ENHANCING DRUG DELIVERY WITH INNOVATIVE SOFT MIST INHALER TECHNOLOGY

Dr Nicolas Buchmann and **Bernhard Müllinger**, both of **Resyca**, discuss the capabilities of soft mist inhalers in terms of usability for patients, sustainability, compatibility with biologics and cost-effective delivery, showcasing these advantages in Resyca's Pre-Filled Syringe Inhaler (PFSI).

Inhaled drug delivery has long been central to the treatment of respiratory diseases. However, traditional inhaler types come with inherent design limitations that can contribute to higher rates of patient use errors, resulting in inefficient delivery, wasted drug product and suboptimal therapeutic outcomes.[1] Often, these inhalers are not designed for next-generation therapeutics, which require more accurate and sensitive delivery technologies, limiting their use in novel life-changing treatments.[2]

Soft mist inhaler (SMI) technology was developed to address these challenges. SMIs generate a slow-moving aerosol cloud, enabling inhalation over several seconds of spray duration. This reduces the risk of co-ordination errors, enhances pulmonary drug deposition and improves usability across diverse patient populations. The potential of SMI technology is particularly exciting for inhaled

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biologics, such as vaccinations and gene therapies, where efficiency, patient usability and gentle aerosolisation are crucial.[3]

The Pre-Filled Syringe Inhaler (PFSI™) by Resyca® is a step forward in SMI technology. By integrating a prefilled sterile syringe, precision spray nozzle engineering and a patient-centric design, the PFSI sets new standards for usability, scalability and drug delivery efficiency.[4]

EXPLORING THE POTENTIAL OF SMI TECHNOLOGY

The effectiveness of certain inhaled therapies depends largely on the proportion of drug that reaches the lungs. This requires not only the right technology but also patient ease-of-use. Instead of relying on propellants or patient-generated force, SMIs deliver a therapeutic aerosol cloud through a mechanically activated system, dispersing the drug over approximately 3 seconds. This longer inhalation window reduces dependency on co-ordination, supporting successful use by certain patient groups, such as children, the elderly and those with disabilities. As the mechanism requires less effort and precision from the patient, SMIs can support improved outcomes through consistent dosing and increased lung deposition.

In addition to facilitating ease-of-use for patients and efficient drug delivery into the lung, SMI technology is creating opportunities for inhaled biologics. These biologics could expand treatment far beyond those for respiratory disease, enabling systemic therapies such as inhaled insulin or messenger RNA (mRNA) vaccines, as well as novel routes to target the central nervous system.

OVERCOMING THE CHALLENGES OF BIOLOGIC DELIVERY

While inhaled biologics offer significant therapeutic potential, their delivery presents unique challenges due to the large, fragile and often costly nature of these molecules. Effective pulmonary administration requires a container closure system (CCS) capable of maintaining the stringent requirements for biologics, as well as gentle aerosolisation to preserve molecular integrity and to ensure efficient lung deposition.

> "THE PFSI CAN BE CUSTOMISED TO ACCOMMODATE DIVERSE TARGET PRODUCT PROFILES, ENABLING TAILORED DOSING AND TARGETED LUNG DEPOSITION TO ADDRESS THE NEEDS OF VARIOUS PATIENT POPULATIONS."

A primary challenge for inhaled biologics is the packaging within the CCS. While biologics require a sterile environment throughout their use, they cannot tolerate preservatives or additives used in more traditional inhaler types. The PFSI uses a prefilled, sterilised glass syringe to maintain stability. This CCS has a valve that opens and then closes immediately as the patient inhales to prevent bacterial entry and maintain sterility for multidose use.

Highly sensitive biologics, such as mRNA and protein therapeutics, are often encapsulated in lipid nanoparticles (LNPs) to protect them from degradation during aerosolisation and to facilitate their delivery to the appropriate region of the lung. After deposition in the lung, these lipid carriers are typically taken up by cells, where they are degraded and can release the biologic payload that exerts its therapeutic effect. However, many conventional aerosolisation methods generate high shear forces that can disrupt or damage LNPs, leading to aggregation or loss of the encapsulated drug, or reduced biological activity.

The Resyca PFSI is uniquely suited to this challenge. Its spray nozzle employs the Rayleigh spray principle to create fine, uniform droplets under low shear forces, preserving the integrity of LNPs and other delicate carriers. A recent study evaluated aerosolisation techniques for preserving the integrity of mRNA-LNPs and optimising pulmonary deposition. The PFSI was shown to maintain mRNA-LNP physicochemical properties with minimal aggregation and superior encapsulation efficiency, while other devices induced particle alterations and mRNA degradation.[5] This gentle aerosolisation makes inhaled biologics clinically viable where other platforms fall short.

