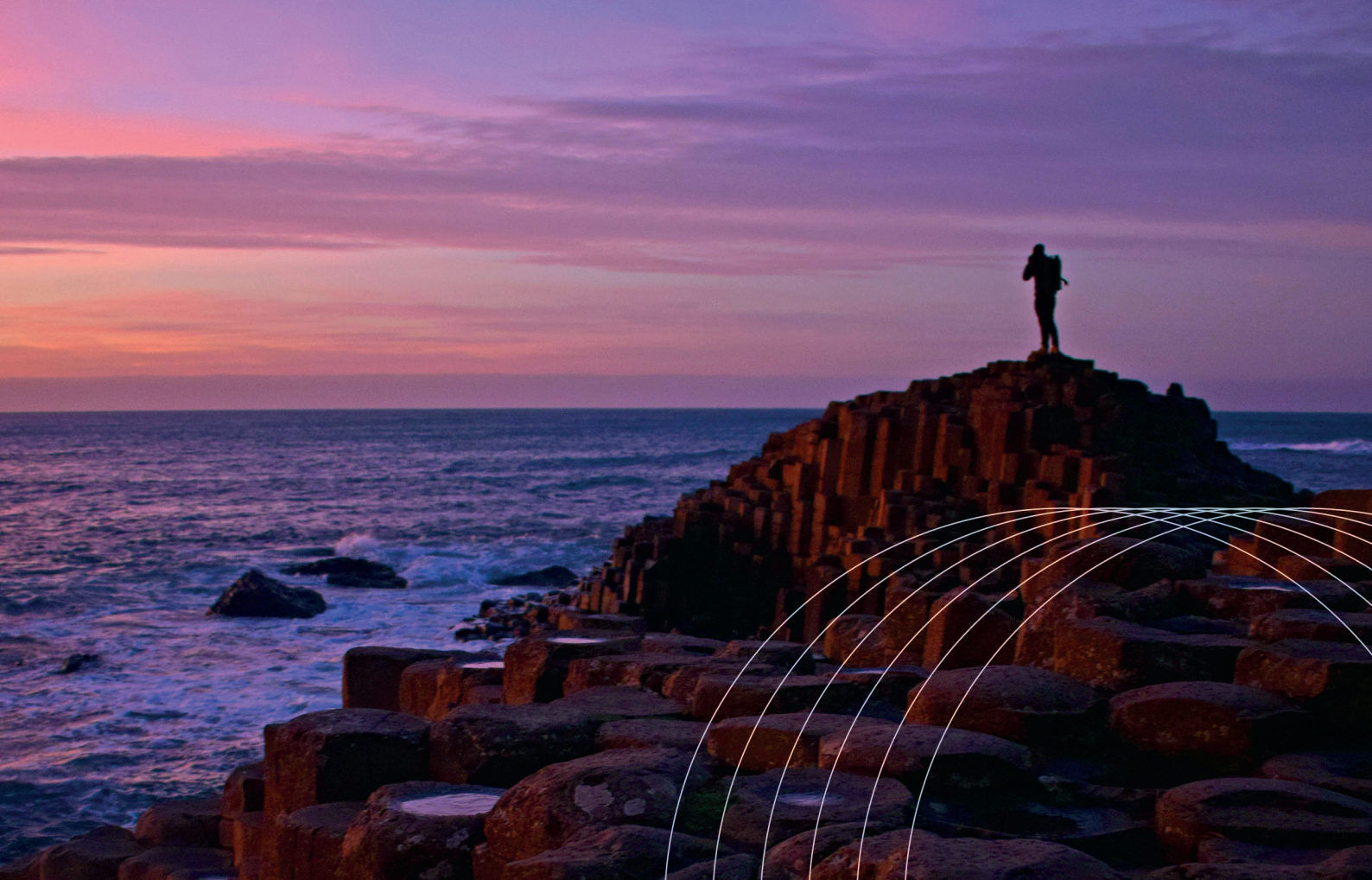




# DESIGNING WITH SUSTAINABILITY IN MIND: ENGINEERING LOW CARBON pMDIs FROM THE COMPONENT UP



**Tony Mallett** and **Richard Turner** of **Bespak** explain the environmental strategies that shape inhalation device development and commercial manufacture when designing for propellants with low global warming potential, allowing patients to receive safe and effective treatment with lower environmental impact.

