# Solstice Advanced Materials on Powering the Global Shift to Low-GWP Inhaler Propellants

**Solstice Advanced Materials outlines its perspective on the transition to low-GWP propellants in an interview with International Pharmaceutical Industry Journal, focusing on regulatory change, manufacturing challenges, and sustainability in respiratory medicine.**

**How would you describe Solstice Advanced Materials' role in the global transition toward low-GWP potential propellants for inhalers?**

Solstice's role is to help the pharmaceutical industry deliver on two priorities simultaneously. First, continued patient access to critical medications – the roughly 300 million people worldwide with asthma and Chronic Obstructive Pulmonary Disease (COPD) who depend on a pressurised metered-dose inhaler (pMDI) need that medication to remain available and effective.[1] Second, environmental progress – pMDIs have historically been a significant contributor to healthcare's carbon footprint due to the use of high-GWP propellants HFA-134a and HFA-227ea.[2]

Solstice's medical propellant HFO-1234ze(E), GMP is the world's first low-GWP propellant in pMDIs approved for patient use in three countries and a region – UK, EU, AU and NZ.[3,4,5,6] It has a GWP 99% less than hydrofluoroalkanes (HFAs). But our role isn't simply to supply a propellant. The pharmaceutical companies reformulating today are taking on complex, multi-year programmes that touch formulation, valve compatibility, manufacturing readiness, and regulatory submission. Much of the technical ground-work for the transition is already in place, and we are now approaching a period where regulatory clarity is expected to drive a significant wave of product transitions. Our focus is on supporting early adopters in the transition with consistent supply, technical support, and product samples, while also planning for the broader industry adoption of low-GWP propellants.

**Although there are other options such as dry powder inhalers (DPIs), why do pMDIs remain an essential part of respiratory care for many patients?**

DPIs require patients to generate a strong, deep inhalation to draw medication into the lungs, and that is a physical capability many patients simply don't have. Young children, elderly patients, people in the acute phase of an asthma attack, and those with advanced COPD often cannot inhale forcefully enough for a DPI to deliver an effective dose.[7]

In rescue and emergency situations, when a patient needs medication quickly and reliably, the pMDI remains the primary go-to solution. So, while substitution to DPIs is part of the conversation, it is not a universal solution. For a significant share of the roughly 300 million patients worldwide who live with asthma or severe COPD, the pMDI is irreplaceable.

Additionally, the sustainability gap between DPIs and pMDIs is rapidly narrowing. With the introduction of Next Generation Propellants (NGPs), pMDIs are becoming capable of potentially delivering a lower carbon footprint than even DPIs (see Figure 1), while still maintaining the clinical advantages that many patients depend on.