> "THROUGH GUIDED INHALATION, THE PFSI CAN ACHIEVE HIGH LUNG DEPOSITION OF UP TO 60%."

ENHANCING PATIENT CENTRICITY

Due to the cost of these next-generation therapeutics, inefficient delivery directly translates to reduced affordability and accessibility for patients.[6] Patient centricity is therefore an important consideration when designing any drug delivery device, as it can only be effective if patients are compliant and can use the device without errors.

Novel SMIs, such as the PFSI, offer flexibility to enhance patient centricity.[7] The PFSI can be customised to accommodate diverse target product profiles, enabling tailored dosing and targeted lung deposition to address the needs of various patient populations. Delivery characteristics such as particle size distribution, metered dose and fill dose can be customised to provide the best possible drug-device combination, for both efficiency and patient usability.

Even with optimised spray technology, inhalation performance varies between patients.[8] To address this, the PFSI incorporates guided inhalation through built-in flow resistance. This feature passively guides patients to perform slow and deep inhalations, a technique that encourages high lung deposition. Importantly, it requires no training and reduces both patient-to-patient and dose-to-dose variability. Through guided inhalation, the PFSI can achieve high lung deposition of up to 60%.[9]

As well as providing flow resistance for improved inhalation, the PFSI has a pocket-sized design for patient convenience, along with a reloadable cartridge, further enhancing the sustainability and affordability of the product. Patients can retain the device body while only replacing the cartridge, significantly reducing plastic waste compared with single-use inhalers.

The device also leaves a low residual volume of around 100 µL, maximising product yield and reducing waste of costly biologics. Together, these features lower both the environmental footprint and the overall cost of therapy.

DESIGNING FOR SEAMLESS MANUFACTURING

For successful adoption, device technologies must demonstrate clinical efficacy and integrate seamlessly with established pharmaceutical manufacturing processes. The PFSI achieves this by using prefilled glass syringes as its primary packaging. Glass syringes are already widely used, well-characterised and supported by global filling capacity. This reduces regulatory risk and development timelines, while also eliminating the need for dedicated facilities.

The PFSI can be used from early clinical studies through to commercial launch, avoiding the need to switch delivery platforms mid-development. This continuity reduces device development risks and regulatory complexity. Furthermore, in an era of evolving environmental regulations and demands, sustainability is also central to the design. Reloadable cartridges and minimal residual volumes reduce waste and environmental impact.

By combining existing, proven technologies with novel engineering, the PFSI enhances drug delivery performance, reduces waste and prioritises patient centricity. On top of this, by combining Resyca's SMI technology with the contract development and manufacturing capabilities of Bespak (Holmes Chapel, UK), developers can take advantage of comprehensive support to bring their SMI concept to life.

UNLOCKING IP PROTECTION AND DEVELOPMENT EXPERTISE

As a novel platform, the PFSI offers compelling opportunities for intellectual property (IP) protection. Unlike many inhalers that imitate existing designs, the PFSI introduces functional differentiation that can result in new patents. This can extend exclusivity for drug-device combinations and enhance the commercial lifetime of therapies.

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The device is well suited to the US FDA's 505(b)(2) pathway and NDA projects, providing flexibility for developers balancing innovation with speed-to-market. Resyca's expert team can further support such development projects, helping developers navigate device strategy, regulatory needs and delivery science to simplify and de-risk the path to commercialisation.

SHAPING THE FUTURE OF SOFT MIST INHALATION

The Resyca PFSI marks a significant advancement in SMI technology. Through proven prefilled syringe packaging, precision spray nozzle engineering, guided inhalation and a reloadable cartridge system, the PFSI addresses the key challenges of developing inhaled therapies.

For patients, the PFSI simplifies use, reduces errors and improves outcomes. For developers, it offers a scalable, customisable and IP-protected platform compatible with existing infrastructure. For healthcare systems, it reduces waste, enhances sustainability and improves the cost-effectiveness of biologic delivery.

With the increasing demand for new inhalation therapies, the need for efficient, patient-centric and sustainable delivery platforms is paramount. The Resyca PFSI is uniquely positioned to meet these needs, enabling precise and reliable delivery of even the most fragile molecules. In this way, it is shaping the future of soft mist inhalation, advancing innovation while keeping patients at the centre.

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