Expert Roundtable:
Navigating the Next Phase of Low Carbon pMDI Development

In May 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) approved the world's first low carbon pressurised Metered Dose Inhaler (pMDI). For an industry that had been discussing the green transition for the better part of a decade, it was a meaningful moment. It was also just a start.

With the first approval in hand, attention has turned to what comes next. At Bespak, we are a specialist inhalation Contract Development and Manufacturing Organisation (CDMO) focused exclusively on inhaled and nasal drug delivery. In this expert roundtable, five of our specialists examine the formulation, manufacturing, hardware and sustainability challenges that stand between first approval and full industry transition.

Meet the panel

- Adam Kite, Commercial Director.
- Ross Errington, Head of Drug Product Development.
- Nick Atkinson, Portfolio Manager for Strategic Engineering Projects.
- Tony Mallett, Platform Development Group Manager.
- Benedicta A. Bakpa, Head of ESG.

THE VIEW FROM THE PANEL

The industry has been talking about the low carbon pMDI transition for years. From your point of view, what has changed, and what has taken longer than expected?

Adam Kite: Market forces are actively reshaping the competitive landscape – tightening HFC supply and rising costs make the direction clear. What has taken longer is commitment from companies at the mid-market level, despite major players already approaching approval.

Ross Errington: It has taken longer than expected for companies to decide. Propellant cost and uncertainty around per- and polyfluoroalkyl substances (PFAS) regulation remain top concerns even as some of the biggest players are already at or near market with their first low carbon products.

Nick Atkinson: Talk has given way to action. The MHRA's approval of the first low carbon pMDI in May 2025 is the industry's first real proof point. That further approvals haven't followed quickly is its own indicator of the complexity involved.

Tony Mallett: The market is definitively starting to shift. What has taken longer is the volume of new filings that still take the HFA-134a bridging route first, which adds time before a full transition is complete.

Benedicta A. Bakpa: The level of commitment has changed: investment has moved from pilots into real programmes. The transition is taking longer because it is a system change, not a component swap – customers increasingly want to understand the full product carbon footprint, not just whether a low GWP propellant has been adopted.

How can the industry ensure that the push for low carbon inhalers does not come at the expense of patient access, safety, or therapeutic efficacy?

AK: Patient access cannot be a casualty of the transition. Low GWP propellant supply chains need to be robust and diversified – any disruption is a clinical risk, not just a commercial one. The commercial case and the obligation to patients point the same way, but only if infrastructure is built early enough.

RE: We must continue to lobby on behalf of patients. The regulatory pathway must be proportionate, and early engagement with health authorities – with a clear narrative around patient equivalence – is critical.

NA: Sharing knowledge about the equipment and facility changes required for low carbon propellants is essential. The complexities of handling flammable propellants are real but manageable – if poorly understood across the industry, they risk becoming an unnecessary barrier to a transition that ultimately serves patients.

TM: Low carbon pMDIs are developed with the same rigour as any new product. Therapeutic equivalence must be demonstrated, quality requirements are unchanged, and safety is always the first consideration.

BB: At Bespak, Environmental, Social and Governance (ESG) performance operates within the same constraints as safety, quality, and supply. Supply risk is patient risk — dual sourcing and material continuity sit alongside emissions reduction, not beneath it. We track ESG performance alongside quality and manufacturing metrics, not separately.

Commercial Landscape and Propellant Strategy
With Adam Kite, Commercial Director

In some ways, market forces seem to be moving faster than regulation. How urgent is the pressure to transition right now, and what are the risks for companies that haven't yet committed?

AK: The competitive dynamics are stark. Early movers are securing access to development expertise, manufacturing capacity, and supply chain partnerships that will become increasingly constrained as demand accelerates. Companies that delay risk not just higher costs but a structural loss of strategic flexibility. The revised EU F-gas Regulation tightens quotas for high-GWP propellants, and with long lead times for compliant equipment and limited specialist manufacturing capacity available, the ability to react quickly diminishes with every year that passes without commitment.

The regulatory direction is clear, but there are still big unknowns, especially around future regulations surrounding propellants. How should companies be making strategic decisions around propellant choice in that context?

