SCALING LOW-CARBON pMDI PRODUCTION WITHOUT DISRUPTING PATIENT ACCESS

Simon Gardner at **Bespak** looks at how the pharmaceutical industry is scaling up production of low-carbon pressurised metered dose inhalers to cut emissions without disrupting patient care. The article considers the challenges faced by the industry, as well as the role of CDMOs in creating sustainable, scalable solutions.

Commitment to protecting the environment is transforming many industries, and pharma is no exception. For the inhalation sector, this has resulted in increased scrutiny of the carbon footprint associated with inhalers and a drive for change – particularly when it comes to pressurised metered dose inhalers (pMDIs). These devices are designed with a propellant gas that acts as a carrier for drug particles, constituting approximately 90% of drug formulations. Current high global warming potential (GWP) propellants are the main source of pMDI carbon emissions. Next-generation low-GWP propellants are now available, but switching to low-carbon pMDI production at scale can be complex.

As a specialist inhalation CDMO, Bespak is working to streamline the development and scale-up of low-carbon pMDI production without disrupting patient access to vital therapeutics.

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MARKET CHALLENGES

Many patients rely on pMDIs, which represent an estimated 71% of all inhalers used in Europe and 87% in North America.[1] Given that pMDIs make up the majority of respiratory drug delivery devices, transitioning to new propellants that reduce their carbon footprint is a massive project with many moving parts. Two next-generation propellants have proven feasibility and a low GWP: HFA-152a and HFO-1234ze. With these alternatives ready to be adopted, the challenge for pMDI manufacturers now is not how to decarbonise, but how to do it quickly at scale without risking supply shortages for millions of patients.

To this end, there is a need for manufacturing facilities that are compatible with the new propellants. For example, HFA-152a is flammable, which together with other controls, necessitates ATEX-certified facilities to ensure safety. Handling flammable aerosols at scale is not an issue in and of itself – mass-produced consumer products using flammable propellants can be found in the cleaning and personal care aisles of any supermarket. However, this change marks a new era for pharma and requires clear guidance to ensure safe handling during manufacturing, storage and transportation.

Additionally, pMDI device components, such as actuators and valves, must be optimised to be compatible with the chemical and physical properties of next-generation low-GWP propellants. These too must be made available across the entire industry from development to commercial-scale projects.

The landscape is further complicated by evolving regulations, which has resulted in some pharma companies being hesitant to take the plunge. Nonetheless, the direction is clear – it is not a question of whether industry will transition, but how quickly and smoothly that transition to low-carbon pMDIs will take place and how companies can work together to effectively drive change.

REGULATORY AND SUPPLY CHAIN DRIVERS

In the EU, the F-gas Regulation of 2024 has been published, which lays out the required phase-down of currently used high GWP hydrofluorocarbon (HFC) propellants starting from 2027 and a total phase-out by 2050.[2] Importantly, the exemption for HFCs used in pMDIs under the previous 2014 EU F-gas Regulation has been removed. HFCs are being phased down in the UK by 79% by 2030 compared with average use between 2009 and 2012 under the Fluorinated Greenhouse Gases Regulations 2015. While pMDIs are currently exempt from this, the guidance may change with the next revision, anticipated during 2026.

Meanwhile, in the US, the Environmental Protection Agency is implementing a phase-down of HFCs under the AIM Act. While an application-specific allowance was renewed for pMDIs over 2025–2030, as lower GWP alternatives gain momentum, it will become imperative to transition before legislation mandates it.[3]

One reason to get ahead of regulation changes is the progressively diminishing supply of currently used propellants. This is occurring because propellant supply feeds a broad industrial base beyond pharma. In fact, pharmaceutical applications of propellants are just the tip of the iceberg, accounting for less than 10% of propellant use, while over 90% of propellants are used for other industry applications, such as refrigerants, air conditioning in automobiles and firefighting.[4] The transition to next-generation alternatives is more advanced in these industries. For instance, the use of the traditional propellant HFA-134a in new EU cars was banned in favour of next-generation propellants in 2011. There have also been HFA-134a industrial-grade plant closures in Europe, and next-generation propellant alternatives to the traditional propellant HFA-227ea have been developed for firefighting.

In light of changing regulations, supply chain concerns, corporate social responsibility goals and an opportunity to gain a corner in the market, major pharmaceutical companies are already forging ahead with next-generation propellants. AstraZeneca has recently obtained regulatory approval for the first inhaled respiratory therapy delivered with a low-carbon pMDI in the UK: Trixeo Aerosphere.[5]

THE ROLE OF CDMOs IN SCALING PRODUCTION

CDMOs play a vital role in expanding the production capacity for low-carbon pMDIs across the pharmaceutical industry. Bespak, for instance, has invested heavily in its manufacturing capabilities for pMDIs using next-generation propellants, embarking on an expansion project to enable clinical and commercial manufacture of low-carbon pMDIs incorporating either HFO-1234ze or HFA-152a. This investment addresses a major market gap and will support both large pharma companies – who want to move fast and take major market positions – and small-to-mid-size pharma companies without the resources to invest in the updated manufacturing equipment needed for both new propellants.

Additionally, Bespak has redesigned pMDI components, including its range of valves to ensure compatibility with low-GWP propellants. A new hybrid valve developed by Bespak builds on the highly successful BK357 pMDI valve, incorporating materials suitable for HFA-152a and HFO-1234ze – specifically ethylene propylene diene monomer seats and a bromobutyl neck gasket in contact with a polybutylene terephthalate core. These changes are essential to reduce propellant leakage from the inhaler,

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presenting a robust barrier internally and externally to moisture ingression. The first low-carbon pMDI product using a Bespak valve has received regulatory approval and is expected to be on market before the end of 2025.

