity to understand and support patients in new ways – gathering insights into aspects of their chronic disease and treatment experience, and supplementing support through ongoing digital solutions. By harnessing digital "life data", there exists the potential to evolve healthcare insight, and deliver benefits to all stakeholders.

The expertise and experience within Merck's MD&S function allows Merck to operate with an ideation to commercialisation model. This includes insight gathering to identify the issue or opportunity, hardware and/or software development, regulatory approval and finally launch at scale that includes ongoing post-launch support. In this way, Merck can help bridge the gap to revolutionising healthcare.

REFERENCES

1. *"Member States spent over €1000 billion on health". Eurostat, Aug 2018.*
2. *Ramsey L, "How the internet is improving healthcare". World Economic Forum, Jan 2017.*
3. *Kirk A, "One in four self-diagnose on the internet instead of visiting the doctor". The Telegraph (UK), Jul 2015.*
4. *Devlin H, "Health apps could be doing more harm than good, warn scientists". The Guardian (UK), Feb 2017.*
5. *Jack A, "Healthcare apps battle to be taken seriously". The Financial Times (UK), Apr 2016.*
6. *"Things are looking app". The Economist (UK), Mar 2016.*
7. *Miller J, "Self-diagnosis on Internet not always good practice". The Harvard Gazette, Jul 2015.*
8. *Wit JM, Koledova E, Dommelen P, "Effect of Adherence on the 2-Year Growth Response to Growth Hormone Treatment in Prepubertal Children with Idiopathic Isolated Growth Hormone Deficiency Participating in the easypod Connect Observational Study (ECOS)". Presented at 10th International Meeting for Pediatric Endocrinology, Washington DC (US), Sep 2017.*
9. *Cancela J, Guedes S, Koledova E, "Real-World Data from Electronic Monitoring of Adherence to Growth Hormone Treatment in Children with Growth Disorders: a Descriptive Analysis". Presented at ENDO, Chicago (IL, US), Mar 2018.*

Drug Delivery Partnerships

January 28-30, 2019
PGA National Resort & Spa
Palm Beach Gardens, FL

THE BUSINESS DEVELOPMENT EVENT BRINGING YOU VISIONARY IDEAS, DISRUPTIVE TECHNOLOGY, AND PARTNERINGONE® TO MAXIMIZE YOUR PRODUCT LIFECYCLE AND GENERATE NEW REVENUE STREAMS.

A PERFECT BALANCE OF SCIENCE & BUSINESS DEVELOPMENT

Source new partnerships and qualify new deals during one-on-one meetings scheduled with the powerful partneringONE networking tool.

Delve into drug delivery technologies and innovation in our drug delivery tracks, scientific workshops, and tech showcase.

BIG IDEAS AND THOUGHT LEADERSHIP ON THE NEXT LEAP FORWARD

JOSEPH TARNOWSKI
Senior Science & Innovation Medical Director
GlaxoSmithKline

URI BARUCH
Head of Drug Delivery
Cambridge Design Partnership

LILLY STAIRS
Head of Patient Advocacy
Clara Health

MOLLY STORY
Senior Director, Global Usability Engineering and Risk Management
Sanofi, USA

SAVE 10% OFF CURRENT RATES WITH CODE DDP18ON

Drug Delivery Partnerships International

@DrugDelivery365
#DDPCONF

www.DDPevent.com

Leading the way with integrated containment and delivery solutions

West
By your side
for a healthier world™

SMARTDOSE®

PRECISE. RELIABLE.
READY TO GO.

FDA Approved

- The first combination product that incorporates the SmartDose platform technology was recently approved by the US Food and Drug Administration (FDA)
- Thousands of doses have been administered using the SmartDose platform
- Proven engineering, manufacturing and regulatory expertise to support your needs

Wearable Injector

- Subcutaneous self-administration
- Ability to deliver high volume and high viscosity drug products

Patient-Centric

- User-centered design
- Connectivity to a variety of software platforms
- Able to link with adherence solutions
- Onboarding and training solutions available

Flexible Technology

- Address a variety of delivery times through adaptable, pre-programmable technology
- Maximize patient comfort through pre-programmable delivery times

West Pharmaceutical Services, Inc. | 530 Herman O. West Drive, Exton, PA 19341 | www.smartdose.com | North America +1 800-345-9800
Europe +49 2403 7960
Asia Pacific +65 6860 5879

West seeks partners for its SmartDose platform. This platform is intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical/biotechnology company.

For more information visit www.westpharma.com

#10182 0317

WE'RE OFF TO SEE THE WIZARD: "USE-LIKE" PROTOTYPING OF DIGITAL CONCEPTS

Here, Tom Lawrie-Fussey, Healthcare Digital Strategist, and Lucy Sheldon, Human Centred Design Consultant, both of Cambridge Design Partnership, introduce "Wizard of Oz" testing, named after the classic novel and film, whereby experimenters can field test concepts at a very early stage by giving the illusion of a finished product, saving potential costly and time-consuming changes further along the development process.

It is a simple fact that product development cycles are always being squeezed. In all industries, the cost of an extended time to market means that pressure is applied at every step of the development process. In response, rapid-prototyping techniques have matured quickly and are able to significantly reduce these timescales. Mechanical components, such as the body of an inhaler or the lid of an injection pen, can now be quickly built, improved and refined.

> "In the world of drug delivery, many digital concepts are multi-user, multi-touch-point and must comply with strict regulatory and data protection constraints. This is a far cry from designing, coding and deploying a consumer app."

The benefits of these techniques are now widely recognised but the rapid-prototyping of other design functions, such as user interaction, are much less well known. For example, when a novel drug delivery system with new digital interactions is in early-stage development there is a huge benefit in early user testing, as it were, using the digital equivalent of 3D printing.

In theory, digital opportunities do not suffer the same scale of risk and cost as is associated with physical manufacturing. However, in the world of drug delivery, many digital concepts are multi-user, multi-touch-point and must comply with strict regulatory and data protection constraints. This is a far cry from designing, coding and deploying a consumer app. With this complexity comes additional uncertainty and longer development times.

One approach to address this challenge is to use concept testing. Typically, stakeholders are surveyed to provide opinions on the utility and future value of a proposed innovation. As the innovation does not yet exist, their opinions are based on a description of what it would be like once it is made. However, this fails to investigate the user experience or, crucially, how it might influence behaviour. This is vital information in healthcare, compounded because digital services are complex and typically comprise of multiple touch-points and stakeholders.

To use an example from Cambridge Design Partnership's own work, CDP has been working on a digital education programme aimed at increasing the level of correct inhaler usage in children. CDP wanted to find out whether videos, interactive games or even songs were the most successful way of encouraging best-practice compliance in young inhaler users. The implications go far beyond the patient's own device. A comprehensive digital service to improve inhaler use must address a range of different drugs and devices, therefore comprising multiple front-end applications. System building blocks include a:

- Secure patient-data hosting solution
- Portal for the payer
- Dashboard for the healthcare professional
- Dashboard for the pharmaceutical company
- Back-end data analytics engine.

In this example, it is hugely advantageous that, in the same way a physical design is frozen before investment in detailed design and manufacturing begins, the digital design is also optimised and pre-validated prior to transitioning into development. If the

Tom Lawrie-Fussey
Head of Digital Health
E: Tom.Fussey@cambridge-design.com

Lucy Sheldon
Human Centred Design Consultant
E: Lucy.Sheldon@cambridge-design.com

Cambridge Design Partnership
Church Road
Toft
Cambridgeshire
United Kingdom

www.cambridge-design.com

proposition cannot be tested in a realistic way early on, then late stage changes are inevitable, adding additional, unnecessary cost and time. What is needed is an approach where each stakeholder can assess the part of the system that they will interact with, long before the design is locked down.

WIZARD OF OZ TESTING IN PRINCIPLE

One approach we use on early ideas is to create the illusion in the user's mind that very early prototypes are in fact final products. This is the theory behind Wizard of Oz testing.

The Wizard of Oz technique enables unimplemented technology to be evaluated by using a human to simulate the response of a system design. The technique is named after L Frank Baum's novel and the classic film, in which the Wizard is ultimately exposed as a normal man sitting behind a curtain, pulling levers and successfully convincing everyone that he is a powerful magician. The experimenter, like the Wizard, creates a believable illusion of a new device or service. This is then deployed to discover how users interact with an idea and, in so doing, provokes genuine responses.

For example, a user may believe they are speaking to a computer using voice recognition, when, in truth, their words are being typed in manually by an experimenter. The goal here is to observe how a user interacts with a voice recognition system, rather than to measure the effectiveness of the technology that drives it.

This method relies on the generation of what are known as "use-like" prototypes, which do not necessarily need to look like or work like the real thing. The "use-like" prototypes must simply create enough of an illusion to elicit reactions from the people using them that are completely genuine. It is the fidelity of the experience and interaction that is important, not the fidelity of the prototype. For the experiment to work, you simply need to create enough of an illusion to elicit these responses, which then identify the successes and flaws that feed back into the design process.

Figure 1: This is a "use-like" prototype developed by Cambridge Design Partnership to trial inhaler use. It is the fidelity of the experience, not the fidelity of the prototype, which is important. The "use-like" prototype consists of a device which collects inhalation profile data and a training app. The app and device were used in combination for inhaler training. The device could be used in isolation to assess the effectiveness of the app and a range of other inhalation training options including current approaches to training as a baseline.

WIZARD OF OZ TESTING IN PRACTICE

Have you ever been on a website, seen a fantastic new product and tried to purchase it, only to be added to a waiting list? Well, this is a form of Wizard of Oz testing in action. You are faced with the illusion that you can buy an, as yet, non-existent product. In showing an intention to buy, you are added to a list of potential customers, helping the innovators investigate the potential commercial success of their product.

For drug delivery device development, there are many advantages to the Wizard of Oz approach, especially when evaluating early digital concepts. Consider again the system aimed at improving inhaler usage in children. The success of any solution is dependent on how all the stakeholders involved benefit, and when combined, how their behaviour impacts patient outcomes. Utilising "use-like" prototypes and Wizard of Oz testing can shine a light on the aspects of the system that need to be further improved and developed. Figure 1 shows a "use-like" prototype which was created by CDP for a Wizard of Oz research programme to help develop and refine new systems to train patients in correct inhaler technique.

In one example of a Wizard of Oz test protocol, children or adults who are not current inhaler users are trained in how to inhale (without reference to the purpose of the training). This research design assumes that the data collected on the learnability of the inhalation technique is relevant to a

"Have you ever been on a website, seen a fantastic new product and tried to purchase it, only to be added to a waiting list? Well, this is a form of Wizard of Oz testing in action."

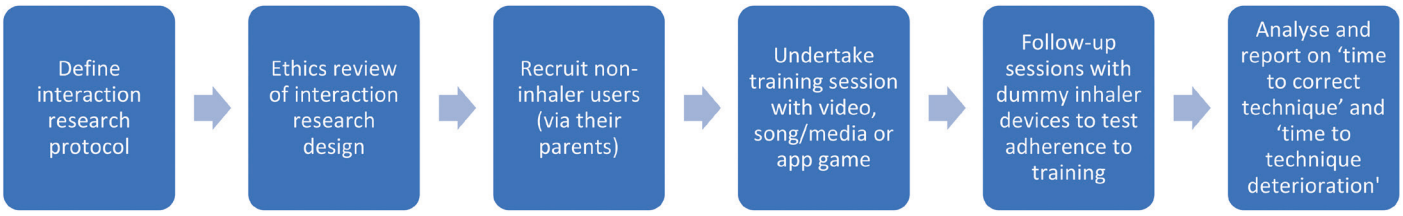


Figure 2: Example research design.

first-time inhaler user. Typically, the cohort is split into two groups; one is trained in line with normal practice (to provide a baseline) and the other group trained using the "use-like" prototype and app in Figure 1. However if data on the adherence over time to the new learned behaviour is required, the study becomes more complex and requires patients to be followed and re-tested at realistic intervals in line with known training decay.

Wizard of Oz testing generates quantitative data on the relative potential of the product concept against a baseline, with a general outline of the research design shown in Figure 2. In addition, observation and interviewing uncovers what users love about the idea, as well as highlighting aspects that they may not value, features they struggle with and areas where improvements need to be made.

Given that this process does not involve administering any drugs or therapies, the approach can be undertaken ethically as market research. Appropriate ethics reviews must still be undertaken nonetheless, but these studies can be implemented relatively quickly and economically.

In parallel with patients themselves, research can be undertaken with stakeholder general practitioners (GPs). They could be presented with various "use-like" representations of information dashboards, in which realistic data visualisation options and anticipated patient scenarios are generated. Faced with believable prototypes GPs can more easily evaluate their desire for new data and researchers can tease out what is most important to them.

"Wizard of Oz testing of new digital concepts is a powerful tool to optimise and learn about the commercial potential of digital concepts at a very early stage."

Further up the chain again, this research method can address the needs of the pharmaceutical company selling the drug. In the same way as with GPs, but this time a simulated live dashboard showing the market usage and effectiveness of the training programme could be used to inspire innovations that optimise marketing and sales programmes.

Wizard of Oz testing of new digital concepts is a powerful tool to optimise and learn about the commercial potential of digital concepts at a very early stage. The method enables development teams to observe customers interacting with a digital product or service, allowing direct feedback on its potential value in the real world while it is still in the conceptual phase.

It is surely far better to start technical development only when digital concepts have proved themselves in Wizard of Oz-style evaluations. It's a smart way of ensuring that your new digital device and service will fully deliver its potential.

ABOUT THE COMPANY

Cambridge Design Partnership is a technology and product design partner focused on helping clients grow their businesses. Some of the world's largest companies trust CDP to develop their most important innovations. Located in both Cambridge (UK) and in Palo Alto (CA, US), CDP specialises in the consumer products, healthcare, energy and industrial equipment markets. Its multidisciplinary staff have the expert knowledge to identify opportunities and tackle the challenges its clients face.

ABOUT THE AUTHORS

Tom Lawrie-Fussey is a Head of Digital Health at Cambridge Design Partnership, and has more than 15 years' product development experience and is a Chartered Engineer with a master's degree. He has been trusted by a myriad of well-known brands during his career, spanning automotive, industrial, FMCG, consumer healthcare and drug delivery. For the past 5 years Tom has specialised in helping clients to navigate their digital roadmap, providing a horizontal cross-sector capability and expertise.

Advising on connectivity and digital services, Mr Lawrie-Fussey has led the development of a number of digital toolkits to help clients to de-risk their digital innovation. One of these, the instrumented user-insights service "diialog™" has grown to serve multiple markets, with various ongoing client projects helping to steer and inform product development investment.

Lucy Sheldon is a Human Centred Design Consultant at Cambridge Design Partnership, and has 15 years' experience developing human-centred medical products, including the application of human factors to drug delivery devices, diagnostic tests, and surgical and therapeutic devices. Ms Sheldon's expertise includes unmet needs exploration through observation, research and structured interviewing; usability engineering including usability testing and the development of usability documentation in line with medical device human factors regulations and IEC14971; and interaction design across physical and screen-based interfaces. Recent projects include usability testing of home-use drug delivery devices, iterative exploration and design for an award-winning low-cost vital signs monitor, and interaction design for a touchscreen surgical interface.

H&T PRESSPART

eMDI
powered by cohero

Smartphone app connectivity to allow real-time tracking and care management

Mechanical Dose Counter

Introducing the next generation MDI

H&T Presspart are pleased to introduce the first market-ready, fully-embedded, intuitive and connected metered dose inhaler (eMDI™) established to optimize care of patients ensuring from asthma and COPD.

The eMDI™ integrates seamlessly with BreatheSmart from Cohero Health, the only respiratory disease management platform that enables tracking of both controller and rescue medications, along with clinically accurate lung function measurement, in real-time.

For more information contact H&T Presspart:

www.presspart.com
eMDI@presspart.com

SUCCESSFUL CONNECTED DEVICE DEVELOPMENT REQUIRES A ROBUST VALUE PROPOSITION

Here, Eric Dessertenne, Chief Operating Officer, Biocorp, discusses the current status of connectivity in healthcare, its future, benefits both in terms of addressing adherence and big data analysis, and emphasises the need for a robust business case. He goes on to describe Biocorp's portfolio of connected delivery systems, including both integrated devices and connectivity add-ons.

INTRODUCTION

We live in an ever more connected world; a fact clear even to the most casual observer. Across industries there is a drive to include smart and connected features into new technology developments to meet a demand for convenience and advanced capabilities from consumers, and for data to analyse from business. Even in the conservative world of pharma and healthcare, where the well-tested and thoroughly understood often seems preferable to cutting-edge innovation in the face of strict regulatory bodies, the drive towards connectivity is inexorable and undeniable.

A recent article in Health Data Management[1] discussed predictions for the coming years in connected healthcare. Amongst them it suggested that, by 2019, more than 50% of life science and healthcare firms will be utilising real-world evidence and, amongst those companies, digital mobile engagement will have increased by 50%; by 2020, adoption of Internet of Things (IoT) based assets in hospitals will have doubled, and 25% of data used in medical care will be captured by the patient themselves; and by 2021 digital healthcare services will account for 6% of all global healthcare expenditure.

> "Adherence is not the sole reason behind the rise of connectivity. Today's world is ravenous for data and the insights that can be gleaned from its analysis."

In today's connected world, the consumer tools of the "wellbeing" industry are being converted into actual healthcare products, in some cases by a natural progression of businesses such as Fitbit, in others by patients making their own "home-made" digital healthcare solutions. Regulators have begun the process of establishing their position, and clinical outcomes for connected devices are starting to arrive. For example, in April 2017, Merck Serono reported results from interferon beta-1a delivered by the RebiSmart™ connected device, which not only achieved a very positive impact on adherence (>95% adherence rate) but, crucially, increased the relapse-free rate to more than 77% over 140 weeks, establishing a clear link between better adherence and lower relapse rate.

