REINVENTING THE pMDI: EVOLVING A PROVEN PLATFORM FOR A LOW-GWP FUTURE

Aptar pharma

Chris Baron of **Aptar Pharma** discusses how lower-global warming potential pressurised metered dose inhalers are moving from development to commercialisation and explains why manufacturing readiness and supply resilience are critical, going on to introduce Aptar Pharma's ZEN30 Futurity®, designed to anticipate current and emerging regulatory expectations.

For more than half a century, pressurised metered dose inhalers (pMDIs) have been a cornerstone of respiratory care, delivering life-saving therapies to hundreds of millions of patients worldwide.[1] Their proven performance, affordability and ease of use have made pMDIs a trusted mainstay for patients and healthcare systems alike, particularly in acute and rescue settings, where reliability and familiarity are essential.[2]

Over time, the platform has demonstrated an exceptional ability to evolve, adapting to regulatory changes and advancing scientific understanding. Today, healthcare systems are facing growing pressures to meet sustainability commitments, and turning their attention towards the environmental impact of drug delivery systems. For pMDIs, this focus is driving a transition towards lower-global warming potential (GWP) propellants, offering a meaningful opportunity to reduce their carbon footprint.[2]

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Figure 1: Low-GWP pMDIs support environmental progress while meeting patient needs.

While its implications are far-reaching, this shift is not about replacing a trusted platform but deliberately evolving it. Successfully navigating this transition requires innovation across formulation, device design and manufacturing, alongside a focus on de-risking development and preserving continuity of care. With the right expertise and integrated support, low-GWP pMDIs can deliver meaningful environmental progress while maintaining the standards that patients and healthcare systems depend on (Figure 1).

THE NEXT CHAPTER IN THE EVOLUTION OF pMDIs

While incremental regulatory milestones have guided pMDI innovation, the most significant shift came with the introduction of the Montreal Protocol. This landmark treaty aimed to phase out harmful greenhouse gases, including chlorofluorocarbons (CFCs), which were widely used in pMDIs at the time. This change catalysed the development of alternative propellants based on hydrofluoroalkanes (HFAs), demonstrating that the platform could evolve while maintaining continuity of care for patients worldwide.[1]

In 2016, the Montreal Protocol was amended to recognise that HFAs are themselves greenhouse gases, prompting the need for new low-GWP solutions.[2] At the same time, regulatory frameworks continue to advance, including a global movement towards restricting per- and polyfluoroalkyl substances on the horizon, shaping expectations around material selection.[3] These pressures are compressing development timelines and adding complexity to innovations, setting the stage for the next generation of pMDIs.

WHY pMDIs STILL MATTER IN GLOBAL RESPIRATORY CARE

Despite the growth of alternative inhalation technologies, pMDIs remain indispensable in global respiratory care. Their continued relevance is rooted in a combination of patient reliance, global accessibility enabled by large-scale manufacturing capacity, cost effectiveness and practical advantages that alternative technologies have yet to match at scale.[2]

For patients, familiarity and preference matter. pMDIs are deeply embedded in real-world disease management, particularly for rescue medications where confidence and ease of use are critical. This is especially true for paediatric and elderly populations, as well as for patients managing acute exacerbations.[2,4]

From a healthcare system perspective, pMDIs remain among the most cost-effective and scalable inhalation solutions available. They have global access, including in regions where alternative devices may be less practical due to cost, infrastructure or supply constraints.[2,4]

While innovation in inhalation therapy continues, replacement of a specific drug delivery technology is not always the optimal solution. For many therapies and patient populations, evolving the pMDI platform offers the most realistic and effective pathway to reducing the healthcare sector's CO_2 footprint, while ensuring both clinical continuity and patient access.[2]

LOW-GWP PROPELLANTS AS A CATALYST FOR INNOVATION

To advance the evolution of the pMDI platform, two next-generation low-GWP propellants, HFA152a and HFO1234ze, have emerged as viable solutions. These propellants offer a reduction in GWP of more than 90% compared with current propellants, supporting industry-wide emission reduction commitments.[2]

While low-GWP propellants enable meaningful reductions in environmental impact, they also introduce technical considerations that ripple across the pMDI system. Differences in vapour pressure, density and solvency between legacy propellants and low-GWP propellants influence multiple aspects of inhaler performance,[2,5,6] including:

- Formulation stability and excipient interactions, which can affect dose uniformity and shelf life
- Aerosol generation and spray characteristics, with potential implications for lung deposition and patient experience
- Extractables and leachables risk linked to device–material interactions, particularly at the level of the metering valve, elastomers and seals
- Manufacturing and filling requirements, including safe handling of flammable materials and ATEX considerations.

These changes make it clear that low-GWP reformulation is not as simple as substitution. Instead, it acts as a catalyst

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for innovation, prompting a reassessment of components that were originally designed around different propellant chemistries.

EVOLVING THE VALVE TO ENABLE THE NEXT GENERATION: ZEN30 FUTURITY®

At the centre of the pMDI system is the metering valve – the interface and engine between device, formulation and patient. Legacy valves were developed for the physicochemical properties of traditional HFAs, and relying on these designs for low-GWP propellants can increase development risk.

ZEN30 Futurity® represents a deliberate redesign of the metering valve, purpose-built to perform reliably with the new low-GWP propellants (Figure 2). Rather than adapting existing designs post hoc, the valve was engineered from the outset to address the challenges introduced by new propellant chemistries.

Figure 2: The ZEN30 Futurity® is Aptar Pharma's pMDI valve, designed and optimised for low-GWP formulations.

"DESIGNED WITH PATIENTS IN MIND, ZEN30 FUTURITY® PRESERVES FAMILIAR INHALER ARCHITECTURE AND DELIVERY CHARACTERISTICS."

