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A SIMPLE AFFORDABLE DPI: MEETING THE NEEDS OF EMERGING MARKETS

In this article, Anselm Ebert, PhD, Business Development Director, H&T Presspart, João Ventura Fernandes, PhD, Business Development Manager, Hovione Technology, Ameet Sule, Head of IPTC, H&T Presspart, and Sunita Sule, IPTC Consultant, H&T Presspart, discuss the rising need for respiratory medication in the developing world. They go on to highlight the novel challenges presented by these new markets and explain how a new DPI, PowdAir Plus™, meets those challenges, offering a solution to the increase in chronic respiratory conditions across the globe.

GROWING NEEDS FOR RESPIRATORY CARE

It is estimated that chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) may affect as many as 334 million people worldwide today,[1] with that number predicted to rise by an additional 100 million by 2025.[2] Whilst the prevalence of asthma and COPD has been historically estimated to be higher in developed countries,[3] it is forecast that many will also become affected in developing countries, as the disease prevalence rate is expected to rise faster in these countries as a result of urbanisation and modifications to lifestyle and the environment.[2] While asthma alone causes over 250,000 deaths every year, the mortality rate of chronic respiratory diseases is known to be mainly correlated with access to essential respiratory care

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and drugs. Hence, mortality rates are currently higher in developing countries such as India, China and South Africa. Thus, there is a growing need to improve access to basic respiratory healthcare and medications in emerging markets.

THE IMPORTANCE OF THE INHALER

Improving population access to respiratory care in developing markets is both a clear, unmet medical need and a major task for manufacturers of respiratory drugs and delivery devices. As the traditional strategy followed by pharmaceutical companies in developing countries has been geared towards providing a barrier to generic competition (via complex products, customised to expensive devices), patients in developing countries have not yet been able to benefit from an industrial strategy targeted to fulfil their needs for improvement in access and treatment affordability. In this aspect, dry powder inhalers (DPIs) are a particularly well suited delivery device platform for emerging markets. In particular, capsule-based DPIs offer flexibility to deliver a wide range of drugs from a single, cost-effective device platform.

In practice, the device has become the largest portion of the final pharmaceutical package cost, making it essential to develop new, state-of-the-art device designs that maximise ease of use whilst minimising manufacturing costs. This facilitates patient access to respiratory medicines in developing markets. Market research predicts that, with key drugs and delivery devices soon to come off-patent in the asthma and COPD space, emerging markets offer considerable potential for inhaled generics.

Driven by the rapidly evolving healthcare industry, Asia Pacific is expected to display the fastest growth, having to look after an increasing patient pool in need of treatments for asthma and COPD. India, in particular, is expected to gain from the increased efforts of its government to reduce overall healthcare expenditure. Other regions such as Latin America, the Middle East and Africa are also observing improved access to healthcare, connected to a rise of the middle class with more disposable income, in turn driving an increased usage of asthma inhalers. Whilst the inhalables market has previously been dominated by metered dose inhalers (MDIs), DPIs have become the fastest growing segment. Whereas most DPIs have been designed for developed markets and their economic structure, with multiple components and complex mechanics, the demand for respiratory treatments is growing rapidly in developing markets, presenting a new set of challenges. By listening to customers, a clear demand can be heard for DPIs that deliver reliable performance, are easy to use and are readily affordable. Whilst the pharmaceutical industry has made extraordinary technological advances with inhalation devices, it is important in some market segments to make sure that not too much complexity is added, making the devices more difficult to use and expensive to manufacture.

a) PowdAir Plus in storage position

b) Step of pushing moveable tray into the open position for loading of the pharmaceutical capsule

c) Step of closing the loaded tray, which allows the capsule to be cut open, and opening the hinged cover for inhalation

Figure 1: Usability of the PowdAir Plus capsule-based DPI: a) storage position; b) loading pharmaceutical capsule; and c) closing the loaded tray.

