Drug Development & Delivery

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Respiratory Drug Development eBook

Respiratory Drug Delivery & Development – Inhalers Trend Toward Sustainability & Targeted Control

Technology advancements, rising prevalence of respiratory diseases, and a growing awareness among patients and healthcare providers are driving the global inhalation market to potentially reach a value of $18.6 billion. With its potential to revolutionize treatment methods, the inhalation market is set to reshape the healthcare landscape.[1]

The effectiveness of inhalation devices relies on their ability to deliver a pharmaceutical directly to the targeted part of the body with precision and calculated dosing. And user error is common, impacting patient well-being. Additionally, devices are typically placed in the nose or mouth, making contamination from viral or bacterial particles possible.[2]

Porous polymers play a key role in overcoming these challenges by controlling the flow of particles within the device. Porex offers porous polymer components and resources to direct flow with precision, meter dosing, and filter out viruses and bacteria. By incorporating Porex's porous polymers in their designs, manufacturers can optimize manufacturing costs while elevating device performance.

While efficacy and safety of medical treatments are always a priority when selecting the best inhaler and drug combination for a patient, environmental impacts have become a key consideration for inhaled therapies like metered dose inhalers (MDIs) and dry powder inhalers (DPIs). A study of inhaler satisfaction and preferences in patients with asthma and chronic obstructive pulmonary disease (COPD) found "environmentally friendly" to be one of the most important characteristics. Patients in a second study, designed to investigate perceived importance of inhaler cost, carbon footprint, and ease of use, rated "carbon footprint" as 3.4 out of 5 (where 1="not important" and 5="very important").[3] Device manufacturer Nemera is seeking ways to find greener alternatives in inhalation design, prioritizing sustainable procurement aimed at reducing GHG emissions.

Learn more about Porex and Nemera and their contributions to inhalation drug delivery and device design in this fourth annual *Drug Development & Delivery* exclusive report.

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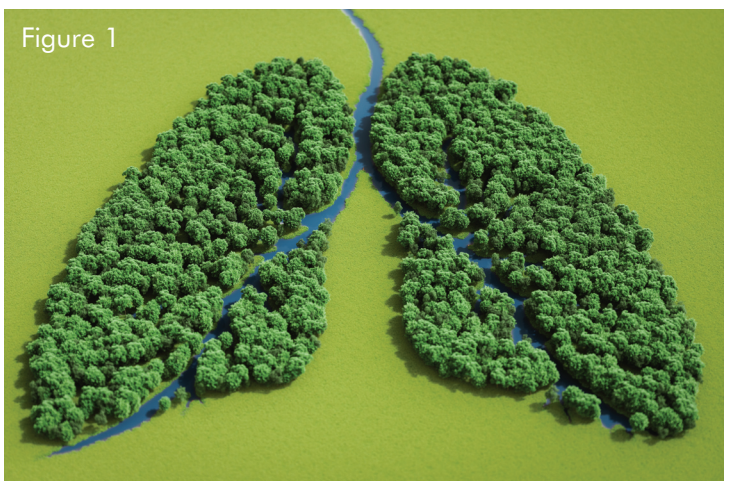
Nemera: Meeting Inhalers' Sustainability Challenges

By: Léa Salfati, Inhalation & Oral, Vaginal, Rectal Franchises, & Gildas Huet, Technology Product Manager for Future Inhalation and Ophthalmic Devices

Figure 1



In 2022, close to 850 million people around the world were suffering from a chronic respiratory disease, notably asthma and chronic obstructive pulmonary disease (COPD).[1] The number of people with these pulmonary conditions are expected to rise, given the increasing elderly population, air pollution, climate change, and evolving lifestyles. Although these are long-term conditions with no permanent cure, the symptoms can be controlled with the right treatment. Drug delivery inhalation devices play a crucial role here.