> "Biocorp has long understood that connectivity in drug delivery devices needs to be considered carefully, designed for a specific usage and presented with a robust business case."

Eric Dessertenne
Chief Operating Officer
T: +33 6 08 02 14 51
E: edessertenne@biocorp.fr

Biocorp
Parc Technologique
Lavaur-La-Bèchade
63500 Issoire
France

www.biocorpsys.com

The underlying factors of the buzz around connectivity in healthcare are well documented. Most often cited, as with the RebiSmart™, is the promise connectivity presents to tackling the adherence challenge, a huge drain on healthcare both in terms of patients failing to reach their desired therapeutic outcomes and in financial cost to healthcare institutions and the pharma industry itself. Connected devices, with the ability to provide patients with calendars, reminders and feedback on their own treatment, offer one of the most compelling answers to this challenge. As such, device designers across the industry have thrown themselves into the task of bringing connected devices to market.

Of course, adherence is not the sole reason behind the rise of connectivity. Today's world is ravenous for data and the insights that can be gleaned from its analysis. Pharma is eager to realise the benefits this presents in healthcare, including gaining insights into real-world use of medication and devices to feed back into future designs, outcome-based payment models, and IoT-integrated manufacturing and logistics to smooth and enhance production and delivery chains.

Connectivity applied in the context of the current healthcare goal of moving treatment from the clinic to the home is a clear winner. This is evidenced by the success of Abbott's FreeStyle Libre blood glucose monitoring (BGM) device, which greatly increased ease-of-use for patients compared with previous BGM technologies and rapidly proved its worth to payers after a successful launch in Europe.

Biocorp has been working in the area of connectivity since 2013. It has long understood that connectivity in drug delivery devices needs to be considered carefully, designed for a specific usage and presented with a robust business case. As such, Biocorp has developed a portfolio of connected devices in both add-on and integrated formats, spanning both parenteral and respiratory drug delivery.

SOLVING CONNECTED CARE FOR DIABETES

Based on the observation that some critical needs of diabetic patients are not being fulfilled, Biocorp has developed Easylog™ (Figure 1) is a connected smart cap that is compatible with all pen injectors, which records and logs the exact dose dialled and injected by the patient, along with the time and date. The data is sent to a mobile app using Bluetooth technology (Figure 2).

Easylog is an add-on device, meaning it can be used with existing products without designing a new product from the ground up and going through a full combination product approval process. The add-on approach enables connectivity to be readily deployed, in effect allowing pharma companies to gain real experience with a connected device in their product portfolio, without any impact on existing industrial processes and infrastructure.

The pen injector market contains a lot of disposable products. By using an add-on such as Easylog, the cost of adding connectivity to a device can be offset to the reusable add-on. Easylog is reusable for up to two years. Disposable pen injectors represent a major portion of the market, especially when looking at diabetes, which itself is the largest market in this area by volume.

Figure 1: Easylog, smart cap for pen injectors.

The diabetes market is, on the whole, already very well connected when looking at BGMs and other monitoring devices. By bringing the pen injector into the connected sphere the missing piece of the puzzle can be filled in, and a comprehensive connected approach to diabetes care can be offered. This is a clear unmet need in the diabetes market and Easylog is in prime position to meet it by adding the recorded insulin injection time and dosage data to the patient's logs, enabling them to accurately track their insulin usage and, in tandem with a connected BGM, their blood glucose levels, all from their smartphone. The promise of completing this "closed-loop" or "semi-closed-loop" system is clear, being able to pull all the information and data from the various key devices into a single platform for analysis, support and real-time decision making.

The main cited drawback of the add-on approach is that it adds an extra use-step for the patient. For example, the patient needs to remember to transfer Easylog from their used pen injector to the new one every time they change device. However, Biocorp has spent a lot of time ensuring that the process is as seamless as possible, making it really

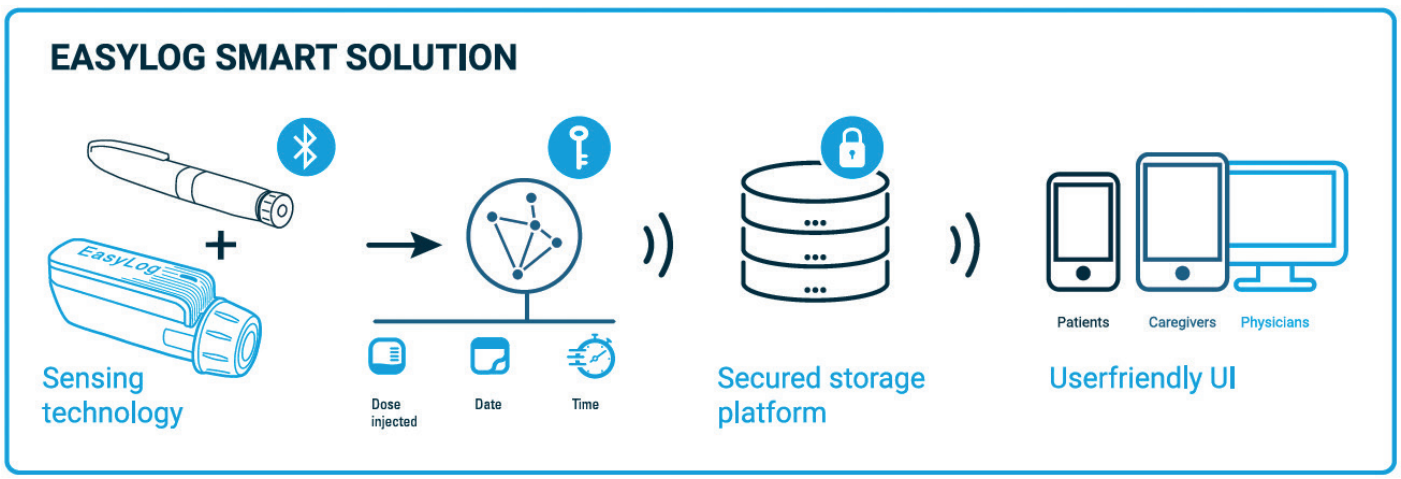


Figure 2: Easylog records injected dose and time, transfers it via Bluetooth to a secure server and outputs useful data to patients and healthcare providers.

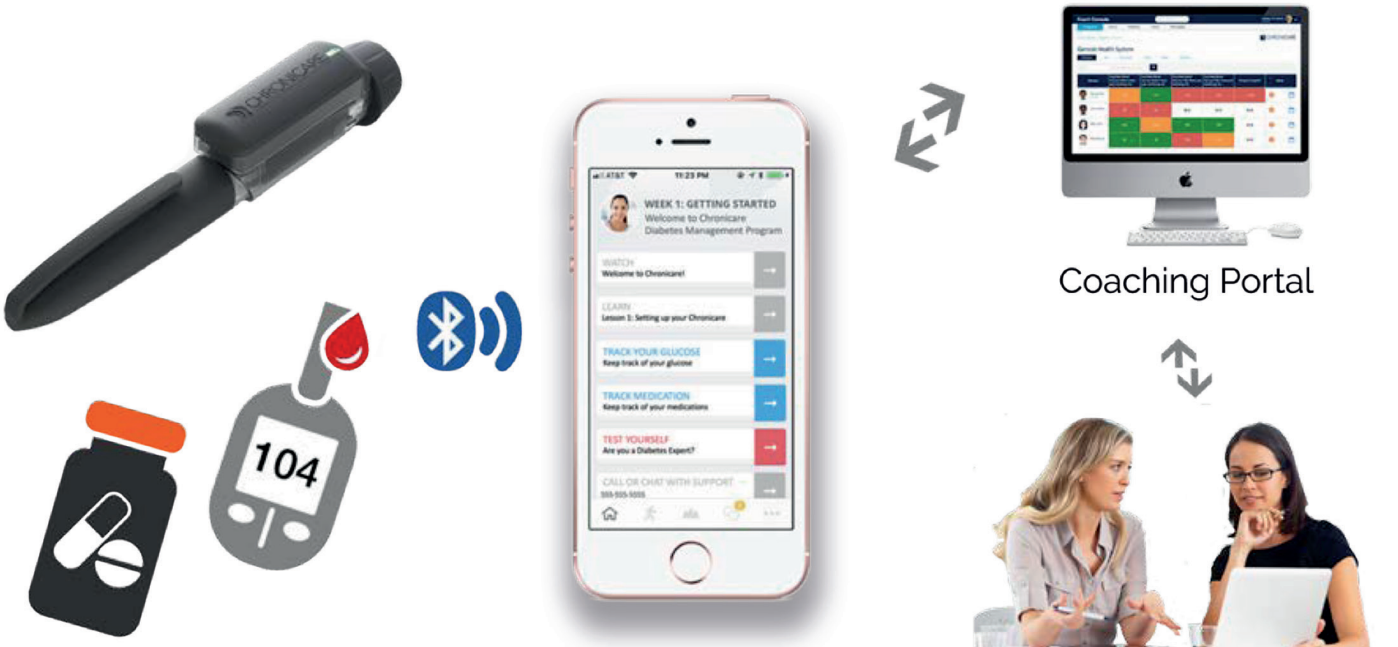


Figure 3: The service provider business case - integrated platform comprising device, app and coaching services.

easy to put the add-on on the new device and requiring no further steps to prepare or activate it. The patient simply puts Easylog onto their device and then uses the pen injector as they usually would.

Easylog will be launched in 2019. At launch, it will be compatible with all major insulin pen platforms currently on the market and connect to any diabetes support platforms, thus fulfilling its purpose of facilitating treatment management for patients. Whilst Easylog will initially be targeted towards the diabetes market, it will in turn be adapted to other indications and markets. Biocorp has already begun tailoring of the technology to other therapeutic areas.

Service Provider Business Model

Rather than offering the Easylog add-on alone, Biocorp offers it as part of a fully integrated platform comprising a connected device, an app, and coaching services (Figure 3). This business model provides additional services to the patient, and real-time data that is valuable for payers (e.g. health plans and large companies in the US). Thus, the device is not an extra cost, but a central piece of a smart services offering. It is a model that is already proving profitable for some companies, for example Livongo (Mountain View, CA, US) and Omada (San Francisco, CA, US).

EMBEDDED CONNECTIVITY TO IMPROVE EFFICACY

Biocorp also has products that take the integrated approach to connectivity, seamlessly building it in as a fundamental part of the design. They include the Datapen™ reusable pen injector (Figure 4) and the Onejet™ disposable autoinjector (Figure 5). The advantage of the integrated approach to connectivity is its ease-of-use and convenience for patients. By embedding the connected technology within the device, it can be made a more intuitive part of the user interface and this is the case with Datapen and Onejet.

Datapen is an electromechanical smart pen injector, compatible with standard cartridges and adaptable to dual-chamber cartridges as well. The electromechanical systems in Datapen provide a more comfortable, precise and easy injection for patients, and the digital elements manifest as an easily understood display with control buttons for optimal dialling and dosage, along with audio and visual cues to support the patient through the injection process. With embedded Bluetooth, Datapen allows for real-time data transfer to companion software for tracking and recording injection data.

Figure 4: Datapen, reusable pen injector.

Figure 5: Onejet, motorised disposable autoinjector.

Onejet is the first motor-driven, disposable and Bluetooth-connected autoinjector for use with standard prefilled syringes (PFS) from 1–2.25 mL. Onejet is supplied assembled and ready to use by the patient which, along with its integrated connectivity, makes Onejet an extremely convenient product from the patient perspective. Onejet, utilises an easy and innovative pairing system to connect to a smartphone app, which receives real-time data from Onejet and processes it to provide treatment history and reminders for patients.

Onejet is designed for use with biologic medicines, so had been engineered to be easily customisable for different product profiles with varieties of volumes and viscosities. The device includes an in-built passive safety system to prevent needlestick injuries and the needle is hidden at all times, before, during and after injection, with needle insertion automatically triggered by a skin sensor. Like Datapen, Onejet

> "As an early adopter of this new era of medical technology, Biocorp is in a prime position to design, develop and commercialise connected devices as part of its "design to production" approach."

features audio and visual signals to help the patient keep fully abreast of the progress of their injection.

TRAINING PATIENTS TO BETTER USE THEIR INHALER

Whilst historically, Biocorp's interest and experience has been in the parenteral sector, it has expanded its connected add-on offering into the respiratory area with Inspair™ (Figure 6). Pressurised metered dose inhalers (pMDIs) are often misused by patients, so Inspair was developed as a smart sensing add-on device for standard pMDIs. The add-on captures airflow data as patients use their inhaler, providing feedback on usage, as well as advice on improving their technique.

Inspair is a two-part device: a cap and a sensor. This design means that Inspair can be universalised across pMDIs as only the plastic mouthpiece needs to be customised to fit a given pMDI, which significantly reduces time-to-market. The design also does not interfere with regular inhaler usage, making it patient-friendly and easy to use. Inspair can also be adapted for other types of respiratory device, thanks to its modular design.

The data captured by Inspair can be fed back to the patient in a number of valuable ways. Key on the subject of proper adherence to medication is that it can be used to help the patient improve their hand-breath co-ordination. Poor patient performance in this respect negatively impacts the dose of medication delivered. Inspair can also feed back the inhaled dose and measurements of inhalation depth and speed, which for certain indications can be hugely valuable for tracking the course of treatment and enhancing ongoing decision-making with respect to patient care.

Much like Biocorp's parenteral offerings, Inspair connects to a companion smartphone app via Bluetooth. The device captures and logs each actuation of the device, together with the time and date to provide patients and healthcare providers with an accurate treatment history, interwoven with assessment of quality of delivery. These features make Inspair a valuable addition to an inhalable offering, either as onboarding for new patients, a data capture tool for clinical trials or as part of a commercial product to help patients manage and track a chronic condition.

Figure 6: Inspair, add-on sensor for pMDIs.

CONCLUSION

Connectivity is very much part of the future of drug delivery and healthcare as a whole, and with it will come new business models, opportunities and challenges. As an early adopter of this new era of medical technology, Biocorp is in a prime position to design, develop and commercialise connected devices as part of its "design to production" approach. With devices following both the add-on and integrated approaches to connectivity, Biocorp is ready to fulfil the opportunities presented by the new digital era.

ABOUT THE COMPANY

For 20 years, Biocorp has been designing, developing and manufacturing medical devices for the pharmaceutical industry, enhancing drug reconstitution, safety, packaging and delivery. Today, Biocorp continues to innovate in medical plastics, bringing new solutions to the market such as the Newguard™, an integrated passive safety system for PFS compatible with nest, and Biopass™, a reconstitution system with an integrated needle ready to inject.

Recognised for its expertise in device R&D, Biocorp has incorporated software development capacities to develop connected drug delivery systems, including the Datapen™, a reusable smart pen injector that automatically transmits data to a treatment mobile app, helping patients to manage their treatment, and a range of add-ons, smart sensors for existing drug delivery devices (pen injectors, MDIs).

In addition to its R&D activities, Biocorp also provides manufacturing services for plastic injection, process assembly and blister packaging.

REFERENCE

1. *Bazzoli F, "Top 10 predictions for healthcare IT in 2018". Health Data Management, Dec 2017.*

ABOUT THE AUTHOR

Eric Dessertenne holds a pharmaceutical degree from the University of Clermont-Ferrand (France), an MBA from ESSEC Business School (Paris, France) and is a graduate of the Therapeutic Chair of Innovation at ESSEC Business School. He began his career in the pharmaceutical industry working for Servier in France in the Corporate Strategy department and then moved to the Chinese subsidiary in Beijing, where he handled positions in the marketing and sales force department. Mr Dessertenne then joined LEK Consulting where he worked as a consultant in the Life Sciences and Private Equity practices. In 2014, he brought his experience and insights on market opportunities to Biocorp as Head of Business Development & Commercial Operations, and was appointed Chief Operating Officer in 2016.

Drug Delivery & Packaging

Pharmapack

INNOVATION • NETWORKING • EDUCATION

EXHIBITION & CONFERENCE **6-7 FEBRUARY 2019** **PARIS EXPO, PORTE DE VERSAILLES, HALL 7.2**

Pharma's dedicated packaging & drug delivery event

INNOVATION
- Innovation Gallery
- Pharmapack Awards
- Innovation Tours
- Start-up Hub & Pitch

NETWORKING
- Networking Areas & Opportunities
- International Meetings Programme

EDUCATION
- Conference
- Symposium
- Workshops
- Learning Lab

85% of visitors have already done or anticipate doing business with exhibitors met at the event

Exhibitors met an average of **64** contacts at Pharmapack 2017, **45%** of these were new

5,300 attendees
400 exhibitors
500+ delegates

NEW FOR 2019!