For the next generation of pressurised metered dose inhalers (pMDIs), sustainability and performance need to be considered hand in hand. As the Kigali Amendment to the Montreal Protocol drives the phasedown of propellants with high global warming potential (GWP), the pMDI industry is transitioning towards low-GWP alternatives, including HFA-152a and HFO-1234ze(E).

However, this transition is about far more than replacing one propellant with another. Low-GWP propellants have different physical and chemical properties that can affect how formulations interact with the device, influencing critical aspects of performance and meaning that components, such as valves, need to be redesigned and optimised.

At the same time, reducing the environmental impact of a pMDI does not stop at the propellant. Materials, manufacturing processes, supply chains and product development also contribute to its overall carbon footprint. Understanding these impacts – and identifying opportunities to reduce them – requires sustainability to be considered from the earliest stages of development and at every level of the device.

As a specialist CDMO for inhaled and nasal drug delivery, Bespak is investing across its capabilities to support this transition, from component engineering and computational modelling to lifecycle assessments (LCAs), increased manufacturing capacity and supply-chain engagement. Together, these capabilities

are helping customers to develop low-carbon pMDIs while maintaining the quality, safety and reliability of the device that patients depend on.

### BUILDING CAPABILITY FOR THE NEXT GENERATION OF pMDIs

The transition to low-carbon pMDIs will require not only new technologies but also the manufacturing capacity, environmental insight and supply-chain capability to bring them into commercial supply. Bespak is investing across each of these areas.

The company's commercial-scale infrastructure has been expanded to support both HFA-152a and HFO-1234ze(E), creating the capacity to manufacture next-generation pMDIs at scale. This investment will be essential as demand for low-carbon pMDIs grows. However, the concept of a low-carbon pMDI starts long before commercial manufacture is considered – every component must be studied and understood to make sure that the device and formulation work together as expected whenever any changes to the drug-device system are made.

Alongside this, Bespak is developing a broader understanding of the environmental impact of its products and processes. LCAs are helping to identify environmental hotspots and opportunities for improvement, while supply-chain assessment and engagement are helping the business to understand and address impacts beyond its own operations.

At the component level, Bespak has dedicated years of collaborative R&D to optimise its market-trusted pMDI valve for low-GWP propellants. This work culminated in the BK357 valve becoming the world's first market-approved valve for a low-GWP propellant in May 2025. Bespak is also introducing its next-generation integrated dose counter, ready for low-GWP propellant pMDIs.

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**"THE TRANSITION TO LOW-CARBON pMDIs WILL REQUIRE NOT ONLY NEW TECHNOLOGIES BUT ALSO THE MANUFACTURING CAPACITY, ENVIRONMENTAL INSIGHT AND SUPPLY-CHAIN CAPABILITY TO BRING THEM INTO COMMERCIAL SUPPLY."**

Building on this component expertise, Bespak combines engineering with computational modelling and simulation (CMS) to understand how next-generation propellants can affect device performance and how device components can be optimised in turn.

### BUILDING NEXT-GENERATION pMDIs WITH COMPUTATIONAL MODELLING

Bringing a low-carbon pMDI into commercial manufacture starts with understanding how the device needs to perform with the new propellant. HFA-152a and HFO-1234ze(E) have sufficiently different physical and chemical properties from existing propellants that nothing can be taken as read.

For Bespak, CMS is an important part of this process. Combined with component engineering and materials expertise, it enables engineers to understand how changes in the propellant affect device behaviour, explore how different design

and manufacturing variables influence performance and refine component designs before moving into extensive physical prototyping.

Two examples demonstrate this approach. Bespak has used computational fluid dynamics (CFD) to understand how different propellants affect valve refill, while finite element analysis (FEA) and meta-modelling have been used to map the wider valve design space.

### Understanding the Propellant: CFD Modelling of Metering Chamber Refill

Immediately after a pMDI is actuated, the metering chamber inside must refill ready for the next dose. If it does not refill fully and consistently, the device can deliver an inconsistent dose. As this event takes place inside a sealed metal assembly in under 300 milliseconds, it is challenging to observe directly.