Designed with patients in mind, ZEN30 Futurity® preserves the familiar architecture and delivery characteristics of pMDIs. This supports continuity of use by minimising changes in patient technique, reducing retraining needs and maintaining confidence in dose delivery. Additionally, carefully selected polymers and elastomers reduce the extractables and leachables risk, while robust moisture-barrier performance protects formulation stability, helping to safeguard not only formulation integrity but also patient safety in real-world environments.

DE-RISKING THE TRANSITION WITH CONFIDENCE AT EVERY STEP

For pharmaceutical companies, transitioning to low-GWP pMDIs introduces interconnected challenges across formulation, device design, manufacturing and regulation. Addressing these challenges in isolation can increase uncertainty and prolong development timelines. Instead, successful transitions rely on an integrated approach that manages risk across the entire pMDI system – not only for today's requirements but with an eye towards what comes next.

Aptar Pharma brings decades of pMDI expertise to support this transition, combining valve design leadership with deep formulation, analytical and regulatory capabilities. From the outset, ZEN30 Futurity® was developed to anticipate both current and emerging regulatory expectations, including from the European Chemical Agency, helping pharmaceutical partners to avoid short-term solutions that could require redesign or revalidation later on. This future-focused, de-risking approach provides greater design certainty as sustainability programmes move forwards.

By enabling formulation and device development to progress in parallel, Aptar Pharma helps reduce trial-and-error and provides earlier insight into how changes in propellant chemistry may affect performance. Advanced development tools, such as Nanopharm's (Cwmbran, Wales) SmartTrack™ platform, integrate *in vitro* testing, *in silico* and computational fluid dynamics modelling, and physiologically based pharmacokinetic simulations. These capabilities allow potential performance changes to be anticipated earlier in development, supporting more informed decision-making and helping to avoid late-stage surprises that could impact development timelines or the patient experience.

This integrated approach extends beyond development into regulatory readiness and supply continuity. Aptar Pharma provides robust documentation packages, including combination product support, Article 117 dossiers and EU Medical Device Regulation-aligned materials, helping pharmaceutical partners to navigate evolving regulatory expectations with greater confidence.

Additionally, in-house elastomer manufacturing and end-to-end supply chain control help to protect quality, timelines and patient access as products scale towards commercialisation.

Together, these capabilities enable pharmaceutical partners to move forwards with greater certainty, accelerating the path to market for low-GWP pMDIs while maintaining product performance and reliability, long-term compliance and patient confidence.

"APTAR PHARMA BRINGS DECADES OF pMDI EXPERTISE TO SUPPORT THIS TRANSITION, COMBINING VALVE DESIGN LEADERSHIP WITH DEEP FORMULATION, ANALYTICAL AND REGULATORY CAPABILITIES."

Figure 3: ZEN30 Futurity®, a proven pMDI platform, evolving for the next generation.

SCALING THE NEXT GENERATION RESPONSIBLY

As low-GWP pMDIs move from development to commercialisation, manufacturing readiness and supply chain resilience become critical. Aptar Pharma addresses these considerations early. ATEX-rated R&D facilities enable safe mixing and filling of formulations that use flammable low-GWP propellants, supporting an accelerated and smooth progression from development to scale-up.

Supply chain resilience is reinforced through end-to-end control, from component manufacturing to global supply. This approach helps to ensure that the evolution of pMDIs remains practical, allowing global availability of essential respiratory therapies while minimising the risk of disruption (Figure 3).

A PROVEN PLATFORM, READY FOR ITS NEXT GENERATION

Each major shift in pMDI history has shown continuity through innovation, responding to new regulatory and sustainability realities without compromising performance or patient confidence. Rather than disrupting a trusted delivery platform, the transition to low-GWP propellants requires careful redesign and forward-looking materials.

Through the purpose-built design of the ZEN30 Futurity®, combined with development, regulatory and manufacturing expertise, Aptar Pharma enables pharmaceutical partners to move forwards with clarity and confidence. By preserving familiar pMDI architecture and consistent performance, the next generation of low-GWP inhalers is positioned to support patient confidence and healthcare system resilience, while contributing meaningfully to reduced environmental impact.

The pMDI platform has evolved before – and with the right expertise and foresight, it is ready to do so again.

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The Future starts now

LOW GWP

ZEN30 Futurity™: A valve designed for a seamless transition to low GWP pMDIs, ensuring reliable, robust performance

The shift to low GWP pMDIs does not have to be complex. Aptar Pharma's ZEN30 Futurity™ valve for pMDIs supports both HFA 152a and HFO 1234ze propellants, simplifying formulation transition while maintaining consistent delivery.

Aptar Pharma's **in-house elastomer production and valve gasket manufacturing** enhances supply chain security and ensures full and transparent change control. Our SmartTrack™ modeling platform helps you demonstrate the bioequivalence of inhaled products to reference drugs without conducting a comparative clinical endpoint (CCEP) study.

This combination of supply chain control, advanced bioequivalence validation, and **regulatory expertise and U.S. FDA understanding** helps to derisk your product submission and approval process.

Backed by over **35 years of expertise in pMDI valve development, manufacturing, and performance**, our ZEN30 Futurity™ helps you derisk your transition and accelerate development of your next-generation pMDI.

Discover what your future holds with ZEN30 Futurity™

- **Engineered for a smooth transition to low GWP propellants**
- **One valve, two propellants**
- **In-house elastomer production**
- **Navigate regulatory complexity with confidence.**

To start your next generation pMDI project, contact Chris Baron, Director of Business Development Pulmonary Category, at: chris.baron@aptar.com or +33 6 3095 5331.

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GWP, global warming potential; **HFA**, hydrofluoroalkane; **HFO**, hydrofluoroolefin; **pMDI**, pressurized metered dose inhaler.