Over the years, several types of inhalation devices have been developed, including pressurized metered-dose inhalers (pMDIs), dry powder inhalers (DPIs) and, more recently, soft mist inhalers (SMIs). In 2021, 1.5 billion inhalers were sold, increasing CAGR by 4%. Among these, pMDIs are the most common, representing about 60% of the inhaler market. However, pMDIs containing hydrofluocarbons (HFCs) have become a big challenge, in terms of sustainability, in recent years. In 1987, the Montreal Protocol on Substances that Deplete the Ozone Layer regulated the production and consumption of chemicals referred to as 'ozone-depleting substances' (ODS). These chemicals damage the stratospheric ozone layer when released into the atmosphere. The use of HFCs is growing by 8% per year, with annual CO^2 emissions projected to increase by 7-19% by 2050. Finding ways to control these HFCs is one of the biggest challenges today, but solutions are necessary to keep global temperature rise at or below 35.6°F this century. In 2016, countries joining the Montreal Protocol in Rwanda agreed to phase down the use of HFCs, adding them to the list of controlled substances and introducing a timeline for gradual reduction by 80-85% by 2040.[2,3]

The Medical and Chemicals Technical Options Committee estimated that 800 million HFC pMDIs are manufactured annually worldwide, using approximately 11,550 tons of hydrofluoroalkanes (HFAs).[4] The Intergovernmental Panel on Climate Change (IPCC) drew attention to pMDIs for their use of propellant gas, contributing to greenhouse gas emissions. There is a clear need to find a greener alternative to this atomization technology that eliminates the use of propellant gas. Dosage forms with lower global warming potential (GWP), reformulations, and innovative drug delivery devices must all be considered. As a leader in inhalation drug delivery device manufacture, it is Nemera's responsibility to find ways to meet these challenges and steer the pharma industry on this journey (Figure 1).

Dry Powder Inhalers: A Sustainable Alternative With Limitations

Dry powder inhalers (DPIs) are devices delivering medication to the lungs in the form of a dry powder. They are an alternative to pMDIs. Today, they represent about 35% of the total inhalers market, after pMDIs. However, this percentage varies by country. In Sweden, only 13% of inhalers are pMDIs and the rest are mainly DPIs. This demonstrates that it is possible to switch from pMDIs to DPIs. A study calculated the potential CO_2 reduction in the UK by moving to the Swedish pattern: 'The predicted reduction of 550kt CO_2eq annually that [has been] calculated by applying the Swedish distribution of inhalation devices to the population in England thus corresponds to approximately 2.6% of the total carbon footprint for National Health Service (NHS) England.'[5]

While this number is very encouraging, DPIs are not suitable for all patients:

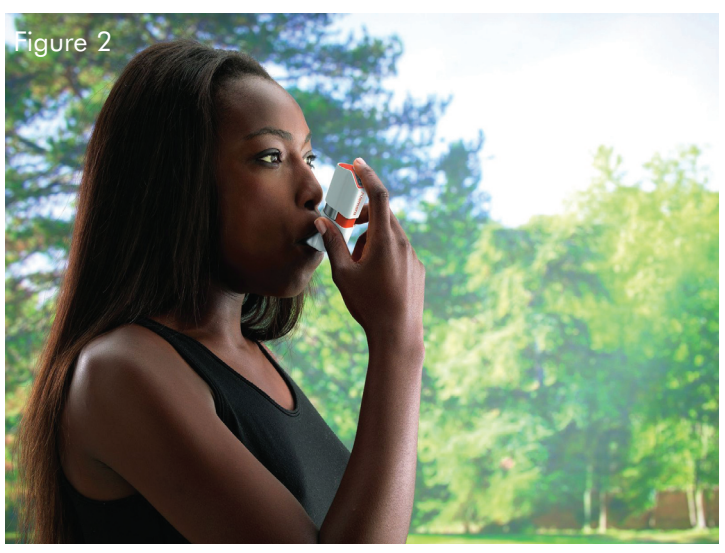
- They require powerful inspiration flow (ensuring that the medication reaches the lower parts of the lungs), meaning breath must be held for 5-10 seconds
- They are not adapted for young children.

Insufficient patient inhalation might lead to reduced dose delivery and incomplete disaggregation of the powder. The deagglomeration principle is triggered by the patient's strength during the inhalation phase, hence it is very user dependent, meaning a potential restricted application area. Furthermore, not all drugs suit a stable, powder formulation that enables a good dispersion during inhalation.

However, DPIs are based on a proven and established technology and still present a more favorable environmental profile. They may not be adapted to every patient's needs, but they are a safe and effective solution. These devices are part of the future of inhalers, even if they have to be complemented by other solutions.