Machinery Zone

SAVE THE DATE
NEXT EDITION
6-7 FEBRUARY 2019

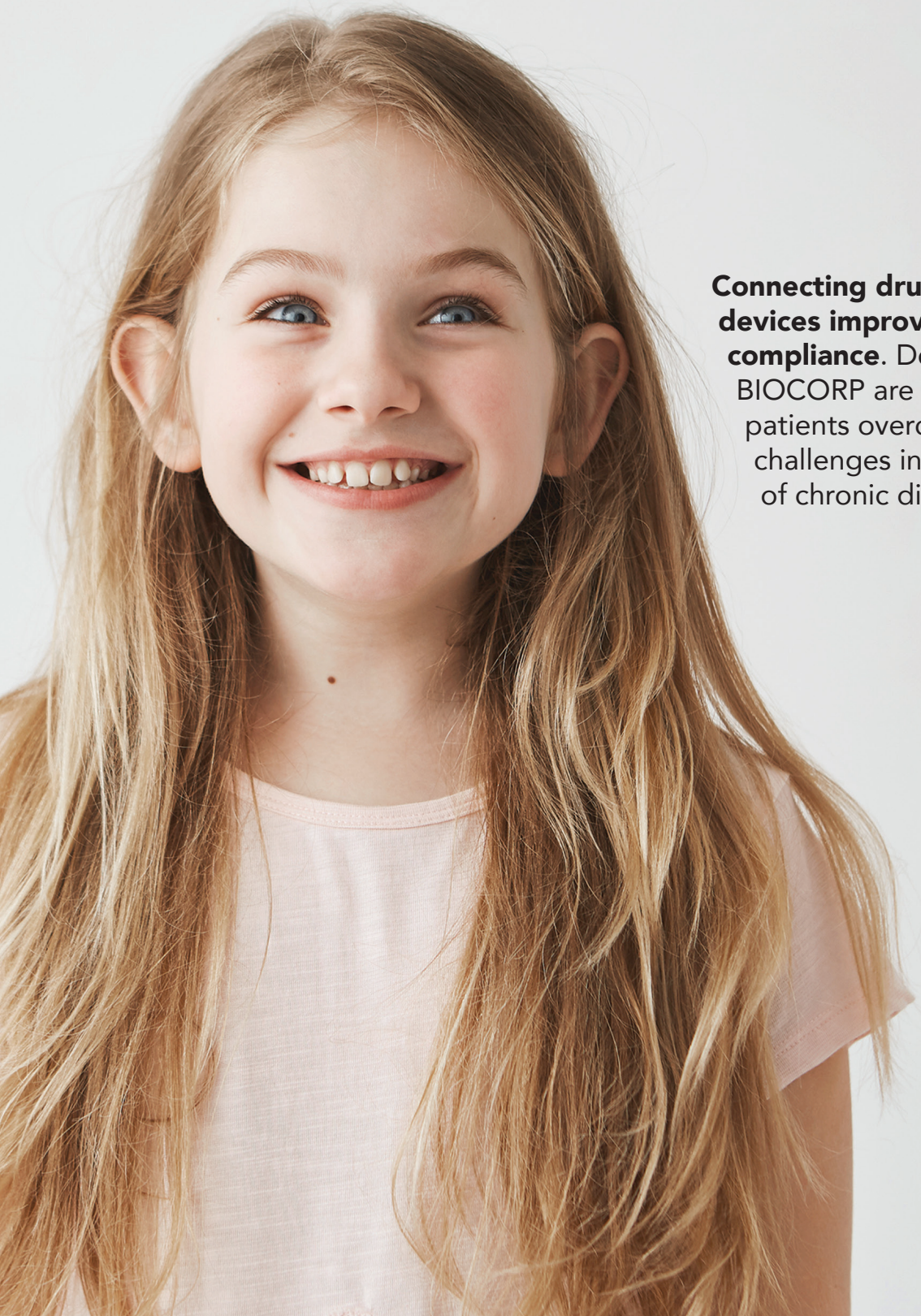
#PharmapackEU

NEWS, WHITEPAPERS & EVENT PROGRAMME ON
WWW.PHARMAPACKEUROPE.COM

UBM

BIOCORP

WE WORK ON **IMPROVING PATIENTS' LIVES**
TO OFFER THEM THE CHANCE OF MAKING
THEIR DREAMS COME TRUE



Connecting drug delivery devices improves patient compliance. Devices from BIOCORP are there to help patients overcome the various challenges in the management of chronic diseases.

Watch our devices videos on
www.biocorpsys.com

EASYLOG
DATAPEN
INSPAIR
ONEJET

SENSIRION
THE SENSOR COMPANY

FLOW MEASUREMENT IN SMART INHALERS FOR CONNECTED DRUG DELIVERY

In this article, Andreas Alt, PhD, Sales Director, Medical, Sensirion, discusses the value of adding sensor technology to inhalers by means of an add-on device, both to help patients track and manage their disease, and to improve compliance by providing feedback on inhalation technique.

Inhalers are the most commonly used devices for treating respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD). With each inhalation the device is designed to deliver a specific dose to the lungs. However, this assumes that the patient is using the inhaler correctly which, more often than not, is not the case.

It is well documented that patients often have problems adopting the correct inhaler technique, which means that they receive insufficient medication. This applies to both metered dose inhalers (MDIs) and dry powder inhalers (DPIs), leading to poor disease control and increased healthcare costs, either as a result of uncontrolled disease, increased drug utilisation for relief medication, preventative therapy or emergency department visits. This remains a serious challenge in the treatment of both asthma and COPD.[1,2]

Global annual costs associated with asthma and COPD management are substantial from both the healthcare payer and societal perspective. Healthcare spending for an uncontrolled patient is more than double that of a controlled patient.[3]

An *in vitro* lung deposition study mimicking real-life patient technique and variable inspiratory flow rates reported that patients make at least one mistake when using an inhaler as often as 70–90% of the time, resulting in only 7–40% of the drug being delivered to the lungs.[4] The two biggest and most serious errors when using an MDI are both related to patient inhalation. The first error is related to the co-ordination between inhalation and triggering the dose release of the inhaler; even a short delay can result in only 20% of the medication being delivered to the lungs.[4] The second most significant error is not breathing deeply enough, which can cause another 10% less medication to reach the lungs.[4]

The opportunity for technological innovation to reduce these common errors, by measuring patient inhalation airflow through the device, is already available. Harnessing such allows for increased drug delivery efficacy, improved medication adherence, reduced healthcare costs and, ultimately, improved patient outcomes.

WHY MEASURE THE INHALATION FLOW PROFILE?

> "...patients make at least one mistake when using an inhaler as often as 70–90% of the time, resulting in only 7–40% of the drug being delivered to the lungs."

As discussed prior, the two most frequent and serious errors patients make when using inhalers are related to their inhalation. Measuring the inhaled airflow through the inhaler, and in the case of MDIs also registering the point in time when the drug is dispensed,

Dr Andreas Alt
Sales Director, Medical
T: +41 44 306 40 00
E: info@sensirion.com

Sensirion AG
Laubisruetistrasse 50
8712 Staefa ZH
Switzerland

www.sensirion.com

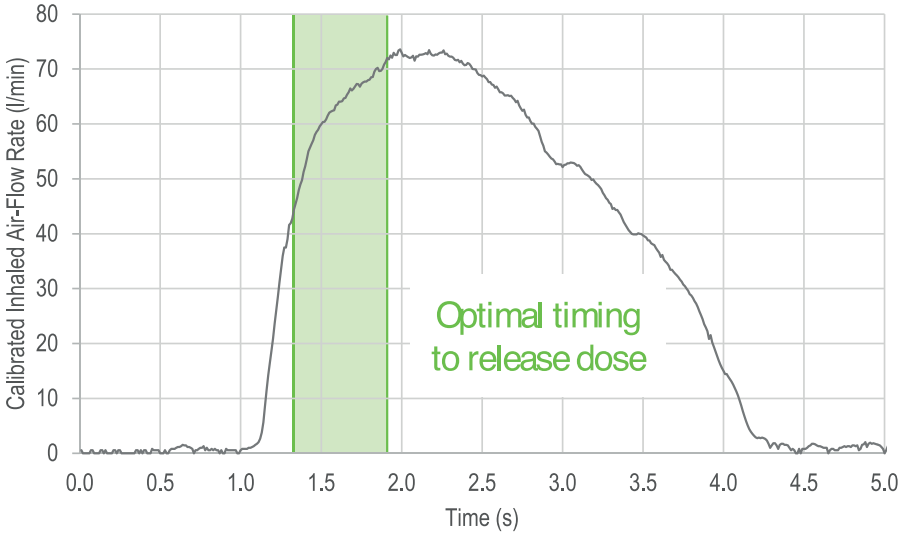


Figure 1: Inhalation flow profile showing the calibrated flow rate in standard litres per minute (l/min) versus the inhalation time in seconds (s).

Figure 2: Figure 2. Schematic illustration of drug deposition when the drug is released in the optimal timing window (left side) and when the drug is released too late (right side).

allows accurate determination of whether the drug was released within the optimal window of the inhalation cycle (Figure 1). This dose-trigger timing versus flow correlation is one critical parameter to understanding if the drug carrying flow reached deep into the bronchi and achieved the desired high lung deposition (Figure 2).

The second critical parameter is the inhaled airflow profile. Borrowing from spirometry, several parameters can be derived from the inhalation airflow profile that provide insights into a patient's inhalation:

- Depth and length of inhalation
- Entire exhalation before inhaling
- Slow inhalation according to instructions
- Lung function and its development over time.

Accurate and calibrated real-time recordings of the inhalation flow profile can provide this information, which can help determine whether or not the patient carried out the inhalation correctly and achieved a high lung deposition of drug product. Other parameters of interest include the inspired vital capacity (IVC) and peak inspired flow rate (PIF), along with the full inhalation airflow characteristics (Figure 3).

"Adapting an inhaler to additionally serve as a spirometer-like device enables all parameters to be derived upon use without any additional effort or time-related burden to the patient."

Subsets of parameters, such as forced inspired volume during the first second of inhalation (FIV1) or the airway resistance (RAW), can also be determined from the inhalation airflow profile. The derivation of the latter is shown in Figure 4 (next page).

Some parameters, such as RAW, can be of special interest for patients with COPD, as it may relate directly to the condition of the disease. Adapting an inhaler to additionally serve as a spirometer-like device enables all parameters to be derived upon use without any additional effort or time-related burden to the patient (Figure 5, next page). Besides monitoring every inhalation through the inhaler for its quality and the correct use of the inhaler, monitoring these parameters over time can also be useful for providing feedback on the effectiveness of the medication, course of the disease, alerting a healthcare professional to problems, or be a great motivational tool for the patient to increase their adherence.

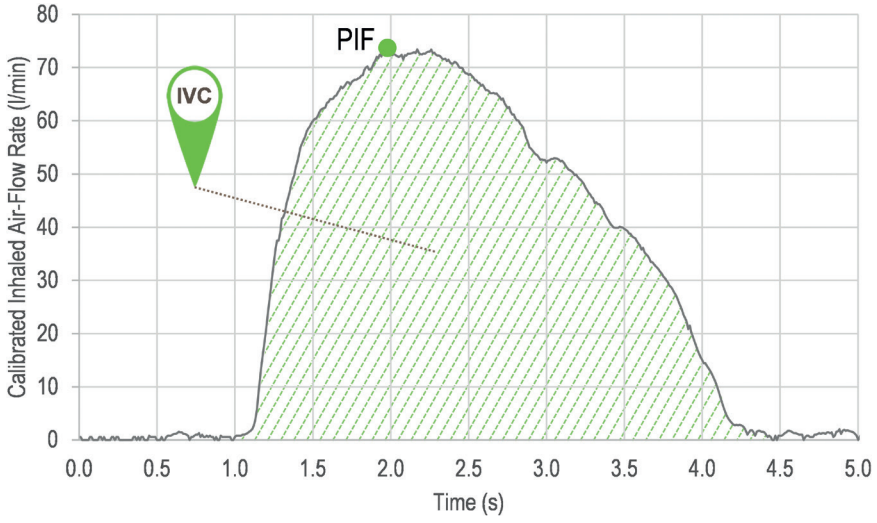


Figure 3. Parameters derived from the inhalation airflow characteristic: inspired vital capacity (IVC) and peak inspired flow rate (PIF).

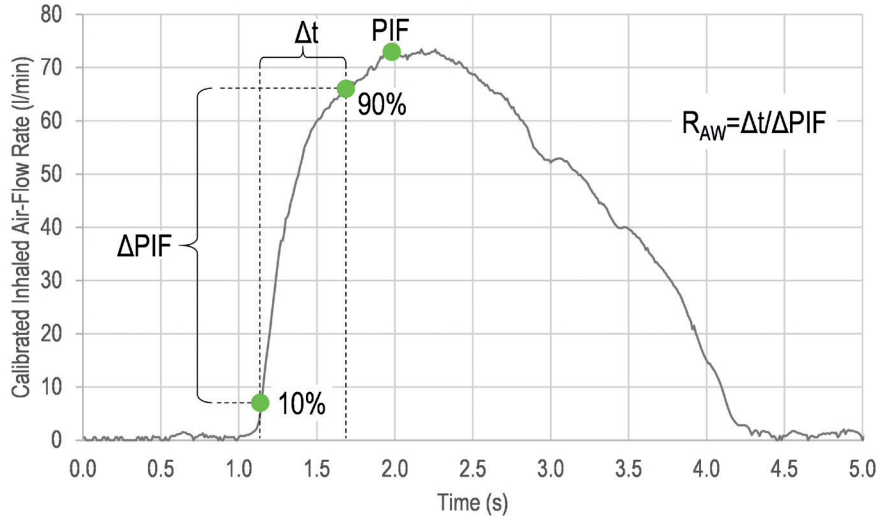


Figure 4. Besides the peak inspired airflow (PIF), the airway resistance (RAW) can be determined from calibrated inhalation airflow characteristics recorded with a sufficient high temporal and flow resolution.

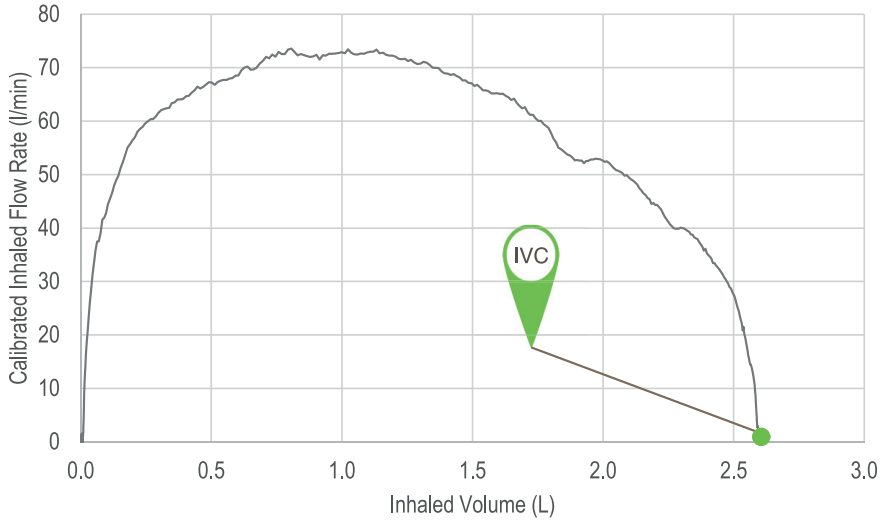


Figure 5. Typical spirometer plot of flow rate versus inhaled volume. The inspired vital capacity (IVC) is the total inhaled volume as the flow rate returns to zero at the end of the inhalation.

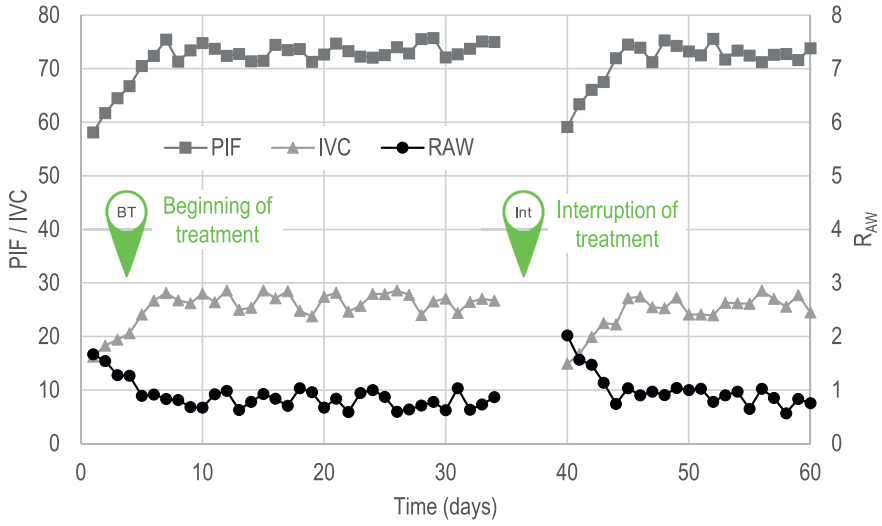


Figure 6. Peak inspired airflow (PIF), inspired vital capacity (IVC) and airway resistance (RAW) monitored over time, providing valuable feedback to the healthcare professional and the patient.

Cohero Health (New York, NY, US) already provides patients with an additional spirometer for exactly this reason, to allow the patients to routinely measure their lung function over the course of the treatment. This assists with direct disease management and sharing the collected data with medical professionals can help patients and clinicians to assess treatment progress. It can also enable a payment-by-results rather than pay-per-dose model. This same development can be observed in the insulin or sleep apnoea industry, where it has led to growing market shares for companies offering connected devices and simultaneously brought down treatment costs and, most importantly, improved patient outcomes.

Figure 6 shows an example of schematic behaviour for PIF, IVC and RAW versus time. It visualises the positive effect of starting the treatment, the stable treatment phase during regular dosage and the negative effect of interrupting the treatment.

Next-generation inhalers – natively incorporating airflow measurements in their design – will facilitate automatic dose release at the optimal point in time, individually tailored to the patient and their specific condition.

HOW TO MEASURE THE INHALATION FLOW PROFILE

Before inhalers natively include electronics and connectivity features by design, existing inhalers and inhaler platforms can be enhanced with the required electronics to achieve connectivity and sensing functionality. This is already being done today by companies such as Propeller Health (Madison, WI, US), Adherium, (San Mateo,

> "In order to avoid revalidation of the inhaler with the US FDA and maintain approval, the key regulatory requirement for all inhaler clip-ons is that the flow path of the inhaler remains unaltered, in order to ensure that it does not interfere with the inhaler's function."