Bespak has also investigated the effect of actuator design on low-carbon pMDIs. One study investigating the suspension of fluticasone propionate in HFA-152a and HFO-1234ze revealed that the spray orifice diameter of the actuator affected the inhaled droplet and average particle size.

These optimised designs are crucial for widespread adoption of next-generation propellants, ensuring the quality and reliability of pMDIs are maintained.

BUILDING PARTNERSHIPS TO ACCELERATE THE TRANSITION

CDMOs can help to address a major market gap by investing in low-carbon pMDI production, but a full transition necessitates collaborations across the value chain. Beyond its own investment in manufacturing infrastructure, Bespak has forged partnerships with major industry players to ensure all the pieces are in place for the green transition. This includes collaborations with Orbia Fluor & Energy Materials (Boston, MA, US), suppliers of the next-generation propellant HFA-152a and Honeywell (Charlotte, NC, US) for HFO-1234ze supply. At the same time, Bespak is working with H&T Presspart (Blackburn, UK) to facilitate pMDI pilot-scale filling capabilities, OzUK (Chippenham, UK) on the feasibility of pMDI formulations, DH Industries (Basildon, UK) on the supply of its advanced Pamasol pMDI production lines, and the Medicines Evaluations Unit (Manchester, UK) to streamline clinical trials for low-carbon pMDIs. Additionally, Bespak has seats on the board of the International Pharmaceutical Aerosol Consortium (IPAC) and the International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS), allowing the company to both influence and communicate the latest regulatory changes that impact low-carbon pMDIs.

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These collaborations have created a cluster of excellence in pMDI development and manufacturing in the UK – particularly in the Northwest of England. This helps to shorten and strengthen the pMDI supply chain, as well as providing the opportunity to reduce the carbon emissions that arise from the transportation of goods between sites.

BEYOND LOW-CARBON CAPABILITIES

Moving away from high-GWP propellants has taken the spotlight when it comes to reducing the inhalation industry's carbon footprint. However, total environmental impact goes beyond the GWP of propellants. A truly low-impact device also depends on the energy, materials, processes and ecosystems connected with its production.

As low-carbon pMDI efforts are scaled up, a holistic approach that considers sustainability across the entire value chain is needed to meet ambitious emission reduction targets, such as those set out by the Paris Agreement. Acknowledging this, Bespak is working to ensure environmental, social, and governance principles are embedded across every level of its business operations.

From a product perspective, Bespak is conducting lifecycle assessments to find new ways to reduce greenhouse gas emissions and resource consumption. Additionally, it is seeking to incorporate renewable electricity, recycled materials and waste reduction wherever possible. Across its two manufacturing sites in the UK, Holmes Chapel and King's Lynn, 97.5% of the electricity is obtained from renewable sources, with 2,300 solar panels installed. Bespak recycles over 65% of waste at Holmes Chapel and over 86% of waste at King's Lynn. Through its partnership with Collecteco (Bristol, UK), Bespak donated decommissioned office furniture and equipment to local charities, avoiding ~26,857 kg CO_2e and diverting ~8,193 kg of waste.

> "TO AVOID PLASTIC WASTE, BESPAK IS ENGAGING ITS CUSTOMERS AND DISTRIBUTION PARTNERS IN CIRCULAR ECONOMY PARTNERSHIPS."

To avoid plastic waste, meanwhile, Bespak is engaging its customers and distribution partners in circular economy partnerships. It is also exploring a mechanical recycling process that will create product delivery trays with up to 80% recycled polymers.

Biodiversity and local environmental health are also emerging factors in pharma sustainability strategies. Bespak is working to understand and improve its impact on local ecosystems, especially the green space surrounding its Holmes Chapel headquarters. On-site biodiversity assessments have been conducted by Bespak at both its sites and these will be used to develop Biodiversity Management Plans. Applying the World Wide Fund for Nature Biodiversity Risk Filter will further help Bespak to identify biodiversity priorities and ensure efforts are targeted towards these.

These initiatives are crucial to build a sustainable foundation for low-carbon pMDIs that will support the inhalation industry in achieving wider environmental goals.

A PARTNER FOR THE FUTURE

Increased environmental awareness, evolving regulations and a diminishing supply chain for currently used HFC propellants have combined to create demand for low-carbon pMDIs. Scaling up production to meet this demand is no

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mean feat, and getting ahead of the curve is crucial to ensure the infrastructure is in place to transition smoothly to low-carbon pMDIs without disrupting the supply of essential medicines. By investing in a strong industry network, strategic manufacturing expansions and low-carbon pMDI expertise – and by embedding sustainability across its operations – Bespak is paving the way for a greener tomorrow.

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Simon Gardner

Simon Gardner, Business Development Director at Bespak, is a chemical engineer by training. He has over 25 years of experience in the global pMDI industry, including process engineering, plant management and business management roles in the medical propellants sector. He is a subject matter expert in propellant market dynamics and environmental regulation, and now focuses on supporting Bespak's customers to transition to low-GWP propellants. Mr Gardner is also an IPAC Board Member.

T: +44 1477 357112
E: enquiries@bespak.com

Bespak Ltd
London Road, Holmes Chapel, Crewe, Cheshire, CW4 8BE, United Kingdom
www.bespak.com

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