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Which important issue should the design of a device tackle? A large independent study completed in 2016, summarising over 140 articles reporting on 50,000 subjects, concluded that "incorrect inhaler technique is unacceptably frequent and has not improved over the past 40 years, pointing to an urgent need for new approaches to education and drug delivery".[4] Furthermore, the Asthma Society of Ireland published figures showing that up to 60% of the 300,000 asthmatics in the country do not have their disease under control.[5] In context, these numbers support the conclusion that a well-designed, easy to use inhaler might reduce the risk of errors caused by incorrect inhaler technique. Looking at developing countries, such as India, COPD deaths have increased by 65% in the last decade.

MAKING IT EASY

At the beginning of 2017 H&T Presspart teamed up with Hovione Technology and launched PowdAir Plus™ (Figure 1).

Figure 2: Easy capsule opening: automatic capsule activation as tray is closed.

PowdAir Plus, a capsule-based DPI, is designed to maximise simplicity and ease of use whilst minimising manufacturing, assembly and production costs (for example, by using no metal parts). A particularly novel design feature is the way that the device opens the capsule automatically once the tray is closed, removing the need for patients to actively pierce the capsule and reducing the number of operational steps. The device is patented with a unique blade technology (Figure 2).

As the industry becomes more customer-focused and aesthetics play a greater role, the visual and haptic design becomes a factor of utmost importance. If patients are going to keep a device on them at all times for frequent use, it must be neat, portable and robust. Most capsule-based DPI formulations are available in transparent or partially transparent capsules. The clear transparent capsule chamber in the PowdAir Plus device (compatible with all Size 3 capsule types) gives visual feedback that the complete dose has been inhaled from the capsule, and its hinged dust lid ensures continuous protection of the mouthpiece. Incorporation of these features has made the PowdAir Plus device simple, compact and discrete.

A patient-centric methodology was followed by Hovione Technology during the design generation of this new capsule-based DPI. In an initial human factors study, a first design embodiment was evaluated and benchmarked against the market-leading capsule-based DPI by 19 COPD patients in terms of use steps, size, shape, capsule handling, mouthpiece comfort and dust cap design. This led to the discovery that patients preferred fewer use steps – in particular the automatic capsule piercing feature – and the more ergonomic shape and size of the proposed new design. However, patient feedback also indicated the need to both further facilitate loading and ejecting the capsule, and integrate a fully hinged dust cap. Based on collected patient preferences and human factors findings, a second design was proposed which integrated the desired

Figure 3: The four parts of PowdAir Plus.

> "Next to the three human factors studies performed by Hovione Technology, H&T Presspart brings professional manufacturing capabilities to the table."

design features, and was subsequently submitted to two new human factors studies with 34 additional COPD patients. The results confirmed the usability improvements and the beneficial impact of integrating patient-focused testing during inhaler device design for achieving maximum ease of use in the final PowdAir Plus DPI.

Next to the three human factors studies performed by Hovione Technology, H&T Presspart brings professional manufacturing capabilities to the table. By employing these, the possibility was opened up to fulfill the market demand for high quality devices at affordable costs (Figure 3). H&T Presspart, being one of the leading suppliers for the respiratory inhalation field, has experience producing high quality products at lean manufacturing costs.

EFFECTIVE DELIVERY

PowdAir Plus is a medium resistance device (50 L/min corr to 4 kPa) capable of delivering both lactose carrier-based and particle engineered dry powder formulations. The X-ray pictures (kindly provided by Prior PLM Medical) (Figure 4) show the effectiveness of the device. The two major positive effects of this delivery method are, firstly, a steady release of the powder during the inhalation period and, secondly, creating a vortex in the capsule itself to disperse and de-agglomerate the powder. The *in vitro* laboratory data of PowdAir Plus with a generic marketed salbutamol formulation exhibits good particle size distribution in line with currently marketed DPIs. The delivered dose data shows flow rate independency at 30, 60 and 90 L/min (Figure 5).