CA, US) and others that have designed a variety of clip-ons for existing inhalers to add connectivity by monitoring parameters such as date and time of usage, as well as evaluating signals from additional sensors such as accelerometers, GPS and many more. In the past, accurate measurement of the flow through the inhaler was challenging due to the lack of sufficiently robust, yet sensitive devices capable of measuring the smallest flows. To avoid revalidation of the inhaler with the US FDA and maintain approval, the key regulatory requirement for all inhaler clip-ons is that the flow path of the inhaler remains unaltered, in order to ensure that it does not interfere with the inhaler's function.

To demonstrate how accurate flow measurement through an inhaler can be realised without interfering with the flow path, Sensirion has developed a functional inhaler clip-on. Figure 7 shows the 3D-printed inhaler clip-on containing the Sensirion flow sensor SDP3x, as well as a Bluetooth Low-Energy communications chip and a battery power source. It is notable that the inhaler housing has not been altered in any way and the flow measurement principle relies solely on the Venturi/Bernoulli principle at the inhaler inlet. The calibrated inhaler airflow shows excellent agreement to an external flow reference and was used for obtaining the flow profiles depicted in this article.

The unaltered and unobstructed inhaler flow path design is enabled by the extreme sensitivity of the Sensirion micro-electromechanical system-based (MEMS-based) flow-chip solution utilised in the SDP3x flow sensor series. This technology is based on the microthermal flow-through principle, the next-generation hotwire flow sensor technology that has been successfully used in medical ventilators for decades. In clip-ons for existing inhalers as well as newly developed inhalers, the key advantages of Sensirion's CMOSens® flow-chip technology can be summarised as:

Figure 7. 3D-printed inhaler clip-on containing the Sensirion flow sensor SDP3x in the side view (left) and top view (right) showing the unobstructed flow path of the inhaler.

"Robust and accurate flow measurement is an important feature for moving towards better disease management and patient outcomes, and is already realisable today."

- Highest sensitivity down to hundredths of a Pascal
- High temporal and pressure/flow accuracy
- Proven device in the medical and automotive industry
- Robust against being dropped and ultra-sonic welding process steps
- Inherently robust against external disturbances by the two-port design
- Low power consumption for portable and battery operation
- World's smallest commercially available flow sensor.

This makes the Sensirion SDP3x flow sensor series the flow sensor solution of choice for accurately measuring the inhalation flow profile in inhalation devices.

OUTLOOK OF FLOW MEASUREMENT IN SMART INHALERS

Adding a diagnostic unit to the drug delivery device that the patient is already familiar with is a powerful tool in asthma and COPD disease management. Improper inhalation technique leads to decreased efficacy through reduced deposition of drug in the lungs, which in turn leads to increasing disease severity and thus a worse patient outcome and an increase in healthcare costs. The solution of guiding the patient and providing direct feedback as well as supporting the patient in controlling the disease and increasing adherence have already been shown to improve patient outcomes by current connected drug delivery devices.

Thus, robust and accurate flow measurement is an important feature for moving towards better disease management and patient outcomes, and is already realisable today. The high percentage of patients suffering from asthma or COPD and misusing their inhaler, when significantly better outcomes would generally be possible with proper disease management, will continue to drive innovation for connected drug delivery. An increasing number of companies are already implementing digital technologies in their products to provide

an enhanced method of managing asthma and COPD, as well as improving the effectiveness of medication. The industry is advancing towards supporting the patient with the optimal treatment for their disease, not solely as a simple medical tool but as a companion device to remind, coach and provide relevant insight into their treatment and the course of their disease.

ABOUT THE COMPANY

Sensirion AG, headquartered in Staefa, Switzerland, 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 ($PM_{2.5}$). 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 AUTHOR

Andreas Alt 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.

REFERENCES

1. *Melani AS et al, "Inhaler mishandling remains common in real life and is associated with reduced disease control". Respir Med, 2011, Vol 105(6), pp. 930–938.*
2. *Press VG et al, "Misuse of respiratory inhalers in hospitalized patients with asthma or COPD". J Gen Intern Med, 2011, Vol 26(6), pp 635–642.*
3. *Sullivan SD, "The burden of uncontrolled asthma on the US health care system". Manag Care, 2005, Vol 14(8 Suppl), pp 4–7.*
4. *Biswas R, Hanania NA, Sabharwal A, "Factors Determining In Vitro Lung Deposition of Albuterol Aerosol Delivered by Ventolin Metered-Dose Inhaler". J Aerosol Med Pulm Drug Deliv, 2017, Vol 30(4), pp 256–266.*

Creating Space for Your Ideas

With the World's Smallest Flow Sensor

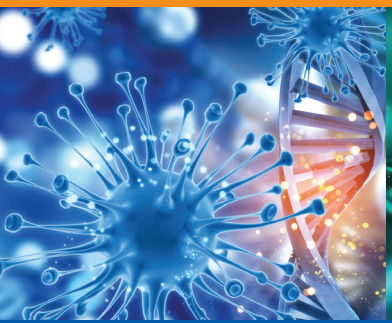
Sensirion consolidates incomparable accuracy, long-term stability and excellent repeatability in a tiny new device called the SDP3x – the world's smallest flow and differential pressure sensor. It's the perfect choice for cost-sensitive mass production, opening up new possibilities in integration and application.

www.sensirion.com/sdp3x

SENSIRION
THE SENSOR COMPANY

Global Excellence in Delivery Device Testing

- Human Factors
- Design Validation Testing
- Needle Testing
- Extractables and Leachables
- CCIT
- Performance Testing
- Packaging / Transit Validation
- Dose Accuracy
- Transit /Altitude Testing
- Trigger Force
- ISO 8009
- Break Loose Force
- Glide Force
- ISO 11608
- ISO 11040
- On Body Delivery Systems
- Connectivity
- Medical Device Performance Testing




Medical Engineering Technologies
Unit 16, Holmestone Road,
Dover, Kent, CT17 0UF, UK

www.met.uk.com
t +44 (0)845 458 8924
e solutions@met.uk.com

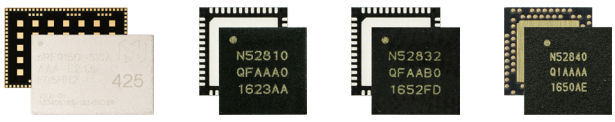
MEDICAL ENGINEERING TECHNOLOGIES
GLOBAL EXCELLENCE IN DEVICE TESTING

NORDIC®
SEMICONDUCTOR

Connecting your drug delivery devices

Nordic Semiconductor delivers the most flexible, mature and reliable connectivity solution on the market, while maintaining low power and high performance in a tiny footprint. All running the latest Bluetooth 5 implementation. Easy-to-use development tools and samples are available through a worldwide distribution network.

Bluetooth® 5 LTE-M NB-IoT



nordicsemi.com

CAPMEDIC™: SIMPLIFYING INHALERS FOR REGULAR AND CORRECT USE

In this article, Rajoshi Biswas, PhD, Architect and Clinical Lead, Cognita Labs, discusses the CapMedic device, which transforms a typical metered dose inhaler into a more user-friendly, efficacious delivery system through its ability to provide feedback on inhaler technique and real-time cues to avoid errors during inhaler use. She also discusses research using CapMedic to estimate the amount of drug successfully deposited in the lung with each use.

THE PATIENT PERSPECTIVE

Metered dose inhalers (MDIs) are necessary for millions of patients worldwide, yet continue to be very challenging to use for most. Seen from a distance, the inhaler looks innocuously simple to use – simply shake and inhale. However, that simplicity hides a very important fact that most people use their inhalers incorrectly. Correct use requires eight to ten steps (as stated in inhaler use guidelines), and study after study has confirmed that patients make several errors, despite repeated training.

> "The incorrect use of an inhaler is clinically important. Unlike pills, which when swallowed ensure delivery of a pre-determined amount of medication, inhalers provide no guarantee how much medication is actually delivered."

The incorrect use of an inhaler is clinically important. Unlike pills, which when swallowed ensure delivery of a pre-determined amount of medication, inhalers provide no guarantee on how much medication is actually delivered. Each error leads to an unknown loss of medication to the respiratory tract, often in the mouth and

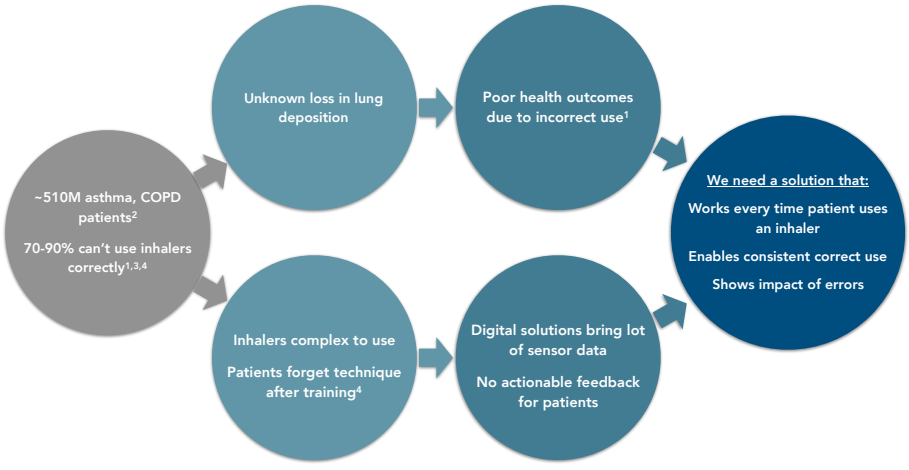


Figure 1: The inhaler misuse challenge and the kind of sustainable innovation needed for patients.

Dr Rajoshi Biswas
Architect and Clinical Lead
T: +1 832 538 3042
E: rajoshi@cognitalabs.com

Cognita Labs, LLC
700 N Main St. Ste C1
Santa Ana CA 92701
United States

www.cognitalabs.com

throat, leading to an unknown amount of medication delivered to the lungs. Perhaps more importantly, incorrect inhaler use has been linked to poor healthcare outcomes. A recent patient study,[1] along with other evidence,[3] demonstrated that reduced asthma control is strongly correlated with errors in co-ordination, orientation and exhalation. As we shall discuss later, many of these errors are hard to spot for clinicians and even harder for patients to recognise themselves. Thus, despite the recommended practice of checking inhaler use on regular visits to the physician, there is little progress in the population-wide improvement of inhaler-use competence.[4]

The difficulty in MDI usability has sparked extensive research and innovation, largely to eliminate difficult steps from the process of inhaler use. Notably, spacers, dry powder inhalers (DPIs) and soft mist inhalers (SMIs) have reduced the burden of correct usage to some extent. However, DPIs and SMIs also suffer from patient misuse and hence much of the discussion and solutions in this article apply to these classes of inhaler too. Furthermore, current digital technologies for inhalers fall short in providing consistent, long-term improvement in inhaler-use competence and quantifiable, actionable feedback on everyday drug delivery. As shown in Figure 1, the importance of improving inhaler use competence cannot be overstated.

WHAT SHOULD WE INVENT?

Inspiration can be taken from the automotive industry. The conceptual design of a "box on wheels" is still no different from the day it was invented, but the experience, safety and efficiency of driving a car continue to evolve. For example, many new features have improved the safety of driving, such as systems that warn the driver if they are drifting out of lane, driving over the speed limit, backing up into an obstacle or if there is a vehicle in their blind spot. Taking inspiration from this analogy, something similar can be done for MDIs by keeping the efficient delivery mechanism but completely changing the patient experience of using it. For example, an inhaler could:

- **Measure what the user is doing (right or wrong)**: For an inhaler, this means not only measuring when it is used (like inhaler caps that measure adherence) but measuring the correctness of use.
- **Teach by informing the user just-in-time**: An inhaler needs to have indicators that teach what to do and how to do it correctly, at the right time.
- **Help build good habits**: By designing feedback to help build good habits, a user's competence could be improved over time.

> "CapMedic's error detection algorithms have been extensively validated with over 1,000 MDI techniques, based on measurements from patients and emulated using a custom robotic testbed."

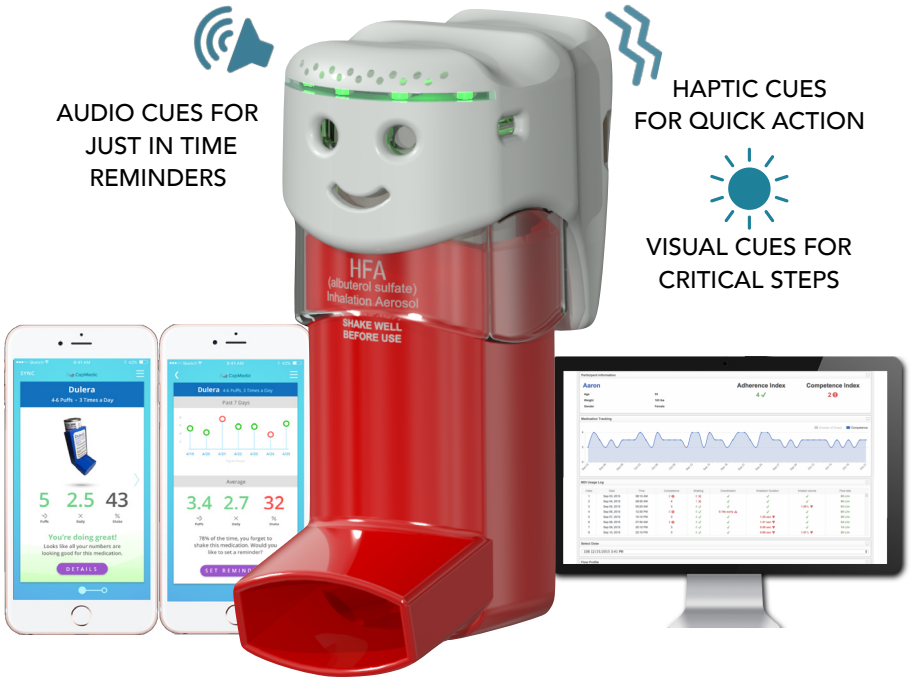


Figure 2: CapMedic can provide instant feedback in three configurable ways: audio instructions, visual feedback and haptic cues.

COGNITA LABS' CAPMEDIC™

Cognita Labs has developed a first-of-its-kind inhaler cap for most on-the-market MDIs, with the following features:

- **Comprehensive measurements**: CapMedic™ enables measurement of nearly all critical steps in MDI usage. Specifically, CapMedic measures seven steps/errors for MDI use, including important parameters like orientation, co-ordination and inspiration.
- **An always-available live-coach**: CapMedic converts these measurements into a highly capable audio-visual-haptic coach. For example, the coach can talk the user through the steps of inhaler use, such as reminding them to shake the inhaler, helping them time their actuation, encouraging deep inspiration and reminding them to hold their breath after inhalation. The coach is reconfigurable via the accompanying app, allowing users to change the method of feedback based on their personal needs (Figure 2).
- **Habit-building design**: CapMedic is a fully integrated design that can operate without an app. This is crucial, for two reasons. First, the coach is always active and in the right place – on top of the inhaler. Second, a coaching inhaler reduces the cognitive load of a user, in that they no longer have to remember to remember the steps themselves. They can simply follow the instructions every time, assured that they will recieve the optimal amount of medication.

NEW INSIGHTS FROM CAPMEDIC

Both Patients & Clinicians Get it Wrong

In a collaborative study conducted at the Baylor College of Medicine (Houston, TX, US), the inhaler manoeuvres of 23 participants, all of whom were experienced inhaler users (19 asthma, 4 COPD, ages

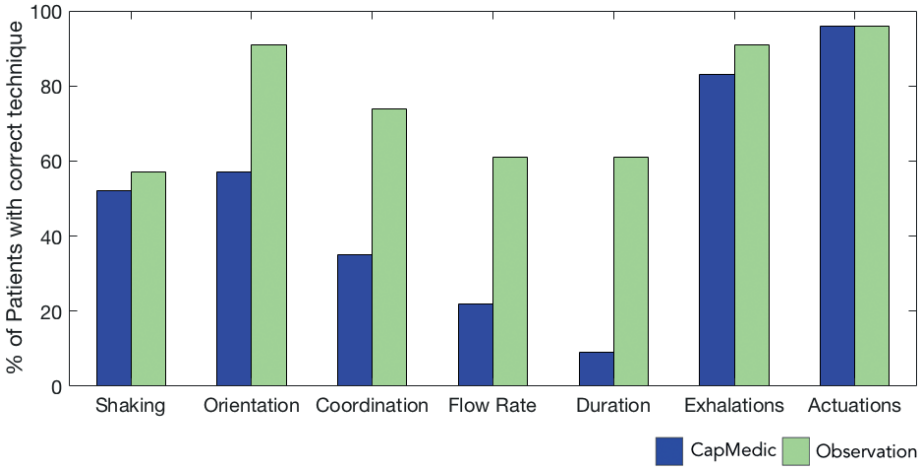


Figure 3: MDI-use competence (correctness of MDI use steps of shaking, orientation, coordination, inspiratory flow and duration of inspiration) and errors (exhalations into the MDI and multiple actuation) measured by CapMedic.

> "The CapMedic on-board coach guides with real-time cues to avoid errors in the first place, and the same sensor suite data can potentially be used to estimate the amount of drug deposition achieved."