To address this, researchers at Bespak and the University of Hertfordshire (UK) have developed an advanced computational model to study the critical refill phase inside pMDI valves.<sup>1</sup> The team simulated the flow behaviour of four propellants: the legacy propellants HFA-134a and HFA-227ea, and the next-generation alternatives HFA-152a and HFO-1234ze(E).

The findings clearly highlighted that the unique physical properties of the propellant directly dictate how quickly the valve refills. For instance, HFA-152a demonstrated the fastest refill speed, achieving over 88% liquid fill within 300 milliseconds, while HFA-227ea proved to be the slowest. These variations correlated with each propellant's specific saturated vapour pressure and liquid density.

The important point from a design perspective is that these differences can be addressed at the component level. By adapting the geometry of the metering valve, engineers can compensate for differences in refill behaviour and support consistent patient dosing regardless of the propellant chosen. The CFD model therefore provides a way to understand a process that is difficult to observe experimentally and use that understanding to inform component design earlier in development.

## Understanding the Component: FEA and Meta-Modelling

Understanding propellant behaviour is one part of the challenge. But the pMDI valve itself is a complex assembly, with more than 100 design inputs potentially influencing more than 20 performance outputs.<sup>2</sup>

Traditionally, understanding how these variables affect performance would require extensive physical prototyping and testing. To explore this design space virtually instead, Bespak used FEA and statistical learning techniques, allowing the engineers to assess the potential impact of different dimensions, materials and manufacturing variations without producing a physical prototype for every combination.

The resulting model was validated against measured manufacturing data, with differences of less than 5% across the performance parameters. This gives engineers greater confidence in using the model to explore design changes and run sensitivity or “what if” studies without repeatedly producing physical prototypes.

While physical prototyping remains essential, particularly for a highly regulated product, the environmental benefit of using CMS to reduce unnecessary prototyping is significant. In one recent application of

this approach, Bespak avoided producing prototypes that would have consumed up to 5 tonnes of plastic. By using simulations to explore and refine designs before committing to physical prototypes, engineers can reduce material use while enabling a more efficient and informed development process.

## LCAs: LOOKING BEYOND THE PROPELLANT

As the industry moves beyond the immediate challenge of transitioning to low-GWP propellants, there is an increasing need to understand the environmental impact of the materials and processes that make up a device. This is where LCAs can provide valuable insight.

By gauging the environmental impact associated with the production of a component, LCAs can help to identify hotspots and focus efforts where they can have the greatest impact. In May 2025, Bespak completed a cradle-to-gate LCA of its BK357 pMDI valve in collaboration with Tunley Environmental (Leeds, UK). The independently verified assessment examined emissions associated with raw materials, upstream transport and manufacturing.<sup>3</sup>

The findings demonstrated the value of taking a component-level approach to sustainability. Rather than making assumptions about where emissions may come from, understanding the footprint of an individual component enabled previously overlooked environmental hotspots to be identified and targeted.

Customers are increasingly seeking transparent environmental data and credible reduction pathways; therefore, by undertaking a verified LCA and publishing a clear decarbonisation strategy, Bespak was able to demonstrate proactive leadership within the inhalation sector. The methodology can also be applied across different devices, processes and portfolios, providing a scalable framework for sustainability-led innovation throughout the pharmaceutical supply chain.

Increasingly, the value of LCAs lies in their integration into product development. When applied early in the design process, LCAs enable sustainability to become a decision input rather than an output, supporting more sustainable design outcomes from the outset.

## WORKING ACROSS THE VALUE CHAIN

Reducing the footprint of a pMDI cannot be achieved by engineering alone. The materials used in individual components come from wider supply chains, making collaboration with suppliers an important part of the process.

Bespak carried out a supply chain assessment to better understand the environmental impacts across its supplier base and identify priority areas for

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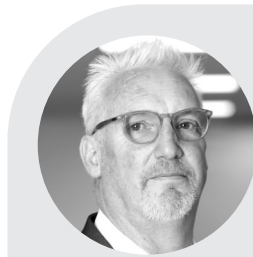
engagement. The assessment highlighted key hotspots for carbon emissions and biodiversity impacts, enabling the business to focus its efforts where they can deliver the greatest value. Building on these insights, Bespak hosted its first supplier engagement workshop, bringing together strategic suppliers to share the findings and discuss evolving sustainability expectations.