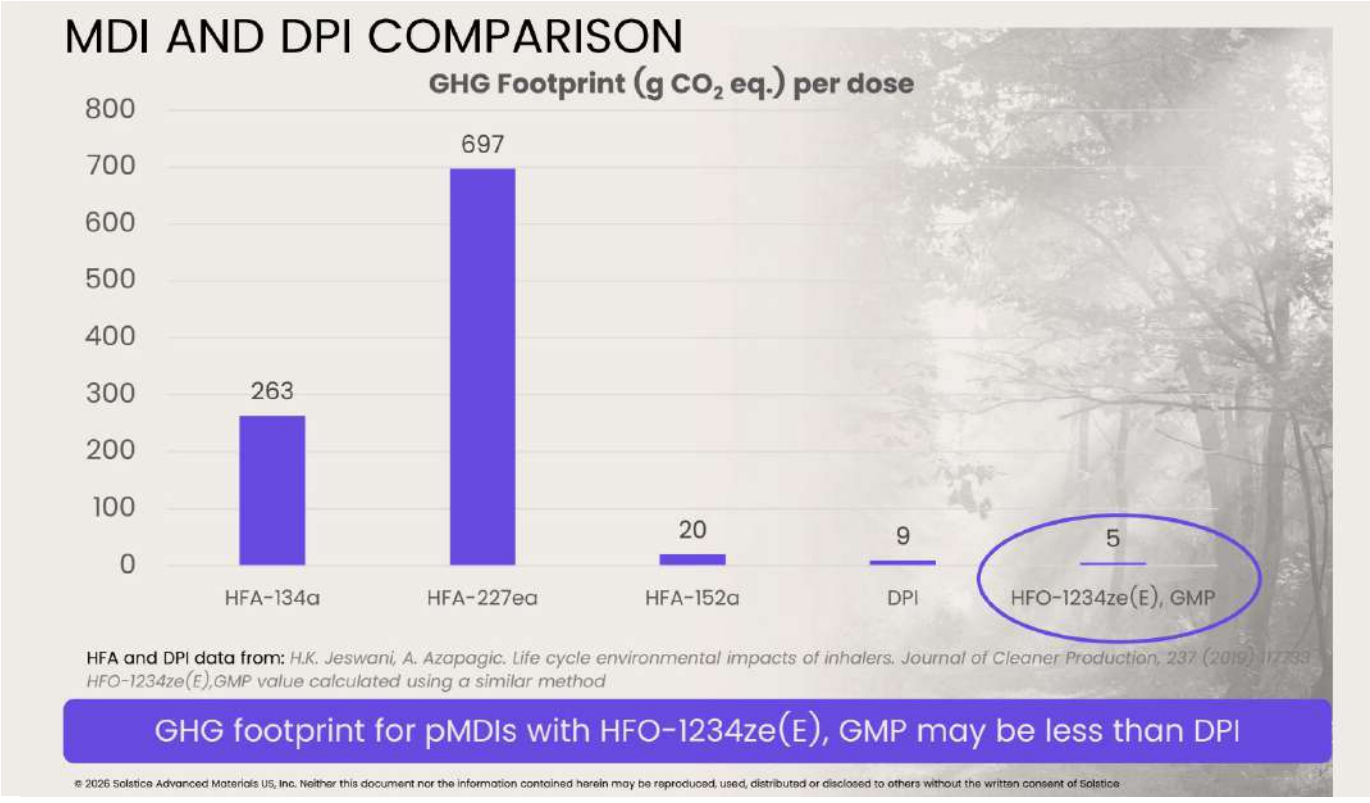


*Figure 1: Greenhouse Gas (GHG) footprint comparison of DPIs to pMDIs with HFA and HFO-1234ze(E), GMP propellants*

**With regulations tightening around legacy propellants such as HFA-134a and HFA-227ea, what are the main implications for manufacturers as they prepare for compliance?**

The Kigali Amendment to the Montreal Protocol established the international phasedown trajectory for hydrofluorocarbons (HFCs), and that is now being implemented through legislative and regulatory frameworks such as the EU F-Gas Regulation, the UK's F-Gas Regulation and the U.S. American Innovation and Manufacturing (AIM) Act.

Manufacturers still using HFA-134a or HFA-227ea may experience shrinking supply, rising cost, and a closing window to complete a pMDI reformulation.

In the United States specifically, the FDA's 505(b)(2) regulatory pathway, which allows applicants to reference existing safety data when bridging an approved product to a new formulation instead of having to generate new data, is emerging as the preferred route for many which will potentially accelerate the industry transition.

**Beyond regulation, what are the main practical and commercial challenges being seen across the industry during the transition to low-GWP propellants?**

The biggest practical challenge is the sheer complexity of an inhaler reformulation programme. At Solstice, we are working with customers to reduce the complexity and timeline of a transition to low-GWP propellant. HFO-1234ze(E), GMP itself is a non-flammable near-drop-in replacement which helps speed up the conversion process in two ways. First manufacturing equipment does not need to be modified to meet ATEX certifications.[9] Second, Solstice has completed numerous compatibility studies with various APIs demonstrating near-drop-in compatibility with existing pMDI formulations.[10]

Beyond complexity, there are two additional challenges that stand out. The first is supplier selection — manufacturers need to align early with the right propellant supplier, the right CDMO, and the right valve innovator, because the technical interdependencies are too high to navigate alone. The second is a strategic question we increasingly hear in conversations with customers: do you wait for the first FDA approvals to fully de-risk your decision, or do you move now and build first-mover advantage in your therapy area?

This is becoming a defining inflection point for the industry: waiting may reduce perceived risk in the short term, but it also increases the likelihood of being behind.

**What are the key attributes that make HFO-1234ze(E), GMP well suited for next-generation sustainable pMDIs?**

The environmental case is the headline: HFO-1234ze(E), GMP has an AR6 GWP of 1.37, which represents a greater than 99 percent reduction compared with HFA-134a.[11,12] It is non-ozone-depleting and, importantly, non-flammable – which dramatically simplifies handling, manufacturing, and storage.