20–65, 6 male, 17 female), were measured.[5] The participants used a CapMedic-equipped inhaler in the presence of a member of clinical staff, who was trained to spot errors in all steps of the manoeuvre. The results summarised in Figure 3 show the errors detected by the trained staff and CapMedic sensor-powered algorithms. For visually noticeable errors – whether the participant shook their inhaler, actuated the inhaler multiple times and exhaled, clinical observations match the CapMedic measurements. However, for four steps, the observation-based count is significantly lower than the errors detected by the CapMedic. CapMedic's error detection algorithms have been extensively validated with over 1,000 MDI techniques, based on measurements from patients and emulated using a custom robotic testbed. Thus, it is likely that the observation-based studies may be under-reporting the number and extent of errors.

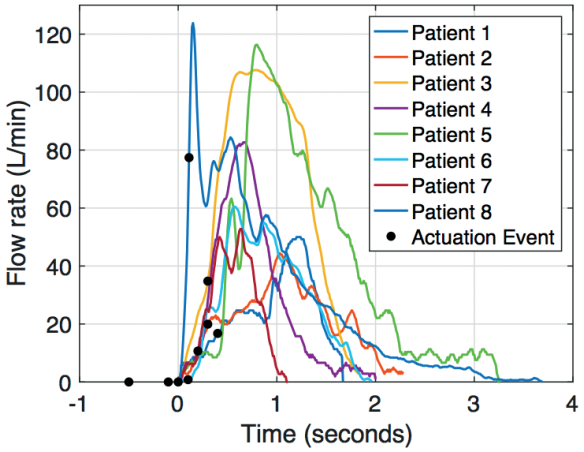


Figure 4: MDI-use technique measured by CapMedic.

Sensors Reveal Inhalation Flow Curves

Beyond error detection, CapMedic provides deep insights based on custom sensor data about each use of an inhaler. An important aspect of inhaler use is the inhalation through the MDI. Using CapMedic's highly accurate inhalation flow measurements, the patient's actual inhalation flow curve can be visualised. Figure 4 shows the flow curves for eight patients, with the black dot showing the precise time of actuation in their inhalation cycle. The flow curves show that these patients have very diverse breathing patterns, which has a significant impact on how much medication is actually delivered to the lungs. Additionally, the patients actuated their inhalers at diverse times, with the co-ordination varying from positive (actuating after the start of inhalation) to negative (actuating before the start of inhalation). Again, this co-ordination error has a significant impact on how much medication is actually deposited in the lungs.

Co-ordination Error – Hard to Detect Visually but with a Significant Loss in Deposition

Using a custom testbed (Figure 5) containing both MDI use emulation and *in vitro* lung deposition measurement

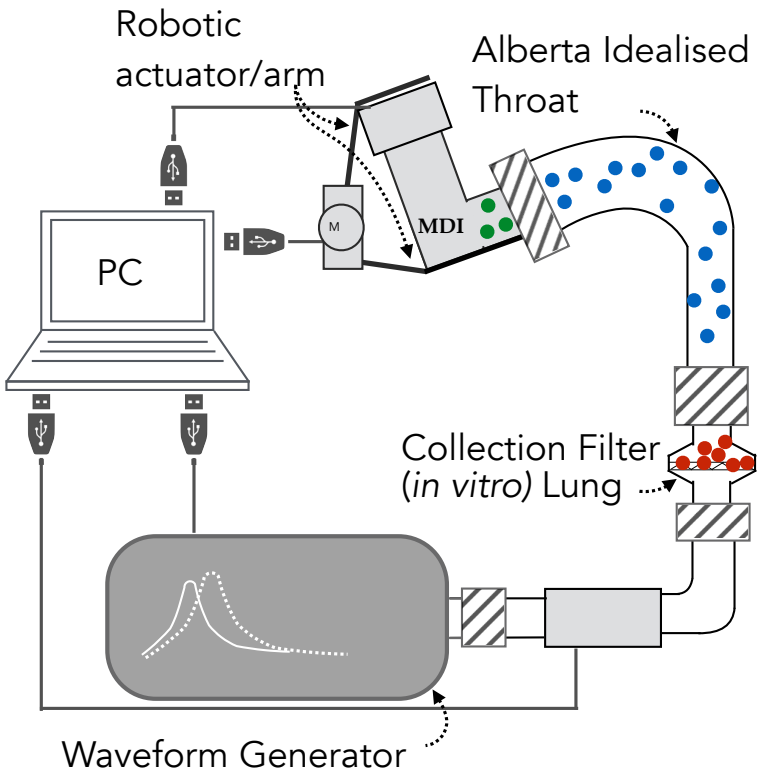


Figure 5: Test-bed for MDI-use emulation and *in vitro* lung deposition estimation.

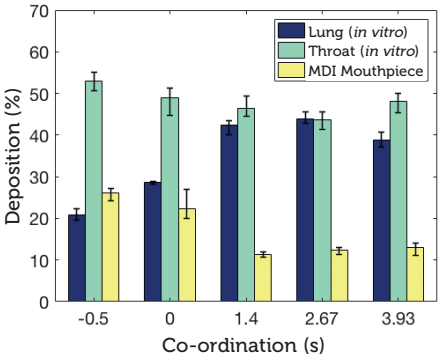


Figure 6: Results showing the dependence of lung deposition on the MDI use parameter co-ordination. Co-ordination refers to the delay in actuating MDI from the start of inspiration (negative when actuated before inspiration).

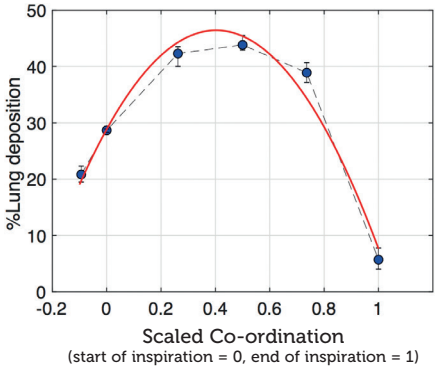


Figure 7: Early results from controlled experiments show the dependence of lung deposition on MDI use technique/errors. Here, coordination is scaled to the duration of inspiration (actuation before inspiration <0, for actuation at start of inspiration = 0, for actuation at end of inspiration = 1).

components, a study at Rice University (Houston, TX, US) evaluated how much medication is delivered in lungs, throat and mouthpiece depending on whether the co-ordination was negative, simultaneous or positive.[6] Figures 6 and 7 show the same data in two different ways. Figure 6 breaks it into the location of deposition in the *in vitro* model, either the lung, throat or mouthpiece. Note that a negative co-ordination of 0.5s, barely perceptible by humans, leads to a large loss in lung deposition, with only 20% of the medication reaching the lungs, compared with the maximum of >40% achieved for a range of positive co-ordination values.[6]

Towards the First "Digital" Drug

Looking forward, Cognita Labs firmly believes that CapMedic holds the potential to change patient care in many ways. First and foremost, by allowing a measurement of both adherence and competence, it may no longer be necessary for patients to bring their inhalers on every visit to their clinician. All that would be needed is a report from the CapMedic cloud detailing the usage data, allowing the clinician to discuss the patient's improvement and challenges with concrete data.

Secondly, perhaps by combining the data collected by CapMedic and modelling the corresponding drug deposition, it would be possible to estimate the lung deposition every time a patient uses their inhaler. This closed-loop solution could become the basis for a "digital drug", where digital feedback provides guidance to the patient that results in higher medication deposition. The CapMedic on-board coach guides with real-time cues to avoid errors in the first place, and the same sensor suite data can potentially be used to estimate the amount of drug deposition achieved.

CapMedic as an enabler of a digital drug could also answer the question "What to do with the sensor data?" beyond retrospective reporting. As the estimate of the delivered drug correlates with health outcomes, CapMedic can simplify everyday MDI competence data to a single actionable estimate of drug deposition with each use. This way, CapMedic can overcome the established difficulties of proper inhaler technique and guide users to use their inhalers correctly, providing meaningful information about drug delivery for every use.

ABOUT THE COMPANY

Founded by leading researchers from Rice University, Cognita Labs has developed patent-pending respiratory innovations to bring high-quality diagnostics and monitoring to the most vulnerable populations, including young children, seniors, and low-resource communities. The CapMedic™ device and cloud platform turns regular inhalers into a personal butler that helps patients use their inhalers regularly and correctly to better manage their disease. PulmoScan is a diagnostic and a monitoring device for detecting small airways changes that cannot be captured by traditional spirometry testing. As opposed to spirometry, PulmoScan allows effort-free <1 min testing, enabling use cases such as pediatric and geriatric diagnosis, home monitoring and volume screening. Cognita Labs' mature devices have been used and validated in various clinical studies.

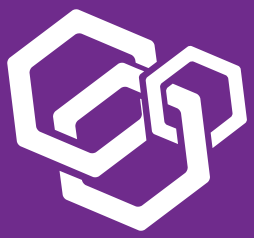
REFERENCES

1. *Price DB et al, "Inhaler errors in the CRITIKAL study: type, frequency, and association with asthma outcomes". J Allergy Clin Immuno Pract, 2017, Vol 5(4), pp 1071–1081.*
2. *Bousquet J, Khaltaev N, "Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach". WHO, 2007.*
3. *Melani S et al, "Inhaler mishandling remains common in real life and is associated with reduced disease control". Respir Med, 2011, Vol 105(6), pp 930–938.*
4. *Hardwell A et al, "Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs)". Prim Care Respir J, 2011, Vol 20(1), pp 92–96.*
5. *Biswas R et al, "Measuring Competence in Metered Dose Inhaler Use Using Capmedic Electronic Inhaler Monitoring Tool". Chest J, 2016, Vol 150(4 Supplement), p 14A.*
6. *Biswas R, Hanania NA, Sabharwal A, "Factors determining in vitro lung deposition of albuterol aerosol delivered by Ventolin metered-dose inhaler." J Aerosol Med Pulm Drug Delivery, 2017, Vol 30(4), pp 256–266.*

ABOUT THE AUTHOR

Rajoshi Biswas is the Architect and Clinical Lead at Cognita Labs. She holds a PhD in Electrical and Computer Engineering from Rice University (Houston, TX, US), specialising in the modelling of aerosol drug deposition, based on quantified patient inhaler-use competence. Through her past collaborations with Baylor College of Medicine (Houston, TX, US) and Texas Children's Hospital, she has focused her efforts at Cognita Labs to develop patient-centric engineering innovations for pulmonary medication monitoring and diagnostics.

Innovative solutions to the greatest challenges in pharmaceutical development



10th Global

DDF Summit

Drug Delivery & Formulation

11 - 13 March 2019 | Berlin

Europe's premier drug delivery and formulation event

The perfect mix. The DDF Summit brings together leading formulation development and drug delivery scientists from both industry and academia to share and discuss their latest work.

Quality content. The agenda is packed with carefully selected talks on topics as diverse as the challenges you face.

Invaluable networking. The DDF community is open, friendly and represents an incredibly valuable network of scientists working at the forefront of their field. There is ample networking time built in to help you make and strengthen connections.

Tailor your experience. 4 parallel streams give you the chance to personalise your agenda and delve deep into the topics pertinent to your challenges. Choose from Small Molecules, Biologics, Technology & Innovation or Device Development.

The right size. This year the DDF Summit will be limited to just 500 people, in order to maintain the quality of the networking and comfort for participants. This means that there will only be 250 delegate tickets available. So, don't waste time in getting yours.

Visit www.ddfevent.com to see the full agenda and book your place

THE DIFFERENCE OF ONE DRUG DELIVERED

FOR BETTER TREATMENT OF CHRONIC DISEASES. Across the healthcare continuum, BD is the industry leader in parenteral delivery devices that help health systems treat chronic diseases. We not only continually advance clinically proven, prefillable drug delivery systems, we do so with a vision to help healthcare providers gain better understanding of how patients self-inject their chronic disease therapies outside the healthcare setting. This is why we partner with leading pharmaceutical and biotech companies worldwide to develop digitally connected self-injection devices—including wearable injectors and autoinjectors—to capture valuable data that can be shared with caregivers. Discover how BD brings new ideas and solutions to customers, and new ways to help patients be healthy and safe. **Discover the new BD.**

BD Libertas™ Wearable Injector

BD Libertas™ Wearable Injector with Smart option

Learn more at bd.com

BD Libertas™ Wearable Injector, BD Libertas™ Wearable Injector with Smart option and BD Intevia™ Autoinjector are products in development; some statements made are subject to a variety of risks and uncertainty.

BD

THE EYES HAVE IT – EYE TRACKING EVOLUTION IN MEDICAL DEVICE DEVELOPMENT

In this article, Philip Lance, PhD, Medical Device Human Factors Consultant, and Phil Seeney, Managing Consultant, both of PA Consulting, discuss the recent surge in the use of eye-tracking technology in the field of human factors, providing an overview of the technique's history and how it may be applied to medical devices in the future.

RECENT GROWTH OF EYE TRACKING

Today we are seeing a rapid increase in the use of eye tracking technology in the development of products across multiple industries, reflected by the surge of publications on the subject (Figure 1). This adoption of eye tracking is the consequence of decades of work developing the technology to a point where it is now more effective and affordable. Certain industries, notably aerospace, automotive, marketing and the human-computer interaction sciences, derive considerable benefit from using eye tracking when developing user interfaces. However, the medical device industry has been slower to adopt and exploit the potential of eye tracking.

> "Eye tracking is a tool used to measure and record the eye movements and gaze positions of an individual as they perform a task or using a device or piece of equipment."

WHAT IS EYE TRACKING?

Eye tracking is a tool used to measure and record the eye movements and gaze positions of an individual as they perform a task or use a device or piece of equipment. These data help us to understand how different designs are actually being used, and then infer how users are interpreting instructions and engaging (or not) with the product, allowing us to identify and address user issues or problems.

Whilst eye trackers differ in form, the fundamental logic is common: capture where the eye focuses its attention and capture the movement between these points of attention. Typical language to describe this is:

- **Gaze:** Where the eye is looking.
- **Fixation:** Where the gaze pauses in a particular position/on a particular area. Most information collected by the eye is during a fixation.
- **Saccade:** The rapid movement (jumps) between fixations. There is little to no information collected during a saccade.
- **Scan path:** A sequence of fixations and saccades, also known as a gaze plot.

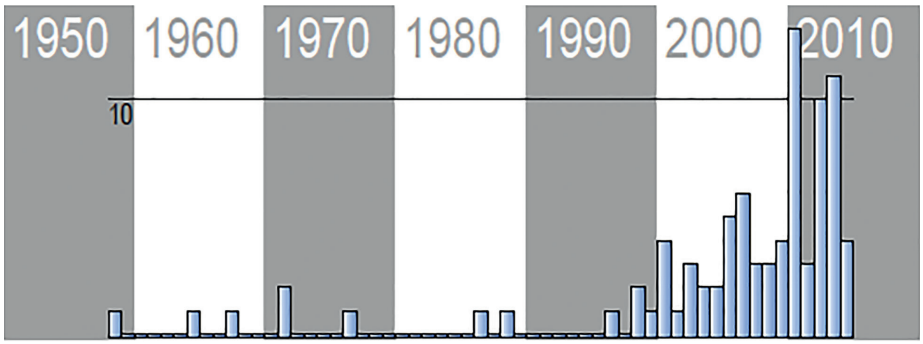


Figure 1: A histogram of all publications of this survey relevant for eye tracking data visualisation techniques. The number of published articles, conference papers and books has greatly increased during the last decade.[1]

Dr Philip Lance
Medical Device Human Factors Consultant
T: +44 1763 285 186
E: philip.lance@paconsulting.com

Phil Seeney
Managing Consultant
T: +44 1763 267680
E: phil.seeney@paconsulting.com

PA Consulting Group
Global Innovation and Technology Centre
Back Lane, Melbourn
Hertfordshire
United Kingdom

www.paconsulting.com

"A popular analysis technique of scan paths is the creation of a heat map, whereby the scan paths of a number of participants are overlaid to identify where there is commonality."

Figure 2: Eye tracking equipment being used in a usability study to observe and monitor.

- **Area of Interest (AOI)**: An area or region on the object being tested that is important for a design hypothesis.

With current eye tracking technology, eye movements across an object can be observed and partially evaluated in real-time. This enables human-factors moderators to observe the gaze of the study participant as it happens (Figure 2).

This observance provides the moderator with an insight into the potential reasoning/thought processes the study participant is following. For example, a participant may be repeatedly returning their gaze to a feature on the device suggesting there is something about this feature that they find confusing or unsettling. Using these insights, the moderator can explore with the participant why they are concerned with a feature. With this information it usually possible for designers and engineers to improve the device's affordance (the property of a user interface to intuitively imply its function).

The power of eye tracking in such situations can be increased by integrating it with other biometric technologies that gather bio-signals, such as electroencephalogram (EEG), electrocardiogram (ECG) and galvanic skin response (GSR), also known as electrodermal activity (EDA). These bio-signals help to provide insights into the emotional state of the participant. For instance:

- EEG monitors the electrical activity of the brain. This can be used to help identify if, when an individual looks at a feature, they have increased concentration or not.
- ECG monitors electrical heart activity, which can indicate the stress levels of the participant, and help recognise if an individual found looking at a feature taxing.
- GSR monitors the electrical characteristics of skin. Skin conductance increases as sweat gland activity increases. Sweat glands are controlled by the sympathetic nervous system, which is subject to psychological or physiological arousal. Thus, by monitoring GSR it is possible to identify when a participant looks at a feature and they become more emotionally aroused. It is not possible yet to tell whether the emotion is positive, such as "happy", or negative, such as "angry".

A range of biometric sensors have been used successfully on several studies, however certain biometric technologies require sensors to be attached to the participant and sometimes this level of intrusion can be detrimental to the aims of the study and their use must be carefully considered. Of these bio-signal gathering devices, GSR requires only a couple of sensors which strap to the fingers and, used judiciously, the results from GSR have been found to be very insightful when used in conjunction with eye tracking.

