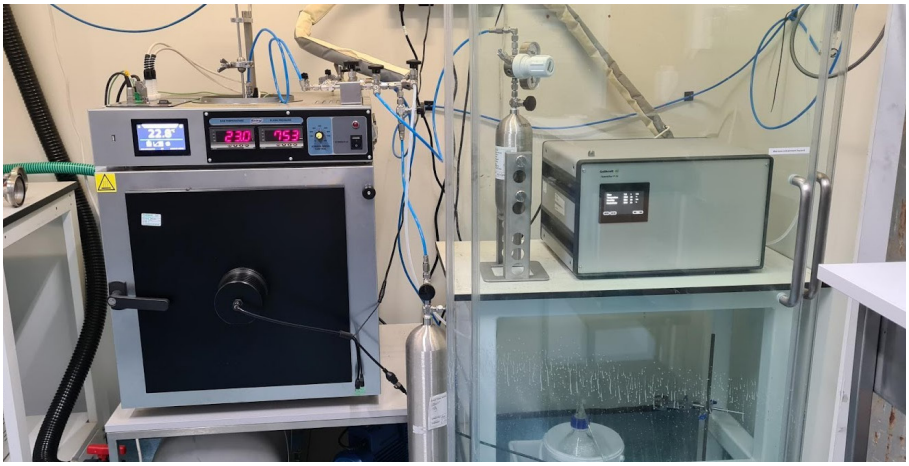
PEER REVIEWED

Safely Navigating the Transition to Low-GWP Medical Propellants

The pressure to reduce greenhouse gas emissions has transformed nearly every industry, and respiratory pharmaceuticals is no exception.

Pressurised metered dose inhalers (pMDIs) have long relied on hydrofluoroalkane (HFA) propellants like HFA-134a to deliver the active medicine directly to the patient's lungs. They are valued for their safety, reliability, and proven track record in supporting asthma and COPD patients.



Flammability testing equipment at Orbia's lab in the UK

However, medical aerosols like HFA-134a and HFA-227ea contribute to the healthcare sector's carbon footprint. For example, in the UK, propellants used in inhalers account for around 3% of the NHS's total emissions.

With environmental targets becoming more of a focus globally, and propellant-free options like dry powder inhalers (DPIs) unsuitable for approximately 30% of patients, the development of lower global warming potential (GWP) propellant alternatives is essential for the future of respiratory care.

At Orbia Fluor & Energy Materials, we have successfully developed a viable propellant alternative in HFA-152a. With a GWP of 124 (100-year timescale relative to CO_2), it offers a dramatic reduction in climate impact by at least 90%, depending on the replaced propellant.

We are currently ready to support product submissions for inhalers containing HFA152a formulations across the UK, EU, and US, with first product approvals and subsequent product launches expected to begin in 2026. This milestone will give GPs and procurement teams the ability to offer more sustainable inhaler options without disrupting continuity of care.

For formulary managers, regulators, and manufacturers working toward Net Zero targets, low GWP MDIs present a practical, clinically robust solution.

Unlike DPIs, they don't require retraining of large groups of patients in how to effectively use the product, or rethinking emergency protocols in respiratory conditions. Instead, they simply replace the higher GWP propellant-containing MDIs with an equivalent lower-impact alternative, once available. The goal is to ensure healthcare professionals have the choice to make environmentally responsible decisions without compromising patient care.

Managing the Flammability Risks

However, creating low-GWP alternatives isn't without complications. HFA-152a is more flammable than its high-GWP predecessors, a characteristic that has raised questions in the industry.

Transitioning to a new propellant often begins with a change in perception, and the term 'flammable' can sound alarming, particularly in a medical context. The reality, however, is far more nuanced. HFA-152a is classified as flammable in air at standard conditions in concentrations between 3.7 and 18.0 w/w%, meaning it can be ignitable in a manufacturing setting, but is not inherently unsafe to handle, particularly in a medical aerosol.

At Orbia Fluor & Energy Materials, our development strategy for HFA-152a has been underpinned by two core principles: the application of proven scientific controls and the execution of detailed material-compatibility studies to ensure both safety and efficacy. Beyond safety, we of course had to evaluate how this compound would behave in the human body, and what impact it might have on the atmosphere.