H&T Presspart's Inhalation Product Technology Centre (IPTC) unit collaborated with Hovione Technology's experts to combine both knowledge and experience regarding device development, powder characteristics and analysis. A joint effort was made for the functional

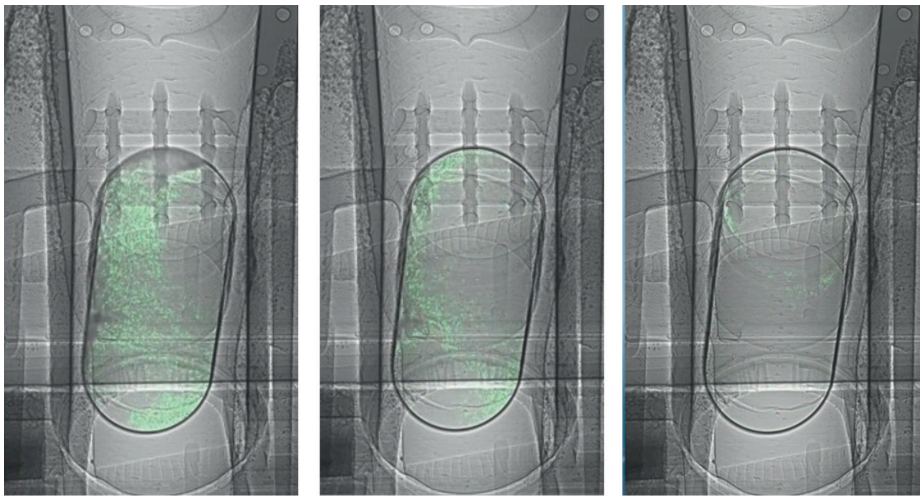

Figure 4: High speed X-ray images of the powder dispersion dynamics inside the capsule during inhalation (kindly provided by Prior PLM Medical).

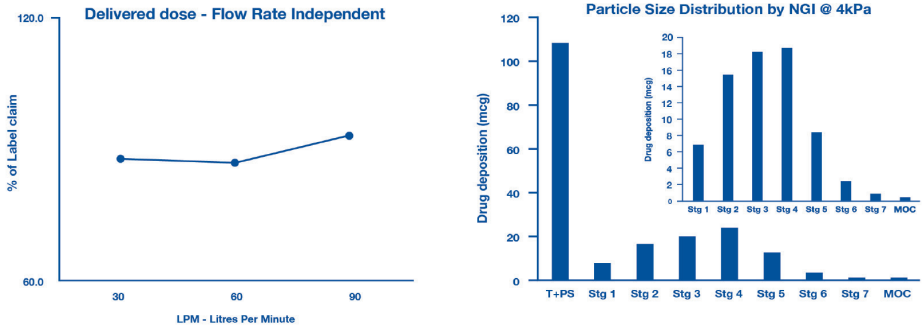

Figure 5: *In vitro* performance data of PowdAir Plus device for a marketed salbutamol capsule-based formulation.

optimisation of the device design, using techniques such as computational fluid dynamics (CFD) and X-ray analysis, leading to the PowdAir Plus DPI.

CONCLUSION

With the prevalence of asthma and COPD on the rise, increased healthcare costs in developing countries will be an undeniable consequence. To help these countries improve basic access to respiratory drugs and care whilst maintaining sustainable healthcare systems for their patients, cost effective solutions by respiratory drug and device manufacturers are needed. Human factors studies suggest that usability issues, incorrect inhalation techniques and a lack of adherence contribute to unsatisfactory treatment results.

On the other hand, as the delivery device itself has become the largest portion of the final cost of pharmaceutical goods, it is essential to develop new, state-of-the-art device designs that maximise ease of use for improving treatment compliance whilst simultaneously minimising its manufacturing cost, meeting the requirements of emerging markets. Nowadays, both generic and originator medication are developed to meet the demand for easy to use, high quality devices, delivering high doses of medication in a reliable and repeatable fashion, for as little cost as possible.