Further insights can be obtained through the analysis of the eye tracking data on fixations and saccades. A popular analysis technique of scan paths is the creation of a heat map, whereby the scan paths of a number of participants are overlaid to identify where there is commonality. Such analyses can inform and provide deeper understanding of the human-device interaction (Figure 3, see over page).

An example of an insight this technique can provide is the identification of a design flaw often referred to as the "vampire effect". This is where an element of the design draws the attention of the user away from more important interactional elements of the device's user interface, potentially leading to an increase in the risk of errors being made by the user.[2] Having identified an element causing a vampire effect, this particular aspect of the design, be it in the instructions for use (IFU) or the product itself, can be redesigned to remove the distraction and improve the affordance of the user interface. Furthermore, a follow-up heat map can demonstrate and potentially quantify the degree of improvement achieved.

A recording of two participants eye movements over an instruction, revealing their fixations and saccades

A heat map built up from their fixations

Figure 3: Analysing the eye tracking data from study participants.

A phrase commonly dropped into device requirements specifications is "must be easy to use", but defining "easy to use" is, in itself, not easy. However, through the use of eye tracking, potential design improvements can be made and evaluated in a way that can demonstrate an improvement in ease of use, such as through the observed improvement in affordance.

WHERE HAS EYE TRACKING COME FROM?

With the recent increase in interest, it would be easy to assume the concept of eye tracking is relatively new. However, eye tracking dates back 150 years. Examples of this early work are cited by Yarbus, such as Lamansky's 1869 work on eye movement when changing fixation points, and Landolt's 1891 work on characterising the jerkiness of eye movements when studying stationary objects. This early eye tracking was done by observation, typically involving some use of optics such as an arrangement of mirrors and telescopes.[3]

The use of still and motion-picture photography was introduced to eye tracking research early in the twentieth century with Dodge and Cline in 1901, building on Lamansky's work. Analysing a series of photographs, they found there is a slight quiver at the beginning and end of an eye movement, identifying that a pair of eyes do not move absolutely together.[4] This work helped form the foundations of our understanding on how eyes move, which is the basis for how we track eye movement today. The use of a series of images quickly moved onto film. In 1905, Judd, McAllister and Steele used film to record the movement of eyes (Figure 4).[5]

It was in the late 1940s when eye movement research moved from characterising and understanding, to being applied to practical problems. Fitts, Jones and Milton of the US Air Force began studying pilots' eye movements during instrument flight – specifically for the purpose of improving instrument and instrument panel design. According to them, this research "provides the answers to many questions encountered in designing aircraft instruments and instrument panels on which a large number of instruments must be arranged in the most effective way".[6] Using eye tracking, they determined how pilots' eyes moved between and fixated on instruments (Figure 5).

However, due to the size and weight of these early film cameras, the cameras that filmed the movement of the eyes could not be mounted on the user's head. This was problematic as it prevented tracking all eye movements, so when the user moved their head position they prevented a clear view of the eyes for the camera. Head-mounted cameras only became a realistic proposition in the 1960s, when the first practical head-mounted eye-tracking equipment was produced.[7]

By the 1970s, eye tracking had progressed from solely studying eye movement to the first attempts at understanding what specific eye movements might mean, relating eye fixations to cognitive processes. In 1971, early pioneers in this work, Norton and Stark, identified and described "scan paths"[8] and, in 1976, Just and Carpenter worked on fixations. Just and Carpenter looked at how the duration of a fixation

Figure 4: Images from Judd, McAllister and Steele's 1905 film, showing the eyes moving whilst the head is kept still.

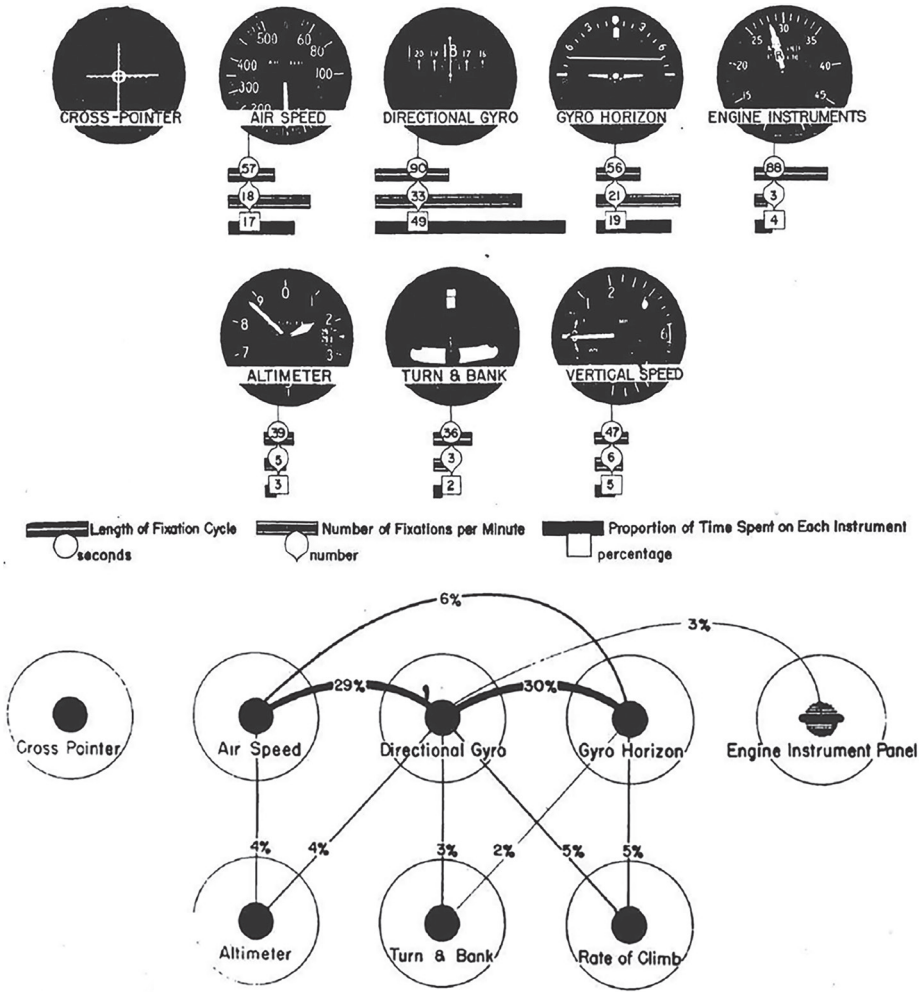


Figure 5: Eye tracking data collected and analysed in 1949 by Fitts, Jones, Milton, revealing a pilot's eye movement between instruments on an aircraft's instrument panel.

might be linked to the mental processing involved. They also investigated scanning strategies, such as looking at a picture with a number of coloured dots. They noticed that whilst not being able to identify all the dots, it was still possible to recognise the highest proportion of dots were red.[9] By the 1980s work on the relationship between eye movement and cognitive load measures was being conducted, such as the 1986 work by O'Donnell and Eggmeier.[10]

Since the 1980s most developments in eye tracking have been in the domain of technology and engineering. However, with the improvement of sensors, materials and optics, eye tracking can now be carried out either remotely, without being intrusive to the study participant, or performed with a pair of simple eye glasses worn by the study participant, as in Figure 2. Additionally, the improved computing power, software and algorithms of recent years have enabled rapid and semi-automatic processing and analysis of results, as in Figure 3.

However, the fundamentals concerned with the meaning and interpretation of eye movements have progressed very little in the last 50 years. Whilst our understanding of the relationship between eye tracking, attention and cognitive processing has developed incrementally since the 1970s, we are still only able to use eye tracking to help gain insights from study participants. Eye-tracking information without context is limited and potentially misleading. For example, two participants (A and B) both read an IFU. The eye-tracking data shows A's eyes followed each line systematically and B's jumped around the instructions. Which participant understood the instructions? Could it be A having read each word in turn understands the instructions, but B who jumped about the instructions missed a lot of detail? Or, could it be A is out of their depth and followed each line hoping to gain some understanding but was left confused, whilst B, already well versed in the subject, quickly scanned for key points just for confirmation? Could it be both are confused or both fully understand the instructions? Currently eye tracking data alone is not sufficient to answer these questions, and still needs traditional human factors techniques to fully interpret the situation.

For eye tracking to reach its full potential, further breakthroughs in our understanding of the meaning of eye movements are needed.

FUTURE DEVELOPMENTS IN EYE TRACKING

Currently, there is increasing focus on improving our understanding of the meaning behind eye movements. Again, it is the early adopters of this technology that are leading the way, most notably the aerospace and automotive industries, researching and obtaining a better understanding of the complex attentional and cognitive processes of users. For instance, the aerospace industry is investigating more deeply how people monitor instruments and why there are lapses in that monitoring.[11] The automotive industry is conducting work to better understand the cognitive load (also known as mental workload) a driver experiences whilst driving, and how different interactions and distractions affect it.[12] Much of this work is driven by a wish to increase safety and reduce user-related errors/accidents. These are also major drivers in medical and drug delivery device development and parallel learnings can be obtained and positively applied.

However, there are limitations to the aerospace and automotive research approaches. Working with comparatively small numbers of study participants cannot provide the quantity of data needed to develop the depth of understanding necessary. Fortunately, a possible answer to this constraint is provided in the emerging discipline of visual analytics, designed to process and analyse vast amounts of eye

"It is the early adopters of this technology that are leading the way, notably the aerospace and automotive industries, researching and obtaining a better understanding of the complex attentional and cognitive processes of users."

tracking data. Using complex algorithms, it allows the data mining of vast databases, which will enable common structures and strategies used by people to be uncovered.[13] By combining miniaturised, low-cost eye tracking equipment with the power of artificial intelligence (AI) and machine learning, huge databases can be created and analysed to reveal insights into how subjects maintain attention, and how they manage varying degrees of cognitive load.

Perhaps with visual analytics it will be possible for eye tracking to tell us if, from the previous example, it was Participant A or Participant B who understood the IFU. Thanks to the potential of low cost electronics, powerful computers and AI, in the future we will have the capability to evaluate and assess the usability of a medical device's user interface just by simply issuing study participants with miniaturised, non-intrusive eye tracking kit and then waiting for the AI to pass its judgement.

On this note perhaps, at some further point in the future, medical devices will have their own eye tracking capability and AI. Maybe then these devices will watch us and decide if we are using them correctly, and interactively train or coach us if we are not!

ABOUT THE COMPANY

PA Consulting Group is an independent firm of more than 2,600 people, operating globally from offices across the Americas, Europe, the Nordics and the Gulf. The company's areas of expertise include consumer and manufacturing, defence and security, energy and utilities, financial services, government, healthcare, life sciences and transport, travel and logistics. PA combines industry knowledge with skills in management consulting, technology and innovation, which it believes allows it to challenge conventional thinking and deliver exceptional results that have a lasting impact on businesses, governments and communities worldwide. PA has extensive experience in product and process development and, as such, provides dedicated human factors inputs to many projects using its state-of-the-art human factors "Observatory".

REFERENCES

1. *Blascheck T et al, "State-of-the-Art of Visualization for Eye Tracking Data". Eurographics Conference on Visualization (EuroVis), Swansea University, UK, June 9-13, 2014.*
2. *Manhartsberger M, Zellhofer N, "Eye tracking in usability research: What users really see," Empowering Software Quality: How can Usability Engineering reach these goals? 1st Usability Symposium, HCI&UE Workgroup, Vienna, Austria, 8 Nov, 2005.*
3. *Yarbus AL, Haigh B (translator), "Eye Movements and Vision". Plenum Press, New York, 1967.*
4. *Dodge RC, Sparks T, "The angle velocity of eye movements". Psychol Rev, 1901, Vol 8(2), pp 145–157.*
5. *Judd CH, McAllister CN, Steele WM, "General introduction to a series of studies of eye movements by means of kinetoscopic photographs". Psychol Rev Monographs, 1905, Vol 7(1), pp 1–16.*
6. *Fitts PM, Jones RE, Milton JL, "Eye fixations of aircraft pilots III. Frequency, Duration, and Sequence Fixations when Flying Air Ground-Controlled Approach System (GCA)". USAF Technical Report No. 5967, Wright-Patterson Air Force Base, Dayton, Ohio, 1949.*
7. *Shackel B, "Note on Mobile Eye Viewpoint Recording". J Opt Soc Am, 1960, Vol 50, pp 763–768.*
8. *Noton D, Stark L, "Scanpaths in saccadic eye movements while viewing and recognizing patterns". Vision Research, 1971, Vol 11(9), pp 929–942.*
9. *Just MA, Carpenter PA, "Eye Fixations and Cognitive Processes". Cogn Psychol, 1976, Vol 8, pp 441–480.*
10. *O'Donnell RD, Eggmeier FT, "Workload assessment methodology". Handbook of perception and human performance, Vol 2: Cognitive processes and performance, Boff KR, Thomas JP, Kaufman L (eds), John Wiley & Sons, 1986.*
11. *Peysakhovich V et al, "The Neuroergonomics of Aircraft Cockpits: The Four Stages of Eye-Tracking Integration to Enhance Flight Safety". Safety, Feb 2018, Vol 4(1), pp 8–23.*
12. *Palinko O et al, "Estimating cognitive load using remote eye tracking in a driving simulation". Proceedings of the 2010 Symposium on Eye-Tracking Research & Applications (ETRA), Austin, Texas, US, Mar 22-24, 2010, pp 141–144.*
13. *Andrienko G., Andrienko N., Burch M., Weiskopf D., "Visual analytics methodology for eye movement studies," IEEE Transactions on Visualization and Computer Graphics, Dec 2012, Vol 18(12), pp 2889–2898.*

ABOUT THE AUTHORS

Dr Philip Lance is an experienced human factors specialist in the field of medical devices and pharmaceutical combination products. With a deep understanding of the usability engineering process, he has applied his human factors expertise to help numerous clients with their development of a wide ranges of devices from invasive surgical equipment and diagnostic equipment to combination products, such as autoinjectors and inhalers. Dr Lance has worked with a wide range of companies from global pharmaceutical companies to small medical device start-ups. Consequently, he has experienced working with a wide range of users from surgeons, nurses, paediatrics and paraplegics to patients with rheumatoid arthritis or COPD. He has helped clients from the outset of the device product development process with early user research, such as contextual inquires and user experience research, through to a device's summative evaluation.

Phil Seeney is a Managing Consultant in the Technology and Innovation Practice within the PA Consulting Group. Mr Seeney developed strong engineering skills in industry transitioning to product design and medical device development after studying at Imperial College (London, UK) and the Royal College of Art (London, UK). He has over 45 years of product development experience covering fast-moving consumer goods, consumer durable and healthcare. For the last 28 years, Mr Seeney has specialised in drug delivery and the development of medical devices. He has a keen interest in the application of technology to improve patient benefits and outcomes and has authored articles on the use of technology in connected drug delivery devices and in the future of inhalation.

Phillips Medisize
a molex company

CONNECTIVITY OPENS THE DOOR TO INNOVATION AND OPPORTUNITY

In this article, Neil Williams, Director of Front-End Innovation and Connected Health, Phillips-Medisize, outlines the need for connectivity in the future of healthcare and details Phillips-Medisize's third-generation Connected Health Platform technology.

Evidence is mounting that connectivity is going to play an increasingly powerful and pervasive role in medicine moving forward. For pharmaceutical companies and drug delivery device developers, integrating connectivity into innovative health solutions offers promising opportunities to improve the experience for both patient and provider, whilst supporting increased medication adherence and therefore facilitating improved therapeutic outcomes.

To optimise their potential, these connected health solutions should be built on three foundational pillars (Figure 1):

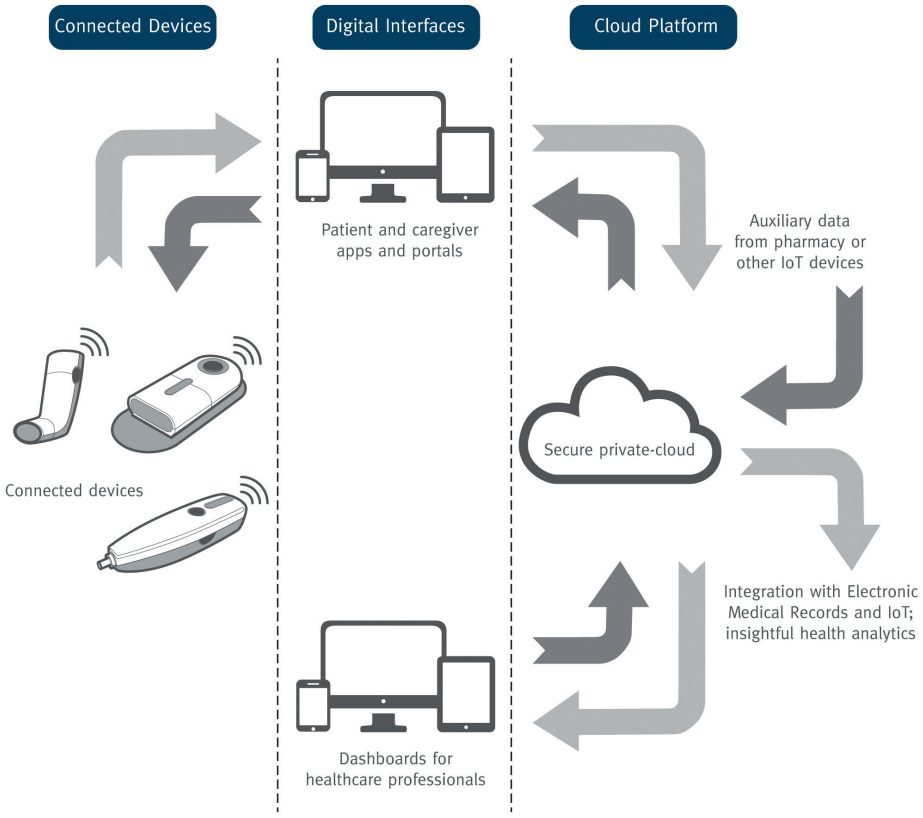


Figure 1: A flexible and low-cost platform, based on the InterSystems HealthShare Health Insights platform that supports enterprise-wide clinical data handling.