From the outset, we recognised the flammability properties of HFA-152a. However, this characteristic is far from unprecedented in the pharmaceutical industry, which routinely handles flammable excipients such as ethanol in inhaler formulations, which can push formulations of non-flammable propellants into the flammable range from levels above 1% w/w. Consequently, while flammability represents a hazard during manufacture, it is a well-characterised and manageable risk when appropriate mitigation measures are applied and has no impact on safety in use.

During the testing phase, we found that laboratory handling of HFA-152a required targeted adjustments – particularly, the use of ATEX-rated equipment and gas detection for operations such as propellant filling and during specific formulation or transfer steps.

This demonstrated that at manufacturing scale, the safe handling of HFA-152a is manageable with a suite of established controls including; ATEX-rated filling equipment; properly classified and zoned areas around filling lines and bulk storage tanks; controlled ventilation systems; continuous leak-detection technology; and comprehensive operator training supported by updated standard operating procedures.

The technology and infrastructure required for these measures already exist and have been proven over decades of application in other aerosol-based manufacturing environments.

In practice, once hazards are fully understood and engineered controls are implemented, our experience has shown that HFA-152a can be managed with the same level of safety assurance as other flammable excipients and propellants in use today.

Building the Foundation for Low-GWP Propellants

Since entering the HFA propellant space in the mid-1990s, following the phase-out of CFCs, Orbia Fluor & Energy Materials has consistently invested in production facilities. At that time, we worked alongside partners to build capacity for supplying the global market with the new generation of HFA propellants. This directly addresses the aims outlined in the Montreal Protocol, which initially highlighted the need to reduce CFC production and consumption by 50% by 1998.

Over the years, we recognised early on that another transition was inevitable. Being a key supplier of fluorinated gases to other industries, we had already seen regulations introduced and implemented in the refrigerants sector, with a phase-down underway, underpinned by the Kigali amendment to the Montreal Protocol, calling for a phase-down of HFAs by more than 80% by 2050. Once we understood that a regulatory-driven phase-down would shape the industry and that innovation would be key to supporting it, we knew we had to develop the next generation of medical propellants.

About 15 years ago, we began evaluating our toolbox of potential molecules. Using our expertise of what makes a successful medical propellant along with an elimination process, we identified the 152a molecule as the best candidate when considering all needed outcomes.

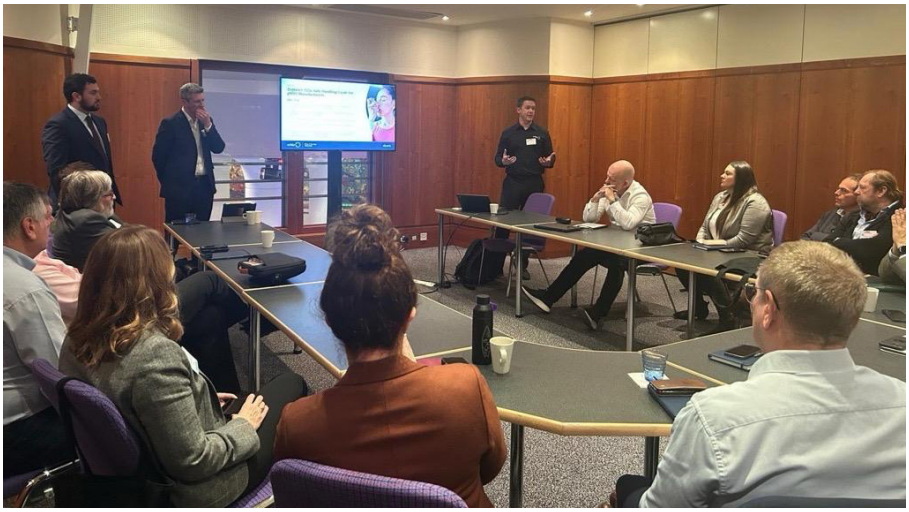
Since then, we have invested tens of millions of pounds to prove the absolute safety of this molecule for medical applications, completing a rigorous 10-year toxicology programme to demonstrate its safety to pharmaceutical companies and regulators worldwide. To date we have proven that HFA-152a has low acute and chronic toxicity, no genotoxic, carcinogenic or developmental effects. It exhibits no respiratory, sensitisation, cardiopulmonary or respiratory effects and juvenile studies support its use in patients from 2 years old.