By combining the strengths of Hovione Technology and H&T Presspart, a unique unit dose, capsule-based DPI, PowdAir Plus, is now available, combining user-friendliness, functionality and affordability to provide for the unmet needs of developing countries for improved respiratory care.

ABOUT THE AUTHORS

Anselm Ebert has a PhD in Neuroscience from Edinburgh University and is Business Development Director at H&T Presspart, the leading supplier of respiratory drug delivery components. Dr Ebert previously worked as a Senior Business Consultant and before joining H&T Presspart was Director of Product Development at Hartmann AG who specialise in the manufacture of medical products.

João Ventura Fernandes is Manager of Business Development at Hovione Technology. He is a Mechanical Engineer, holds a PhD in Engineering Design and has accumulated ten years of product development experience across the aerospace and pharmaceutical industries. Dr Ventura worked previously in jet engine development at Volvo Aero and Rolls-Royce. He joined Hovione in 2014 to lead DPI development, quickly becoming a skilled inventor and business developer.

Ameet Sule, Director, Inhalation Product Technology Centre, H&T Presspart, is a pharmaceutical professional having worked in the industry for more than 20 years, specialising in the development of inhalation products and devices.

Sunita Sule, Inhalation Product Consultant, is a pharmaceutical professional who has over 25 years of experience in the pharmaceutical industry, with core expertise in formulation and device development of inhalation products.

ABOUT THE COMPANIES

H&T Presspart offers pharmaceutical customers high-precision injection moulded plastic components and deep drawn metal cans for respiratory drug delivery systems.

The company has more than 45 years' experience and a worldwide reputation for competence, quality and innovation in the pharmaceutical and other industrial sectors. H&T Presspart Inhalation Product Technology Centre (IPTC) supports new product developments and strategic initiatives with its customers. Founded in 1970 and acquired by the Heitkamp and Thumann group in 2002, H&T Presspart has three European manufacturing sites in Germany, Spain and the UK, with sales offices in China, India, South America and the US.

Hovione Technology offers access to innovative, attractive and globally competitive inhalation devices that maximise simplicity of use, safety, drug delivery performance and industrial manufacturability. With more than 20 years' experience in inhalation device development and a track record for developing successfully marketed, novel and effective inhalation devices, Hovione Technology offers device development services and access to a family of disruptive, patent-granted inhalers for both acute and chronic treatments.

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ON drugDELIVERY

2017/18 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
Dec 2017	Connecting Drug Delivery	Nov 20th 2017
Jan 2018	Ophthalmic Drug Delivery	Dec 11th 2017
Feb 2018	Prefilled Syringes & Injection Devices	Dec 22nd 2017
Mar 2018	Skin Drug Delivery: Dermal, Transdermal Microneedles	Jan 20th 2018
Apr 2018	Pulmonary & Nasal Drug Delivery	Feb 19th 2018
May 2018	Injectable Drug Delivery: Devices Focus	Mar 19th 2018
June 2018	Connecting Drug Delivery	Apr 23rd 2018
July 2018	Novel Oral Delivery Systems	May 21st 2018
Aug 2018	Industrialising Drug Delivery Systems	Jun 25th 2018
Sept 2018	Wearable Injectors	Jul 23rd 2018
Oct 2018	Prefilled Syringes & Injection Devices	Aug 27th 2018
Nov 2018	Pulmonary & Nasal Drug Delivery	Sep 24th 2018
Dec 2018	Connecting Drug Delivery	Oct 29th 2018

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PowdAir PLUS

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Innovative, ergonomic and simple to use

H&T Presspart are proud to present PowdAir Plus™, a new generation of uDPI, precision built from 100% plastic with no metal parts.

PowdAir Plus™ is an innovative, discreet, patented capsule based dry powder inhaler designed for advanced simplicity, ease of use, affordability and consistent medicine dose delivery.

PowdAir Plus™, with a transparent chamber for visual dose delivery feedback, automatically activates the capsule as the tray is closed and is suitable for all capsule types in size 3.