Neil Williams
Director of Front-End Innovation and Connected Health

Phillips-Medisize
Milton Hall, Ely Road
Milton, Cambridge
CB24 6WZ
United Kingdom

www.phillipsmedisize.com

1. Patient-centric drug delivery devices
2. Empathetic patient engagement, including regulated "Software as Medical Device" (SaMD) and Mobile Medical Applications (MMA) and portals
3. A robust health information-sharing and analytics platform that enables actionable insights.

"Phillips-Medisize combines its experience in electronics integration and connected health with its expertise in electronics hardware, software engineering and printed circuit board manufacturing and assembly."

Not surprisingly, the three pillars are closely intertwined. By integrating connectivity into innovatively designed, patient-centric drug delivery devices, such as injectors and inhalers, pharmaceutical companies can make it easier and simpler for people to take their medication on-time and monitor their condition. These connected smart devices can track medication administration, collect patient data and instruct and support patients with reminders, incentives, educational content and access to peer communities. The goal is to help patients, caregivers and healthcare professionals (HCPs) improve not only medication adherence but also disease management and, ideally, outcomes.

At the same time, a robust information-sharing and analytics platform enables pharma companies to connect and aggregate medication and diagnostic information across their medicines and therapy areas on a single-enterprise private cloud platform. Such a platform also allows them to integrate data from multiple other sources, such as diagnostic devices, biometric sensors and electronic medical records. HCPs can review patient medication adherence, biomarkers and patient-reported outcomes to help manage the patient's condition, boost adherence and improve outcomes (Figure 2).

"The CHP is an advanced analytics tool that enables customers to quickly generate views of their data, as well as create a data presentation layer for exporting/exposing data to third-party reporting systems."

Figure 2: Enabling patient data and service ecosystems.

TACKLING THE MEDICATION ADHERENCE CHALLENGE

Poor adherence to medication is a costly challenge worldwide, most importantly in terms of unnecessary human suffering and significantly reduced patient health, but also financially. An estimated 50% of medications for chronic diseases are not taken as prescribed, resulting in up to 70% of emergency department admissions. A review in the 2017 Annals of Internal Medicine reports that an estimated 125,000 deaths in the US alone are linked to patient non-adherence to prescribed medications. In turn, this accounts for an estimated cost of approximately US$290 billion (£224 billion) to the US healthcare system.

While there are no easy answers to boosting medication adherence, improving the user experience can play a crucial role. The opportunity to build drug delivery devices and patient apps on an advanced connected health platform drives innovative design that, in turn, creates solutions for patients, caregivers, providers and payers.

To help its customers bring better drug delivery devices and connected health solutions to market quickly and confidently, Phillips-Medisize combines its experience in electronics integration and connected health with its expertise in electronics hardware, software engineering and printed circuit board manufacturing and assembly. Its innovative third-generation Connected Health Platform (CHP) provides a unique opportunity for pharma companies and drug delivery device developers to reduce the risk and cost of developing connected health solutions and accelerate time to market.

SECURE CONNECTED HEALTH PLATFORM OFFERS MULTIPLE BENEFITS

This scalable cloud-based platform addresses key challenges our customers and their patients face:

"Despite the differences in American and European medical coding systems, it's possible to compare patients with, for example, diabetes in the US with those in Germany or the UK."

- **Information-sharing and analytics capabilities.** The Phillips-Medisize CHP is built on InterSystems HealthShare Health Insight. InterSystems is a global leader in healthcare software and integration. Designed for connected drug delivery devices, bio-sensors and regulated SaMD/MMA, and fully documented to support 510k and combination product submissions, the platform provides a medical device data system (MDDS) that connects pharma companies, providers, patients and payers through a unified healthcare record and powerful analytics spanning the care continuum.

  The CHP is an advanced analytics tool that enables customers to quickly generate views of their data, as well as create a data presentation layer for exporting/exposing data to third-party reporting systems. The ability to change or fine-tune dashboards quickly and easily without the need for expensive, time-consuming software development efforts offers a big advantage.

  Previously, dashboards had to be created as part of the core software development phase, after which changing them was time consuming. The ability to revise dashboards "on the fly" saves time and money, offers valuable flexibility and makes it easy to connect with other supported external analytic systems.

  In addition, the CHP can integrate medication, diagnostic and therapy data from multiple sources, make it actionable and normalise it across geographies for global comparisons. For instance, despite the differences in American and European medical coding systems, it's possible to compare patients with, for example, diabetes in the US with those in Germany or the UK. The CHP can also identify the data or keep it anonymous, depending on the patient's preferences.
- **Scalability.** Phillips-Medisize's CHP is massively scalable enterprise-wide. Having a flexible, scalable platform in place eliminates the need to create a customised solution from scratch each time a new drug is introduced, as has traditionally been the approach. This typically results in creating multiple databases which then must be connected in some way to provide a common view of the data. With the CHP, all data can be connected to a single cloud platform per client, but data can be viewed discretely or collectively.

  Once an initial project and infrastructure are developed for a customer on the CHP, adding additional infrastructure for future projects is highly cost-efficient. Also, as the patient population increases, the price per user declines, further minimising the cost barrier to integrating connectivity in health solutions for common chronic conditions.

  In addition, whether drug device developers or pharma companies are collecting, storing and managing data for a thousand patients or hundreds of millions, they can count on the same level of safety and security.
- **Collaboration.** Clients typically are deployed in their own private cloud. However, clients sometimes have cross-industry partnerships and want the ability to share data. We can combine them into a cost-effective collaborative environment.

PROVEN EXPERIENCE FOSTERS INNOVATION

The innovative CHP from Phillips-Medisize incorporates more than a decade of experience developing connected health solutions, including one of the first wireless autoinjectors approved by the US FDA as a combination product for medication tracking. There's still a steep learning curve when it comes to connected health solutions, given that most companies have not yet integrated connectivity into drug delivery devices. But that's changing – Phillips-Medisize is currently working with partners who expect to bring products to market at an accelerated pace.

"Whether drug device developers or pharma companies are collecting, storing and managing data for a thousand patients or hundreds of millions, they can count on the same level of safety and security."

Phillips-Medisize's experience has proven that innovation flourishes at the intersection of market needs and emerging technologies. Pharma companies and drug delivery device developers need to push the boundaries in the design, development and manufacturing of connected health solutions to continue to enhance the patient and provider experience – and sharpen their own competitive edge.

ABOUT THE COMPANY

Phillips-Medisize, LLC, a Molex company, is an end-to-end provider of innovation, development, manufacturing and post-launch services to the pharmaceutical, diagnostics, medical device and speciality commercial markets. Post-launch services include a connected health app and data services. Backed by the combined global resources of Molex and its parent company Koch Industries, Phillips-Medisize's core advantage is the knowledge of its people to integrate design, moulding, electronics and automation, providing innovative high-quality manufacturing solutions.

ABOUT THE AUTHOR

Neil Williams is the Head of Connected Health and Director of Front-End Innovation at Phillips-Medisize, based in Cambridge (UK). Mr Williams consults for biopharma clients, innovating and executing strategies to enhance stakeholder engagement through connected drug delivery devices and software. He has over 23 years' experience covering medical devices, telemetry, digital x-ray, clinical decision support, secure mobile working, patient engagement and health analytics for businesses including Philips Healthcare, Microsoft, Elsevier Health Sciences, Hospira, Hearst Health and ZOLL. Prior to Mr Williams' commercial career he trained at Leicester University Hospitals in Operating Department Practice and was faculty for numerous post-graduate advanced life support programmes.

5 THINGS TO CONSIDER
WHEN MANUFACTURING CONNECTED DRUG DELIVERY DEVICES

The estimated number of connected drug delivery devices continues to increase and the impact of this trend could be significant, explains Phillips-Medisize, a Molex Company

While digital connectivity or connected health can improve the coordination and delivery of patient care, original equipment managers need to keep these five things in mind when creating connected drug delivery devices:

1. **Development strategy and design consideration**
2. **Situation analysis and patient compliance**
3. **Connectivity ecosystem**
4. **Wireless subsystem**
5. **Security of device and information**

As the Internet of Things continues to become an integral part of people's lives, the opportunity to use it within drug delivery device applications remains promising. The manufacturers and device designers must identify, investigate and overcome these challenges so that the implementation of wireless and other related smart technologies can be achieved. When done successfully, connected systems enable the patient and caregivers to have a 360° view of both the patient and the disease – not only to manage adherence, but to improve results by understanding the effect of the regimen.

Phillips Medisize
a molex company

www.phillipsmedisize.com

DARE TO BE DIFFERENT: INNOVATION VERSUS THE STATUS QUO

In this article, Barb Taylor, Senior Director of Marketing, Portal Instruments, discusses the need to differentiate drug products in an ever more competitive market by providing a delivery device that fits comfortably into a patient's everyday lifestyle, and how Portal Instruments' Prime needle-free injector does exactly that.

If you ask a physician how they decide what medication to prescribe, the first answer is almost always:

- Efficacy and safety – will this drug work for my patient and help their symptoms?

The second is:

- Insurance – is it covered and what are the costs? Can the patient afford this drug?

And lastly, physicians consider a widely overlooked dimension:

- Ease of use – how does this treatment fit into the patient's day-to-day life? For injected products, can a patient administer a self-injection, or would they be better at an infusion centre? Do they have support at home to help them remember to take their medication and to manage any anxiety they may feel? Conversely, are there kids or pets at home? Would that make self-injecting at home more stressful and less desirable than other means?

> "With the emergence of biosimilars and increasing competition, there is a threat that safety and efficacy alone may not meaningfully differentiate products."

1937 – "Penetration of Tissue by Fuel Oil Under High Pressure from Diesel Engine" C.E. Rees

1947 – First clinical evaluation of "Hypospray" device

1954-1997 – Widespread use of jet injection

Polio, cholera, small-pox

1997 – US Military sees Hepatitis B outbreak from shared jet injector

2013 – Single-use flu vaccine approved for 0.5 mL injections

"Hypospray." TIME Magazine, 29 Aug, 1960

"Peace Gun" Smithsonian Institute

Figure 1: A brief history of needle-free devices.

Ms Barbara Taylor
Senior Director of Marketing
T: +1 617 500 4348
E: barb.taylor@portalinstruments.com

Portal Instruments, Inc
190 5th Street
Cambridge
MA 02141
United States

www.portalinstruments.com

With the emergence of biosimilars and increasing competition, there is a threat that safety and efficacy alone may not meaningfully differentiate products. Access and payer strategies are certainly important, but that is a difficult area by which to differentiate oneself. What may make the difference with physicians and patients in such a competitive space is the drug delivery device. Drug delivery that fits into a patient's day-to-day life, with minimal pain, disruption and hassle is an important consideration for doctors as they choose what to prescribe. Needle-free drug delivery can solve that lifestyle challenge and presents a significant improvement in the way that injectables are delivered.

The concept of a "needle-free" device has been around for decades (Figure 1). First assessed in the 1930s and made popular via Star Trek's "Hypospray", the broader use of needle-free injectors did not occur until the 1980s. These legacy needle-free delivery systems were powered by mechanical or gas-based means with limited pressure controls and poor regulation of injection depth and volume, which resulted in low-volume, painful and loud injections.[1] As such, needle-free drug delivery was not widely adopted.

PORTAL PRIME DEVICE – NEXT GENERATION NEEDLE-FREE

Portal Instruments is reinventing needle-free drug delivery (Figure 2). Portal Instruments' Prime device administers the drug through a computer-controlled, highly-pressurised jet stream. The narrow jet pierces through the epidermis and delivers the drug into the subcutaneous space (Figure 3). One of the advantages of Portal's needle-free device over needles is the jet-stream's 200 µm diameter, whereas commonly used needles have a diameter of 400 µm (27 gauge), as shown in Figure 4. The drug is delivered from a one-time use, sterile ready-to-fill (RTF) cartridge that is provided to the fill/finish manufacturer in a standard 16 x 10 nest and tub. The design of the cartridge and nest and tub format enables seamless, easy product filling.

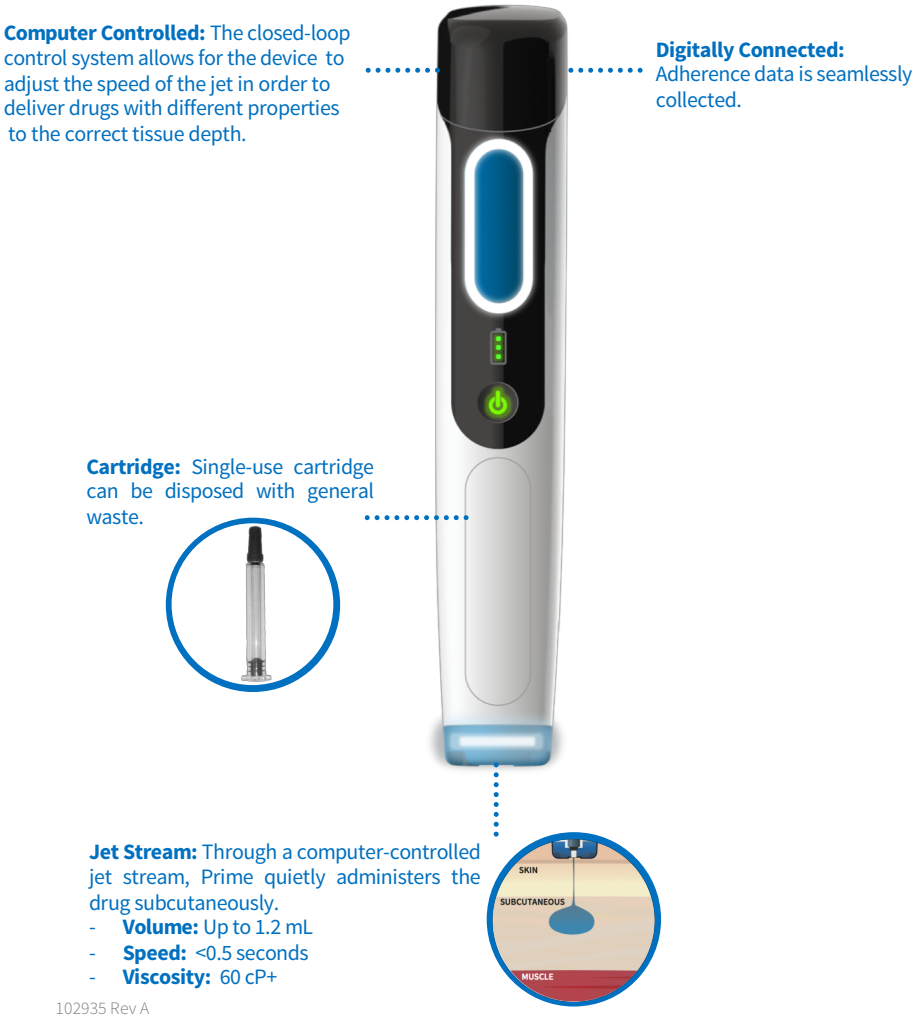


Figure 2: Next generation needle-free drug delivery.

> "The Prime device has been successfully tested with a wide array of drugs, from small molecules to peptides and mAbs over 60 cP."

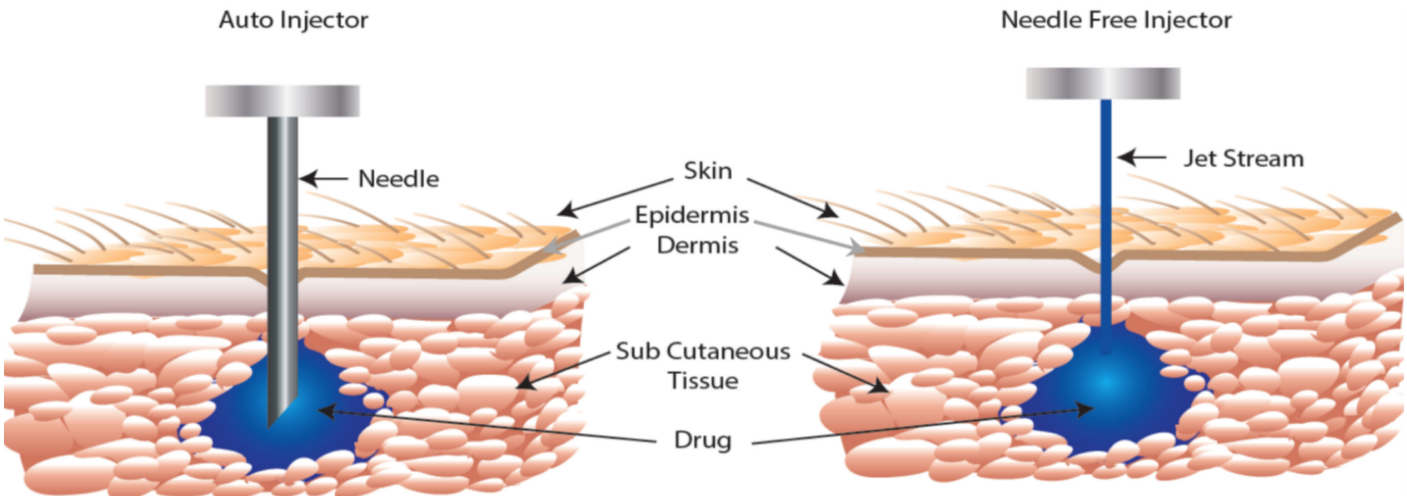


Figure 3: A high pressure, narrow jet pierces through the epidermis, delivering drug into the subcutaneous space.