The overall toxicity of HFA-152a has been proven to be cleaner than any other HFA propellant already in use. A testament to the physical properties that led to its selection as a next generation medical propellant.

In addition, we began investing in production, because a good candidate is only useful if it is produced in sufficient quantities. In the early 2020s, we built a small-scale facility to supply the volumes needed for product development, clinical trials, and regulatory approval.

By investing in production, we gave the industry the foundation it needed to move forward in the early stages of transition. And just last year, we announced plans to build a larger facility that will produce enough propellant for a global switch of current customers to Zephex® 152a.

Construction is underway, and the larger scale plant is expected to be operational in the second half of next year at our Rocksavage site in Runcorn, United Kingdom. The response so far from our customers and the industry on this has been positive, and so we look forward to leading the global transition from the UK.



Collaborative workshop hosted by Orbia at DDL 2024, with Bespak and DH Industries on the topic of flammability

Ensuring Confidence in the Sector

Whilst adapting the technical procedures we use to manufacture this product is imperative to a healthy transition, we also need to consider other implications that could affect the transition to a new sustainable propellant.

Transitioning an industry to a flammable propellant such as HFA-152a requires more than technical adaptations; it demands a cultural shift within organisations. This transition is not solely about redesigning manufacturing equipment or updating supply chains, it also involves reshaping perceptions and building confidence around the safe use of flammable materials.

Success depends on actively managing expectations, addressing concerns openly, and embedding comprehensive education on flammability into everyday practice. By reframing flammability as a well-understood, controllable factor rather than an unfamiliar threat, organisations can foster the mindset needed to ensure a smooth and secure transition.

Building this confidence involves increasing awareness among operators, engineers, and maintenance teams, and drawing on the extensive experience of consumer aerosol manufacturers who have worked safely with flammable propellants for decades.

To address this, we are investing in both technical systems and workforce capability – developing standard operating procedures specifically for flammable propellants, delivering training programs that educate flammability as a manageable and routine issue, and ensuring transparent communication of laboratory and production data. These measures are designed so that safety protocols are understood, trusted, and applied with confidence.

My own role as Pharma Application Development Manager bridges laboratory research and external communication, translating experimental findings into practical, operational guidance for customers. This dual focus on both technical preparation and workforce procedures ensures that concerns over flammability do not become barriers when it comes to the wider industry being confident in its transition to our next generation propellant.

The Impact of Collaboration

The integration of HFA-152a into the

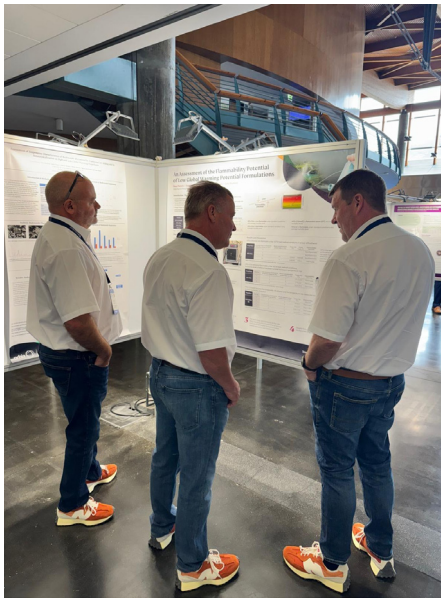
pharmaceutical supply chain will be inherently multidisciplinary, and will require close cooperation between manufacturers, suppliers, and engineering specialists.

Because of this, Orbia Fluor & Energy Materials has partnered with Bespak and DH Industries to produce a comprehensive safety handling guidefor HFA-152a, incorporating best practices for bulk storage, in-factory management, and pMDI line operations.

