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Managing supply Continuity During the pMDI Transition to Next Generation Propellants

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Introduction

Pressurized metered dose inhalers (pMDIs) are a long-established and important inhalation therapy that rely on hydrofluoroalkane (HFA) propellants rather than patient inhalation effort, making them critical for patients who cannot inhale strongly or deeply. Environmental regulation is driving a transition from current propellants (HFA-134a and HFA-227ea) to next-generation alternatives, (HFA-152a and HFO-1234ze(E)), which, while improving sustainability, introduces technical, regulatory, and supply chain risks that could threaten continuity of patient care if not carefully managed.

Current Regulatory Restraints

Global regulation of inhaler propellants is tightening and unevenly developed: the US EPA's AIM Act and emerging state laws, Europe's stringent F-Gas phase-down, and similar measures in other regions are reducing allowable fluorinated gases (F-Gases) [1],[2], with both current propellants and HFA-152a subject to quotas in many jurisdictions (unlike HFO-1234ze(E)). Regulatory guidance remains sparse—so far, only the EMA has issued clear expectations [3], and while the UK approved the first next-generation propellant (NGP) pMDI in 2025, the FDA has not issued formal guidance—creating uncertainty. Beyond F-Gas rules, proposed PFAS restrictions could further constrain propellant and coated can availability, although HFA-152a currently falls outside draft PFAS definitions [4].
Taken together, these evolving F-Gas and PFAS-driven policies create a complex and shifting regulatory landscape for propellant selection.

RISKS TO PROPELLANT AND FINISHED PRODUCT SUPPLY CHAINS

Propellant Production Constraints

Propellant manufacturers are striving to maintain supply of existing propellants for as long as needed [5] and making significant investments into the commercialization of NGPs [6, 7]. The US AIM Act and EU F-Gas phasedown schedules reduce allowances annually, to reach 15% by 2036 and 21% by 2030 of historic baseline levels, respectively, which will impact global capacities.

In addition to emerging PFAS restrictions, constraints are emerging for existing suppliers associated with the demands of maintaining dual supply and production capacity of both current and NGPs, presenting significant capital cost. In some cases, delays in finalizing environmental regulations could result in investment lag in capacity expansion.

Finished Product Production Constraints

Reformulating a pMDI requires extensive testing to demonstrate therapeutic equivalence and aerosol performance evaluation to obtain regulatory approval as well as bridging studies. The flammability consideration for HFA-152a and all ethanolic NGP formulations, places further pressure on a limited number of bespoke pMDI manufacturing equipment suppliers for special filling lines either by way of new or upgraded facilities [10], who already typically operate with long lead times.

Manufacturers of finished products need to maintain current pMDI supply while building capacity for the NGP products. Such dual production is expensive and operationally complex.

Component Supplier Constraints

Companies developing pMDIs with NGPs face formulation challenges as components need to be validated.

Valves require optimization to manage moisture, leakage and material compatibility associated with the NGPs.

Canisters are adaptable to the transition, but fluoropolymer canister coatings face a supply chain risk due to the current proposal of ECHA's PFAS regulations.

Actuator geometry impacts pMDI performance [8], due to physico-chemical differences some optimization is needed for NGPs [9].

Device component suppliers, also must navigate changes for NGPs, while maintaining current component supply for existing pMDIs.

MITIGATION STRATEGIES- CURRENT AND FUTURE

Risk	Stakeholders	Current successes / contributions	Future requirements	
Propellant and component production restraints (and logistical)	Component suppliers (Aptar, Bespak, H&T Presspart, RxPack, Kindeva)	Next-gen valves with improved material compatibility and leakage. Offering sustainable non-PFAS coated canisters.	Continued expansion of global production for NGP products to ease bottlenecks and support all next-gen device platforms	Strengthened cross industry collaboration, education, advocacy, and engagement to ensure uninterrupted global supply of pMDIs.
	Propellant Suppliers (Orbia F&EM, Solstice AM)	Maintenance of current propellant supply. Initial expansion of NGP manufacturing capabilities to appropriate guidance.	Understand and potentially mitigate the impact of regulations (and accompanying label requirements) on the pMDI propellant and component supply chains and subsequent impact on pMDI availability.	
	Environmental regulatory bodies (EPA, ECHA, NMED)	Issuing regulations to restrict the manufacture, and use of F-Gas and PFAS with accompanying label requirements [1][2]		

Risk	Stakeholders	Current successes / contributions	Future requirements	
Finished product production constraints (and logistical)	Propellant, Component Suppliers and Service providers (Orbia F&EM, Solstice AM, Bespak, DH Industries, Kindeva)	Investment in robust non-clinical safety programs to support regulatory confidence. (propellant suppliers) [11][12]. Issuing process safety guidance and advising on ATEX facility upgrades [13]. Initial expansion of NGP manufacturing capabilities to appropriate guidance	Continued expansion of global production for NGP products/services to ease bottlenecks and support all next-gen device platforms	Strengthened cross industry collaboration, education, advocacy, and engagement to ensure uninterrupted global supply of pMDIs.
	Pharmaceutical Companies (GSK, Chiesi, AstraZeneca)	Coordinated portfolio transitions to NGPs, reinforcing regulatory readiness and demand. Investment in robust clinical programs to support regulatory confidence.	Expansion of NGP product development and commercialisation aligned with suppliers	
	Aerosol Consortia (IPAC-RS, IPAC)	Collaborating on awareness workshops/webinars and guidance with members and regulators to reduce uncertainty. [14]	Advocate for propellant quotas, moderation of PFAS regulatory impact and improvements to regulatory harmonization to reduce duplicated studies and non-essential labelling.	
	Medical Regulatory bodies (EMA, FDA, MHRA)	Providing targeted guidance and collaborating on awareness workshops to reduce uncertainty (FDA/EMA/MHRA).	Improve regulatory harmonization and clarity	
	Environmental regulatory bodies (EPA, ECHA, NMED)	Issuing regulations to restrict the manufacture, and use of F-Gas and PFAS with accompanying label requirements	Rationalize non-essential labelling for pMDIs.	

Moving Forward

There's an industry-wide need for suppliers and pharmaceutical companies to join forces and work collaboratively through trade groups and consortia, to advocate for:

- Protected medical-use propellant quotas
- Moderation of emerging PFAS environmental regulation impacting propellants and canister coatings
- Clarity on labelling requirements
- Increased regulatory harmonization-push for clearer guidance from regulators outside the EU

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