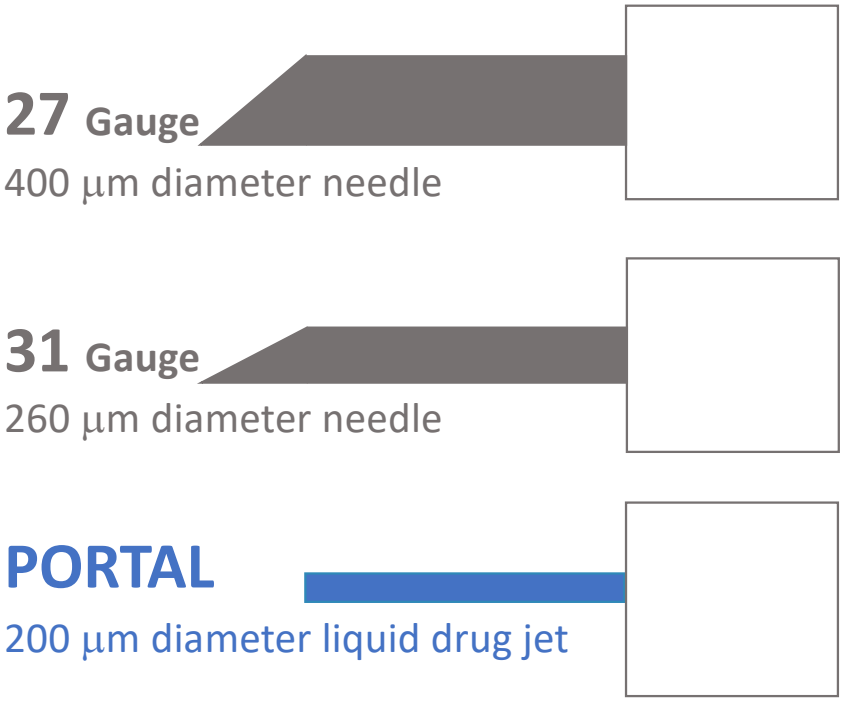


Figure 4: Diameter comparison of Portal's Prime device versus needle & syringe.

> "With data and analysis, teams will be able to identify challenges related to adherence, predict trends in patient populations, and use that data to create a better patient experience."

In Prime's closed-loop system, the computer-controlled motor and internal feedback control system work together to sense the pressure and adjust the velocity of the jet-stream accordingly. The device also provides feedback to the patient to lead them through the injection process, and to confirm that the injection has been completed.

The Prime device has been successfully tested with a wide array of drugs, from small molecules to peptides and mAbs over 60 cP. Regardless of the viscosity, the subcutaneous injection is able to be administered in less than 0.5 seconds.

CONNECTIVITY & ANALYSIS TO DRIVE OUTCOMES

As with many modern advanced drug delivery technologies, the Prime needle-free device logs all injections and can be automatically connected to a secure cloud server, presenting patients with the ability to track their injections without having to input their data manually. Portal's vision is for this data to provide real-time adherence insights which can ultimately be used by healthcare teams, and others, to drive better outcomes. For example:

- Pharmaceutical partners can analyse aggregated and anonymised data to enhance pharmaceutical lifecycle management and use the quantitative insights to launch specific, targeted campaigns that drive population penetration and adherence programmes.
- Patient service providers can quickly identify "late doses" before they become "missed doses" and be proactive in reaching out to patients who may need support.
- Patients may choose to share this data with their physicians in order to have a more well-rounded picture of the progression of their disease. This insight may create more efficient physician visits and more tailored treatment plans.
- Payers could use this adherence data to inform value-based contracts that are dependent on adherence.

With data and analysis, teams will be able to identify challenges related to adherence, predict trends in patient populations, and use that data to create a better patient experience. It may also lead to trends that were previously undetected becoming noticeable.

DARE TO BE DIFFERENT

It is not uncommon for companies to tout innovation as a core pillar. There are several areas in which companies can innovate beyond the science of drugs to strengthen their positions as leaders. Drug delivery is an obvious choice for innovation as it can involve cutting-edge technology, lead to patient and physician preference, and set oneself apart by being radically different from a field of autoinjectors or prefilled syringes that are all fairly similar. Nevertheless, choosing to go with a new delivery solution may feel unfathomably risky versus staying with the tried-and-true needle and syringe.

Fortunately, Portal instruments has identified and systematically de-risked the major concerns while developing its needle-free injector:

- Over 16 mAbs have been successfully tested for structural and functional integrity

- Animal models have been built to analyse the fluid path and disbursement
- Pain and preference studies have been conducted in Institutional Review Board (IRB) approved human clinical trials
- Numerous human factors studies have been conducted.

For companies that would like to test a particular asset with the Portal needle-free device, there is a straightforward evaluation process. The main question that pharmaceutical firms should be asking themselves is – what if my competitors go needle-free? Is there more risk in the status quo or being on the forefront of innovation?

ABOUT THE COMPANY

Portal Instruments is a clinical-stage connected drug delivery firm, commercialising a next generation, needle-free drug delivery platform to transform the treatment experience for patients suffering from chronic diseases such as ulcerative colitis, multiple sclerosis, rheumatoid arthritis and psoriasis. Portal is looking to develop strong partnerships with pharmaceutical firms seeking to gain an edge by offering their therapeutics fully integrated with a digital, patient-centric delivery system.

REFERENCES

1. *Ravi AD et al, "Needle Free Injection Technology: A complete insight". Int J Pharm Investig, 2015, Vol 5(4), pp 192–199.*

ABOUT THE AUTHOR

Barbara Taylor is the Senior Director of Marketing at Portal Instruments. With over 20 years' experience in health tech strategy and marketing, she brings to Portal expertise in healthcare software development, new product introduction, lifecycle and service strategy and business model innovation. Prior to Portal Instruments, Ms Taylor was at a number of large and small firms including Philips Healthcare and Mercer Management Consulting. Ms Taylor holds an MBA from the Kellogg Graduate School in Evanston, IL, US, and a BS in biology from the University of Michigan in Ann Arbor, MI, US.

ON drugDELIVERY

2019 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
Jan 2019	Ophthalmic Drug Delivery	PASSED
Feb 2019	Prefilled Syringes & Injection Devices	Jan 3rd 2019
Mar 2019	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Feb 7th 2019
Apr 2019	Pulmonary & Nasal Delivery	Mar 7th 2019
May 2019	Injectable Drug Delivery	Apr 4th 2019
Jun 2019	Connecting Drug Delivery	May 2nd 2019
Jul 2019	Novel Oral Delivery Systems	Jun 6th 2019
Aug 2019	Industrialising Drug Delivery Systems	Jul 4th 2019
Sep 2019	Wearable Injectors	Aug 1st 2019
Oct 2019	Prefilled Syringes & Injection Devices	Sep 5th 2019
Nov 2019	Pulmonary & Nasal Drug Delivery	Oct 3rd 2019
Dec 2019	Connecting Drug Delivery	Nov 7th 2019

SAVE THE DATE! DDL2019

December 11-13th, 2019
EICC, Edinburgh, UK

DDL2018

DRUG DELIVERY TO THE LUNGS

12/13/14 DECEMBER 2018

Edinburgh International Conference Centre, Edinburgh, Scotland, UK

The **Drug Delivery to the Lungs Conference (DDL)** is Europe's premier conference and industry exhibition which is dedicated to pulmonary and nasal drug delivery.

The focus is on providing a forum to present through podium and poster presentations recent developments in the field of inhalation therapy.

700+Delegates ▶ Annual DDL Award Lecture
100+Industry Exhibitors ▶ Networking Receptions
Emerging Scientist Award ▶ Poster Prizes

Areas of particular interest for DDL2018 include:

- Insights in respiratory medicine
- Real-world challenges for inhaled medicines
- Respiratory development: Thinking outside the box
- The Pat Burnell young investigator competition
- Aerosol science: physics meets pharmaceutics
- Novel formulations and process technology

Visit www.ddl-conference.com to find out more

Contact the team: sheila@ddl-conference.com / nikki@ddl-conference.com +44 (0)1275 849019 / www.ddl-conference.com

Needle Free Injections

Portal Instruments

Adherence Tracking

Patient Preferred*

Ultra-Fast Drug Delivery**

Adaptive To Drug Viscosity

Portal Instruments Connected Needle Free Injector

helping patients take control of their chronic disease

Portal Instruments Inc. • 617.500.4348 • www.portalinstruments.com • info@portalinstruments.com

*Kojic, N., Goyal, P., Lou, C.H. et al. *AAPS PharmSciTech* (2017) 18: 2965. https://doi.org/10.1208/s12249-017-0779-0

** The Portal device can deliver 1ml of drug in 1/3 of a second per Portal internal studies

NORBERT HABERLAND, DATWYLER

Norbert Haberland, PhD, born in 1956 in Germany, received his MSc degree in Chemistry and Technology of Rubber and Plastics from Moscow Institute for Fine Chemical Technology in 1981. In 1986, he gained his PhD in chemical engineering from the same institute. Dr Haberland is a member of the German Rubber Association, where he worked for many years as Chairman of the North Rhine-Westphalia section. For his dedication and contribution to the German Rubber Association, he became member of the Rubber Hall of Fame in 2012.

After diverse management positions in material development, technical management, and general management in globally active rubber companies, Dr Haberland has been working for Datwyler Group since 2010, and is currently Vice-President New Processes & Products, with a focus on advanced technologies and innovation.

Interviewed here, Dr Haberland discusses Datwyler's interests in the field of wearable technology in the healthcare sector.

Q Mr Haberland, what is your view on wearable healthcare solutions, especially in the context of digital health?

A Digital health has been gaining lots of traction in recent years. It is currently one of the big trend topics in the industry, offering many opportunities to pharmaceutical and medical companies, as well as their suppliers. At Datwyler, we have been exploring the field of digital health since 2014. It has become an important new business field for us. We see lots of potential for innovative healthcare solutions, especially regarding wearables, such as injection or monitoring systems. Therefore, we are continuously working on innovations in this area. But even more important to us is that patients can profit from this development. Improving patients' lives is one of our top priorities.

Q How does Datwyler contribute in the field of wearables?

A Datwyler is predominantly perceived as a significant player in the area of drug packaging and the development and manufacturing of medical device components for the administration of drugs (Box 1). However, we have also been exploring the area of wearable devices and digital health. For us, wearables are paving the way for new avenues of drug delivery. With partners and customers, we started to work on innovative wearable solutions. Among the results are our new soft dry electrodes (Box 2). The soft dry electrodes are our proposition for comfortable long-term EEG monitoring. As the name "wearable" suggests, the electrodes are made to be worn on the body for a long period of time, which can stretch over several days or even weeks.

BOX 1: PARENTAL PACKAGING AND PLUNGERS

Datwyler offers state-of-the-art solutions for parenteral packaging, including prefilled syringes and pen systems. Datwyler's plungers, a key component of these drug delivery systems, are compatible with all types of parenteral containers and are made of specialised bromobutyl-based formulations with all the physical, chemical and mechanical properties essential for the safe and easy administration of the drug product. These components are manufactured in line with Datwyler's first line standard, the highest manufacturing standard in the industry.

The production takes place in a fully automated cleanroom environment, including validated washing and the latest generation of 100% camera inspection techniques. For sensitive drugs, such as biologics and biosimilars, Datwyler also offers elastomeric closures with Datwyler's Omni Flex coating. Omni Flex is the first coating to offer excellent barrier properties and to eliminate the closure as a source of silicone oil-based subvisible particles. As a result, the plungers offer an optimised extractables and leachables profile, preventing chemical reactions with the drug and securing the drug's integrity and efficacy. Even after several years of storage, maximum plunger barrel seal integrity is guaranteed.

BOX 2: SOFT DRY ELECTRODES

Datwyler's soft dry electrodes are the company's proposition for long-term EEG monitoring with a focus on patient comfort. The electrodes are based on a flexible conductive polymer and customisable design, ensuring comfort during monitoring. The electrodes allow dry signal acquisition, which eliminates the use of gels and decreases skin irritation significantly. The specific design and characteristics allow usage without special skin preparation. Patients can be monitored anywhere – a hospital environment is not necessarily needed.

Q What are the advantages of the soft dry electrodes?

A Patient safety and comfort are our main concern. Therefore, during the development of the soft dry electrodes, we focused on high-quality materials which are waterproof, flexible, biocompatible and offer a high degree of comfort for the patient. Due to the flexible conductive polymer and customisable design, the soft dry electrodes ensure maximum comfort during monitoring. In addition, dry signal acquisition eliminates the use of gels and decreases skin irritation significantly. The special design allows usage without any skin preparation and does not necessarily require hospitalisation during monitoring.

Q Do you have any other examples of wearable healthcare products?

A We are co-operating closely with the Interuniversity Microelectronics Center (IMEC) in Belgium on research in the wearables sector. This programme is focused on developing advanced materials for intelligent electrodes for brain monitoring platforms. IMEC has conducted research to realise eye movement tracking technology to help diagnose and monitor the progression of neurodegenerative diseases. Together, we developed a standard pair of eyeglasses, which includes wireless eye-tracking technology (Box 3). The smart glasses use electro-oculograms (EOG), which measure the electrical potential across particular points on the skin around the eyes during eye movement. The glasses use five dry-contact electrodes.

BOX 3: EYE-TRACKING TECHNOLOGY

Datwyler is co-operating closely with the Interuniversity Microelectronics Center (IMEC) in Belgium and the Holst Center in the Netherlands to research intelligent electrodes for brain monitoring platforms. Patients with neurodegenerative diseases often experience symptoms of abnormal eye movements. IMEC has conducted extensive research to develop eye movement tracking technology to help diagnose and monitor the progression of these disorders. In co-operation with Datwyler, it developed a wearable device concept which integrates wireless eye-tracking technology into a standard pair of eyeglasses. The smart glasses use electro-oculograms, which measure the electric potential across particular points on the skin around the eyes during eye movement. The glasses use five dry-contact electrodes developed by Datwyler.

Q It sound like partnerships are a key driver for developing new products. Is that correct?

A Absolutely. Partnerships are incredibly important to us. Above all, these partner companies encourage synergies which enable the development of high-tech medical solutions. A recent example is our partnership with Coldplasmatech (Griefswald, Germany), a start-up focusing on plasma research and technology. Together we developed an intelligent wound patch, which uses the regenerative characteristics of cold plasma. The patch is suitable for the therapeutic treatment of chronic wounds which are infected with multi-resistant germs. Cold plasma can eliminate germs and gently improve wound healing through disinfection and cell activation. The patch can be directly applied to an open wound – only a few sessions are needed for recovery and each takes no longer than two minutes. The whole patch is thrice covered with liquid silicone in a complex injection moulding process to ensure maximum safety.

Q What long-term advantages do you see in the wearables sector?

A Our ambition is to continuously master current challenges in the market and turn them into new opportunities for our customers. As a specialist in developing solutions for drug administration, we believe that combining wearables with drug administration could result in new therapeutic measures and devices, which can not only provide more comfort and flexibility for patients, but also contribute significantly to creating a safer healthcare environment.

DATWYLER

Dr Norbert Haberland
Vice-President, New Products and Processes
T: +41 41 875 1313
E: norbert.haberland@datwyler.com

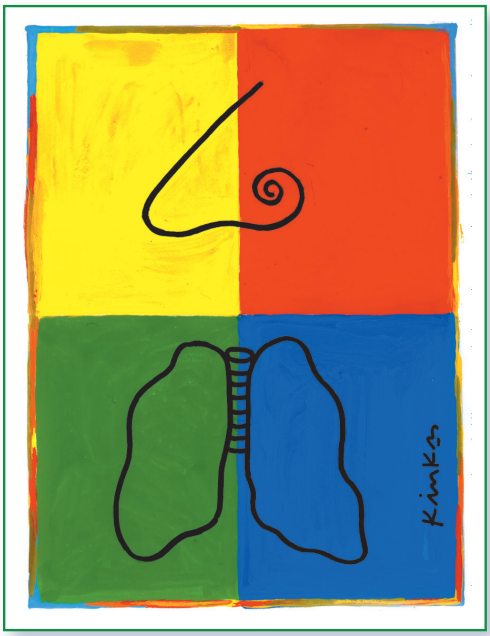
Datwyler Pharma Packaging USA Inc
9012 Pennsauken Highway
Pennsauken
NJ 08110
United States

sealing.datwyler.com

ATTEND • PRESENT • EXHIBIT • SPONSOR

RDD EUROPE 2019

Respiratory Drug Delivery



MAY 7-10, 2019

Estoril Congress Center

Lisbon, **PORTUGAL**

Palace of Pena - Sintra-Cascais Natural Park

rddonline.com/rddeurope2019

RDD Europe is a conference jointly organized by

RDD Online Respiratory Drug Delivery

Aptar pharma

VCU RDD Peter R. Byron Graduate Student Award

All graduate student poster presenters attending RDD Europe 2019 are eligible. Details on conference website.

Nemera

we put patients first

e-Devices

Electronic and connected devices to answer patients' needs

Our electronic concept devices showcase several features to make patients' life easier such as delivery assistance, live feedback and adherence aid to their treatments.

Nemera's innovation department leverages multi-skilled teams to develop tailored electronic solutions across multiple device platforms.

www.nemera.net • information@nemera.net • +33 (0)4 74 94 06 54

• INHALATION • EAR NOSE THROAT • PARENTERAL • OPHTALMIC • DERMAL

DCA

DDL2018
Stand: 310

Helping our clients connect with the future

www.dca-design.com