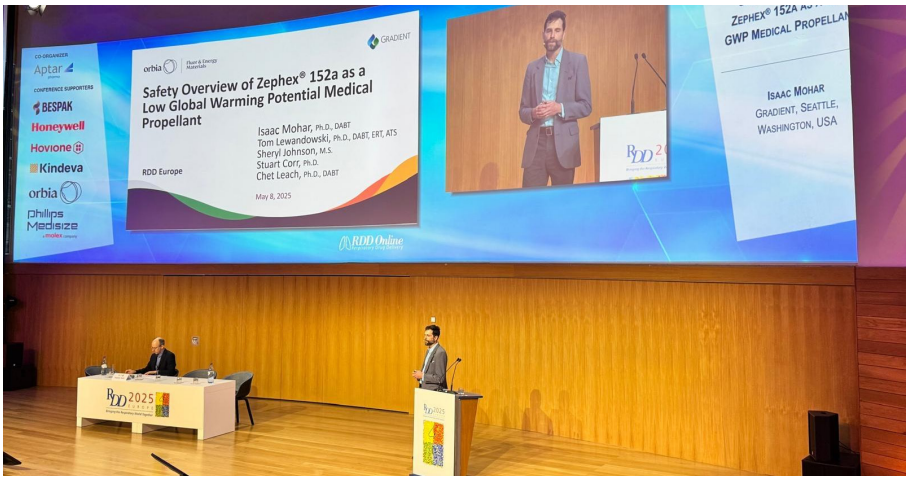
This document is an excellent example of essential industry collaboration, ensuring that the guidance covers everything from bulk storage and safe handling protocols, to incorporating low-GWP propellants into pMDI manufacturing environments.

What's more, this collaboration extends beyond written guidance and into active industry engagement. Together, our teams attend at key sector conferences – including the Drug Delivery to the Lungs (DDL), Respiratory Drug Delivery (RDD) and International Society for Aerosols in Medicine (ISAM) Congress – sharing operational experience, technical findings, and safety data in real time. For example, at ISAM this year, Orbia detailed the timeline of Zephex 152a from its inception, covering its formulation behaviour, toxicological safety and current regulatory and commercial status.

Our experts also participate in regulatory and scientific forums such as IPAC-RS and FDA-hosted events, as well as delivering targeted presentations at DDL, Respiratory Drug Delivery (RDD), and other global platforms.



Orbia's poster presented at RDD Europe 2025 on the flammability potential of Zephex 152a



Podium shot of Dr Isaac Mohar, toxicologist and immunologist, delivering a paper on the safety of Zephex® 152a at RDD Europe 2025

In this transition, collaboration is just as much about ensuring that patients can continue to rely on their inhalers as it does about achieving technical readiness. By working side by side with our partners to share knowledge, address safety concerns, and smooth the path to implementation, we're helping to make sure that no patient experiences a break in treatment. At the same time, we're creating the foundations for the safe, confident adoption of low-GWP propellants across the industry.

Maintaining 134a Supply During the Transition

While the industry prepares to adopt HFA-152a, it is vital to ensure that patients continue to have uninterrupted access to existing inhaler therapies that rely on HFA-134a.

A sudden shortage of 134a could also jeopardise patient care, particularly for those who cannot use DPIs or other alternatives. Recognising this, Orbia Fluor & Energy Materials has committed to maintaining a reliable supply of HFA-134a throughout the transition period for as long as the market requires it.

This dual approach – introducing HFA-152a while securing ongoing 134a availability – provides healthcare providers with the flexibility to make the shift at a pace that ensures patient safety and continuity of care.

Our production facilities have been optimised to manage both propellants molecules simultaneously, and our supply chain teams work closely with pharmaceutical partners to anticipate demand fluctuations, prevent shortages, and maintain confidence in medical propellant and subsequent inhaler availability.

By guaranteeing a consistent 134a supply, we are helping the sector navigate the transition smoothly, giving clinicians and patients time to adjust to low-GWP alternatives without disruption to treatment.

This commitment underscores our patient-first philosophy that environmental innovation should not come at the expense of care.

REFERENCES

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2. https://www.kouraglobal.com/

Sheryl Johnson

Sheryl Johnson, Pharma Application Development Manager at Orbia Fluor & Energy Materials, is a highly respected authority in the pharmaceutical aerosol industry with almost two decades worth of experience in medical chemical development and research. She is on the board at the International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC RS), frequently contributed to the publishing of papers, and speaks at events such as the International Aerosol Society Congress. Now, with nearly 15 years experience at Orbia Fluor & Energy Materials, she serves as Pharma Application Development Manager, overseeing the safe production of research and clinical products containing zephex 152a.