Nemera holds a leading position in the manufacture of DPIs. The company set foot in the inhalation space by manufacturing for the number-one player in the inhalation DPI market (IQVIA, 2021). This initial success then snowballed into other collaborations with blockbusters in the pharma industry and generic players that specialize in inhalation (Figure 2).

Figure 2



About the Authors

Léa Salfati is a graduate of the ESC Rennes school of Business with a Master of Science in International Marketing. She brings over five years of marketing experience in the pharmaceutical industry, she notably worked as Category Manager for COOPER and IPRAD (Biocodex). At Nemera, Léa is in charge of the Inhalation & Oral, Vaginal, Rectal franchises.

Gildas Huet graduated as a generalist engineer from ICAM (Institut Catholique des Arts et Métiers in France) with a specialization of Biomedical Engineering at Aalborg University in Denmark. He has worked since 2004 in research and development of medical devices, starting with the development implantable devices, to drug administration devices for parenteral application. He joined the Insight Innovation center at Nemera in 2016 as Senior Design Engineer for the development of the Safe'n'Sound® safety device, and since 2020 works as Technology Product Manager for Nemera's own IP future Inhalation and Opthalmic devices.

Soft Mist Inhalers: The Emerging Greener Option

A new type of device is the soft mist inhaler (SMI). This generates a fine, slow-moving aerosol of a liquid formulation. This technology reduces the need for patient coordination and inspiratory effort and allows better drug deposition in the lungs, compared to pMDIs and DPIs. SMIs are also compatible with a wide range of drug formulations, including solutions and suspensions, making them suitable for delivering various medications for different respiratory conditions. Last, but not least, they are propellant-free. SMI devices are particularly suitable for those taking pMDI treatments who cannot switch to DPIs.

SMIs are a great fit from both a treatment efficacy (great reach to the lung) and environmental footprint (as they do not involve any gas) standpoint. In addition, their design enables the administration of a liquid formulation, which is a necessary galenic form for certain molecules.

Currently only the Respimat® SMI from Boehringer Ingelheim is available on the market. As it does not contain propellant, the carbon footprint is clearly lower than pMDI and equivalent to DPI, with less than 780g CO_2eq per device. Furthermore, this can be reduced by half by using the refilled cartridges principle.[6,7]

Many device manufacturers are currently developing new alternatives for SMIs. This segment will grow significantly in the coming years. The main challenge is to generate droplet sizes of below 5μm to reach the lung, which is no easy task when designing such a device.

Nemera's Commitment to Sustainability

Nemera's ambition is to embed itself in discussions around the inhalers of tomorrow, striving to ensure R&D effort focuses on sustainability and environmental factors. The company is also committed to support its pharma partners on their sustainability journeys.

Sustainable procurement is one of the strategic pillars of Nemera's strategy. It is an integral part of Scope 3 in the measurement of greenhouse gas (GHG) emissions, which represent the main part of indirect emissions. This means that implementing a sustainable purchasing strategy will enable Nemera to reduce its GHG emissions in the long term.[8]

With the help of EcoVadis benchmarks and methodology, Nemera has developed a set of objectives up to 2030 (Figure 3). Our action plans will include detailed CSR criteria for requirement specifications, contracts and suppliers, including supplier audit checklists, and performance evaluations. Finally, we have created a set of internal and external KPIs to track and measure our progress. We are ready to work on pilot projects to develop less impactful resins and are looking for customers who would like to join us in this adventure. At Nemera, we believe that the challenges of sustainable development must be met together. This can only be achieved by integrating the entire value chain. Thanks to collaboration with our partners, and commitment from all stakeholders, we will succeed in transforming our industry.

Figure 3

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About the Author
Nadia Hajjar, is the Category Manager for Life Sciences solutions at Porex and has over 10 years of international healthcare experience in the areas of Manufacturing, R&D, Operations, Product Development, Marketing, and Business Development.

Porex: Achieving Cost Savings & Enhancing Inhaler Performance with Porex Porous Polymers

By: Nadia Hajjar

Inhaler manufacturers have found a valuable solution in porous polymers to enhance device performance and reduce costs. These versatile components play a crucial role in filtration, wicking, and capillary action within inhalers, thereby improving drug delivery efficiency and effectiveness. By incorporating Porex's porous polymers in their designs, manufacturers can optimize manufacturing costs while elevating device performance.