This builds on the collaborative approach already seen in Bespak's development work. Its research with universities has brought together academic expertise and practical experience to pMDI component development, while the BK357 valve LCA combined Bespak's understanding of its component and manufacturing processes with the specialist environmental expertise from Tunley Environmental.

Collaboration also extends beyond individual projects. Bespak's Holmes Chapel site is positioned within the Northwest of England's established pMDI R&D and manufacturing cluster, bringing together specialist expertise and capabilities across the inhalation sector for global applications. This creates a strong foundation for knowledge sharing and innovation, while enabling Bespak to develop solutions, capabilities and best practices that can support the global transition to low-carbon pMDIs. Through its work with customers, suppliers, academic partners and others across the value chain, Bespak is helping to turn sustainability ambitions into practical, scalable solutions, strengthening its position as a trusted innovation partner for the global pharmaceutical industry.

### MAKING SUSTAINABILITY PART OF THE DESIGN

The development of low-carbon pMDIs illustrates a broader shift in how sustainability can be approached within inhalation drug delivery. Environmental considerations can be addressed alongside engineering, manufacturing and supply-chain decisions, rather than only being considered once a product has already been designed. For Bespak, this means bringing together component engineering, computational modelling, LCAs and collaboration across the value chain to support better-informed



**Richard Turner**

Richard Turner is Senior Commercial Director at Bespak, with more than 25 years' experience in the respiratory drug delivery industry and particular expertise with pressurised metered-dose inhaler (pMDI) technologies. Mr Turner works with pharmaceutical companies globally on the development, industrialisation and commercialisation of pMDI platforms. A long-standing participant and key opinion leader in the respiratory community, Mr Turner brings a commercial perspective grounded in his extensive experience of translating emerging inhalation technologies into robust, scalable and commercially viable drug delivery solutions.



**Tony Mallett**

Tony Mallett is a Platform Development Group Manager at Bespak with over 23 years of experience within medical device development, covering all aspects of CDMO solutions. Mr Mallett's expertise encompasses all stages of new product introduction, servicing many products such as pMDIs, dose counters, dry powder inhalers, *in vitro* diagnostics, patch pumps, gas- and spring-powered autoinjectors, nasal devices and nicotine replacement therapy devices.

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## "THE DEVELOPMENT OF LOW-CARBON pMDIs ILLUSTRATES A BROADER SHIFT IN HOW SUSTAINABILITY CAN BE APPROACHED WITHIN INHALATION DRUG DELIVERY."

decisions throughout development and manufacturing.

This forms part of Bespak's wider environmental, social and governance strategy, supported by validated science-based emissions targets and actions across its operations. The aim is to make sustainability a practical consideration in the decisions that shape products, processes and partnerships.

The result is a more integrated approach to pMDI development. It is not simply a question of which propellant is used, but of how the device is engineered, what it is made from, how it is manufactured and how those choices affect its overall footprint. For Bespak, that means designing sustainability from the component up.

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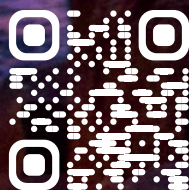
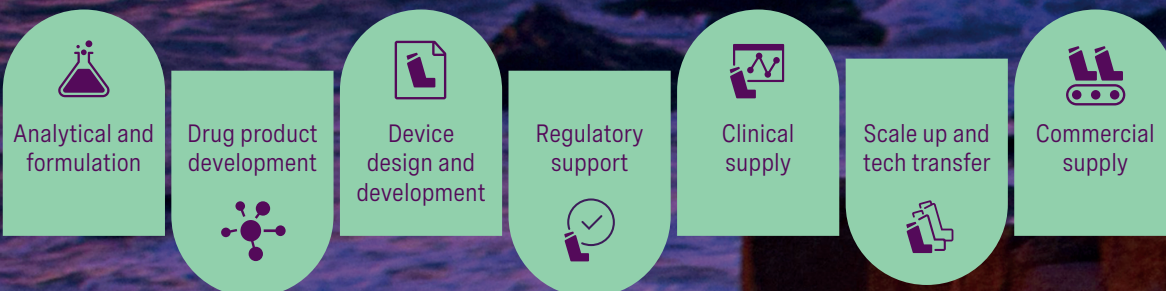


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