On the safety side, we have an established preclinical toxicology profile and clinical data supporting its use in pMDIs. As Nilesh Wagh, our Global Lead for Product Stewardship and Regulatory, often points out: "Given that HFO-1234ze(E), GMP is proven to be safe for pMDIs , the conversation in the regulatory community has quickly shifted to how to get approved products with low-GWP propellant to market as quickly as possible".[13]

In summary, HFO-1234ze(E), GMP combines an established regulatory profile, non-flammability, and near drop-in compatibility which enables companies to manage the technical, regulatory, and capital aspects of pMDI reformulation under a tight timeline.

**How significant is the ability to use existing manufacturing infrastructure for pharmaceutical companies in practical terms?**

Minimising required capital investment is one of the most underappreciated advantages of HFO-1234ze(E), GMP. For a pharmaceutical company reformulating a metered dosed inhaler, the propellant decision cascades into everything. HFO-1234ze(E), GMP functions as a near drop-in replacement for HFA-134a and HFA-227ea, which means manufacturers can use their existing pMDI filling and production infrastructure without major modifications. In addition, HFO-1234ze(E), GMP is non-flammable so ATEX certification is not required. There is a published case study by Recipharm, now Bespak, that expertly breaks this down in practice.[14]

Alternative propellants under development may be flammable, which means manufacturers face the choice of retrofitting existing lines with explosion-proof equipment or building new facilities altogether.

**Solstice Advanced Materials is working with companies across innovator pharma, CDMOs and generics. What does that tell you about the current stage of the industry's transition?**

It tells you that the transition is no longer hypothetical – it is broad, it is underway, and it now spans the full pharmaceutical ecosystem. Companies across the industry from innovator pharma to CDMOs and CROs have already announced that they are

working with Solstice HFO-1234ze(E), HFA and HFO-1234ze(E), GMP propellants, the next generation propellant.

We work with companies of very different sizes and business models because we believe sustainable respiratory care benefits from a wide range of options reaching patients. It also reflects our focus on engaging early, before final propellant and development decisions are locked-in, so that we can help shape the most efficient and scalable path forward.

**With regulatory approvals expected to accelerate later this decade, what is Solstice doing to ensure propellant capacity keeps pace with demand?**

The current understanding across the industry is that there will likely be a large cluster of approvals around the same time. To put the scale in context: in the UK alone, around 42 million pMDIs are prescribed every year with global volumes many times that figure.[15] Many companies have publicly committed to transition to low-GWP propellants to support their sustainability commitments. The next step is to actually make it happen.

When approvals start landing in close sequence across that scale of demand, the propellant supply chain will need to be ready. Solstice is ready today with commercial supply.

**Europe is currently ahead in adopting sustainable pMDIs. What factors will influence the pace of adoption in other regions?**

The EU established a clear transition pathway earlier than other regions, and that gave manufacturers the confidence to commit to reformulation programmes. That is why we are seeing the first approved low-GWP inhaler product on the European market today.

In addition to regulatory clarity, much of the active development work and technical capability in inhalation continues to be concentrated in Europe and the UK, which has further accelerated progress in those regions.

In the United States, with the quota relief for HFA under the US AIM Act potentially expiring in 2030, we expect manufacturers to evaluate the 505(b)(2) regulatory pathway, which allows applicants to reference existing safety data when bridging an approved product to a new formulation.

Beyond Europe and the US, regulatory filings are already progressing in markets like China, and we expect other geographies will follow as their regulatory frameworks mature. Manufacturers planning for global launch are increasingly thinking about a sequenced approach: Europe first, then the US, then the rest of the world.

**Looking ahead, what would a successful transition to sustainable pMDIs mean for patients, manufacturers and the wider healthcare sector?**

For the roughly 300 million patients who depend on pMDIs worldwide, it means continued, uninterrupted access to a device they rely on every day – without compromise to clinical performance. For manufacturers, it means meeting regulatory obligations and sustainability commitments simultaneously, without rebuilding their supply chains or capital infrastructure. For the wider healthcare sector, it removes a significant source of high-GWP emissions from one of the most prevalent chronic disease categories in the world.

That last point matters strategically. Healthcare's own carbon footprint is increasingly under scrutiny – in the UK, the NHS has reported that pMDI inhalers account for approximately 3% of its total carbon footprint, making respiratory care one of the most visible decarbonisation in the system.[16,17] A successful pMDI transition therefore sets a precedent for how the industry can decarbonise without disadvantaging the patients it serves.

Beyond decarbonisation, this transition also creates a foundation for continued innovation within respiratory care – from improved formulation approaches and more precise dose control to the potential expansion into more complex therapies over time.

That, ultimately, is what we are working toward at Solstice – and why we continue to innovate.

For more information:
https://go.solstice.com/mdi_2026

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