AK: Propellant selection is a genuinely complex, multi-factorial decision. Significant uncertainties persist – including potential PFAS restrictions on HFO-1234ze and the pace at which those questions will be resolved. Active engagement with the International Pharmaceutical Aerosol Consortium (IPAC) and International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS) provides access to real-time regulatory intelligence. Equally important is close alignment with CDMOs that have practical experience supporting these transitions – their insight is invaluable in managing both compliance risk and the strategic choice between HFA-152a and HFO-1234ze.

Formulation Science and Development Realities
With Ross Errington, Head of Drug Product Development

What are the biggest formulation challenges specific to the new low GWP propellants, and how does this transition compare to what the industry faced during the CFC-to-HFA shift?

RE: The technical path should be more tractable than the CFC-to-HFA transition – the required changes are already well-characterised. The bigger challenge is often internal. There is a tendency to apply a 'change nothing' approach until a formulation failure makes change unavoidable, and in many cases, it is senior management, rather than technical teams, who are the blocker. That instinct misses a real opportunity: the transition is a chance to improve products and reduce costs. Advanced modelling tools can significantly reduce physical iterations, and they become particularly important where patent activity limits the most straightforward routes to formulation stability.

The clinical and regulatory pathway for these new products is still being defined. What does that mean for development timelines in practice, and where do programmes most commonly underestimate what is required?

RE: The central uncertainty is what clinical data will be required and what *in vitro* bioequivalence (IVBE) evidence health authorities will accept. Differences of opinion can arise both within companies and between regulators, meaning the amount of testing required is frequently underestimated. In the worst cases, unanticipated clinical trials can add one to two years to a programme. Early engagement with health authorities – and a clear narrative demonstrating patient equivalence – is the most effective way to avoid that scenario.

Manufacturing Infrastructure and Scale-Up
With Nick Atkinson, Portfolio Manager for Strategic Engineering Projects

HFA-152a is flammable, which represents a genuine operational shift for pharma manufacturing. What does getting a site ready for this actually involve – and is the industry approaching it the right way?

NA: There is a common assumption that handling flammable propellants requires only ATEX-rated equipment – that is, equipment that cannot generate an ignition source. In reality it goes much further. Skills, training, culture, and ways of working must change across the whole manufacturing organisation: supply chain, production, labs, and development. Something as specific as who is permitted to carry out maintenance work – limiting it to those with the right ATEX training – is the kind of change that often gets underestimated. Beyond a certain inventory threshold, Control of Major Accident Hazards (COMAH) and Seveso regulations must also be addressed, and these can impose significant constraints on sites with inadequate separation distances from neighbouring properties.

Manufacturing capacity for low carbon pMDIs is limited across the industry. How real is the risk of a bottleneck, and what should companies be doing now rather than waiting for regulatory deadlines to force the issue?

NA: The risk is very real. Existing filling equipment is unlikely to be suitable for flammable propellants, and equipment purpose-built for this is constrained across the industry. Companies that wait for regulatory deadlines will find themselves competing for limited capacity at precisely the moment demand peaks. Partnering early with a CDMO already investing in this infrastructure is the most practical way to ensure access to the capability that will be needed.

Valve Hardware and Device-Level Carbon Reduction
With Tony Mallett, Platform Development Group Manager

Adapting the BK357 valve for low GWP propellants is not a straightforward swap. What are the key technical decisions involved, and how do you validate that a new configuration performs as well as what it replaces?

TM: Low GWP propellants introduce material compatibility challenges with implications across the supply chain. We use physical test data and simulation to accelerate development, assessing device geometry changes virtually before committing to physical build. All functionality requirements are driven from the same specification as the original product, though depending on formulation route, shot weight adjustments may be needed. Fill and finish brings significant equipment investment – particularly where HFA-152a flammability must be managed. Final confirmation comes through Design Verification at sub-assembly level and Product Validation at system level.

Beyond switching propellants, where are the biggest opportunities to cut the carbon footprint through device design?

TM: Our Life Cycle Assessment (LCA) of the BK357 valve identified the aluminium ferrule as the most significant carbon hotspot – in both production and the finished product. Candidate replacement options are currently under test with positive early

results. Simulation enables redesign of other functional areas, delivering material reduction and process changes that each carry carbon benefits. For all New Product Introduction (NPI) programmes, LCA reviews are conducted at every development stage, keeping carbon footprint central to design decisions from the outset.