Filtration, Wicking, & Capillary Action: Enhancing Inhaler Performance with Porous Polymers

Inhalation devices require precise filtration to ensure medication purity and prevent contamination. Customized porous polymers enable enhanced filtration efficiency by controlling pore size, effectively filtering out contaminants, and improving patient safety. Additionally, these components excel in promoting efficient wicking and capillary action, ensuring optimal fluid transfer within inhalers. By leveraging porous polymers, manufacturers can achieve cost savings, enhance material purity, and optimize drug delivery, ultimately benefiting patients by improving the efficacy and reliability of inhalation therapies.

Design Challenges & Solutions

Design Challenge 1: Contaminant Removal

Maintaining a high level of purity in inhalation devices is crucial for ensuring the effectiveness of therapies. In the case of portable oxygenators used in at-home care, the design challenge lies in effectively removing contaminants from the air while providing a quieter operation. Custom porous polymers can provide a three-in-one solution by absorbing and diffusing the sound generated by compressed air, resulting in a more silent operation. At the same time, these porous polymers act as efficient inlet filters, removing contaminants and maintaining air purity. By incorporating a multifunctional component, manufacturers can achieve contaminant removal and noise reduction utilizing the same component, while reducing design complexity and cost.

Design Challenge 2: Backflow Inhibition & Precise Delivery

When delivering medication to the central nervous system via nasal spray, backflow contamination and precise delivery are critical design challenges. Custom components made of clean and biocompatible materials prevent leachables and extractables from contaminating the device and ensure safe delivery to the patient. They also can customize flow rate to inhibit backflow contamination and enable precise and focused delivery to spaces such as the nasal cavity. These components can also be tailored to meet the specific requirements of chemical compatibility, formulation viscosity, and metered dosing rates to ensure reliable and safe delivery.

Design Challenge 3: User Error Reduction & Consistent Deposition

In dry powder inhalers (DPIs) and portable nebulizers, reducing user errors caused by subjective inhalation techniques is a significant challenge for achieving consistent drug deposition. Poor inhaler technique and irregular respiration can lead to backflow and inconsistent delivery. Custom components can overcome these challenges by preventing backflow through unique formulations and customized pore structure, thereby creating independent inspiratory flow rates that mitigate risk within the device. Our components also provide methods for aerosolizing the drug, while acting as a sterile barrier. This feature ensures accurate dosing and consistent deposition in the lungs, while ensuring sterility for the lifetime of the device.

Design Challenge 4: Fine Particle Filtration & Volumetric Efficiency

Soft mist metered dose inhalers (MDIs) present a design challenge in achieving effective fine particle filtration while maintaining high volumetric efficiency. The smaller particle size generated by MDIs requires efficient filtration to prevent aerosol residue in the mouth after inhalation. Custom components made from porous polymers can reach submicron filtration levels, effectively managing particle fractions and ensuring the desired therapeutic effect. Additionally, these components offer high volumetric efficiency, allowing effective use of the reservoir and optimizing medication release.

By addressing these design challenges with custom components made from Porex porous polymers, inhalation device manufacturers can improve performance, ensure purity and sterility, reduce user errors, and achieve cost savings through reduced complexity and increased efficiency. Porex components can also offer solutions for mixed particle sizing with large- and small-molecule combinations, optimizing effective drug delivery regardless of the formulation. These versatile components provide a reliable and efficient solution across various inhaler components, offering comprehensive value in developing inhalation devices.

Enhancing Inhalation Drug Delivery with Porous Polymers

Incorporating Porex porous polymers into inhalation devices presents a significant opportunity for inhaler manufacturers to achieve cost savings while enhancing device performance. These components ensure the highest quality, safety, and efficacy by addressing key design challenges related to contaminant removal, precise dosing, optimal drug deposition, and medication waste reduction. With Porex's expertise and collaborative approach, manufacturers can unlock the full potential of their inhalation devices, delivering improved patient outcomes and cost-efficient solutions in the evolving field of respiratory therapies. To explore the benefits of Porex porous polymers in your inhalation device projects, please visit Porex.com.

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