ESG Strategy and Accountability
With Benedicta A. Bakpa, Head of ESG

The propellant gets most of the attention, but it's only part of the story. What does a truly sustainable pMDI look like — and where are the next significant levers beyond propellant choice?

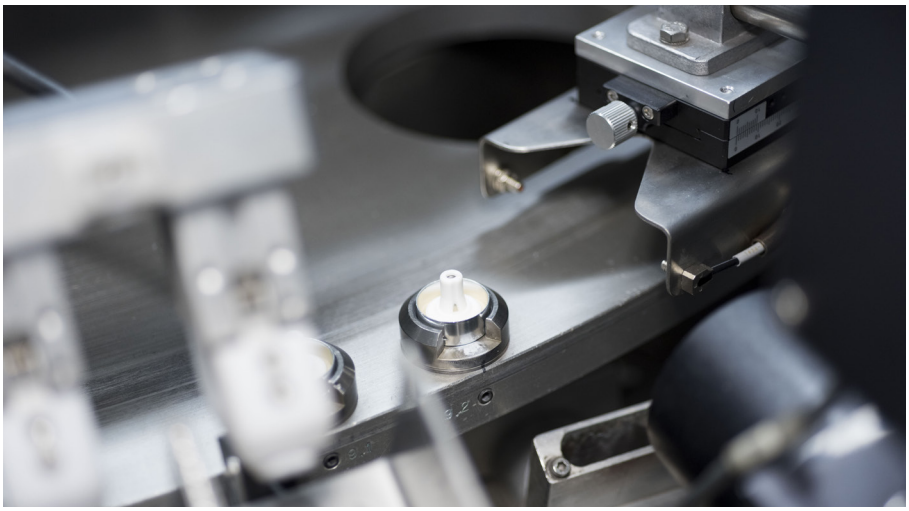
BB: For a pMDI to be genuinely sustainable, it must be optimised across the full product lifecycle. Key decarbonisation levers include transitioning to lower-GWP propellants; improving operational efficiency and increasing renewable electricity sourcing to reduce Scope 1 and 2 emissions; lowering Scope 3 emissions through material selection, supplier engagement and logistics optimisation; and advancing device design to reduce overall lifecycle impact. This requires sustainability to be embedded in every New Product Introduction (NPI) programme. Further opportunities exist in packaging design and warehouse storage, including revised pallet configurations to reduce logistics-related emissions. Dose efficiency also matters: improved product performance reduces lifetime emissions per patient. End-of-life recovery of residual propellants remains an industry-wide challenge that requires greater collaboration across manufacturers, healthcare providers, waste management partners and regulators. While Bespak does not directly control end-of-life treatment, we recognise the role we can play in supporting industry-wide solutions.

ESG reporting in pharma is under increasing scrutiny. How does the industry ensure that sustainability commitments translate into meaningful, measurable action rather than just good intentions?

BB: At Bespak we approach this in structured phases. We begin by defining a credible baseline using Greenhouse Gas (GHG) Protocol methodology, committing to the Science Based Targets initiative (SBTi), and setting validated near- and long-term targets. We then make investment, procurement, and product design decisions with ESG impact in mind, while driving operational improvements across manufacturing, quality systems and supply chain operations, with progress measured through performance management tools. We also focus on transparent reporting of year-on-year progress against GHG targets, highlighting gaps and corrective actions, and assigning accountability at executive level with delivery linked to performance management.

Most pharma companies are working through or have completed these phases. The ones making real progress treat ESG not as a reporting exercise, but as something embedded in how the business makes decisions every day.

Looking Ahead
The first approval settled one question: the transition is technically achievable. What it leaves open is whether the rest of the industry will move quickly enough. Supply of existing propellants is already contracting ahead of any pharmaceutical mandate, regulatory deadlines are fixed, and the work still ahead demands significant investment of time and resource. At Bespak, we have been building that capability since 2018. For organisations earlier in the process, decisions made now will determine readiness when it matters.



Adam Kite

Commercial Director at Bespak with over five years' experience in medical device commercial management, supporting product development, commercialisation and lifecycle management to help customers achieve market success.

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