



Airborne Advantage

Biotherapeutic therapies are being approved at an increasing rate and are widely expected to dominate the pharmaceutical market across most routes of administration.

Biotherapeutics are often based on genetic code rules which might benefit from advances in generative artificial intelligence. This predicted enhancement may enable more precise disease-mechanism-focused treatments and improved prevention. Yet only a small

Dr Mireia Puig-Sellart, PharmD, PhD, inhaled biologics specialist at Phillips Medisize, explores the biological rationale, technological advances and clinical momentum behind inhaled biologics.

number of biologics are marketed as inhaled and nasal products. This has long been attributed to the perceived risks associated with delivering large, delicate molecules through a complex respiratory route. However, progress in inhalation device technology and formulation science now allows biologics

to be delivered to the lungs with high efficiency, helping reshape the landscape for inhaled therapeutics.

LIMITATIONS OF PARENTERAL ADMINISTRATION OF BIOLOGICS FOR LUNG TARGETING

Biologics can sometimes be



administered parenterally with the intention of reaching the lungs, but this approach typically offers only modest delivery to lung tissue. In practice, only a very small fraction of an injected antibody tends to reach the respiratory tract, meaning the rest of the body is exposed to a therapy that is meant for a much more specific target.

It is also important to recognise that injectable biotherapeutics, like vaccines, do not engage the mucosal immune system within the respiratory tract. This is significant as the respiratory tract is the primary entry point for airborne pathogens, and the mucosal surfaces of the nose and lungs interact with these agents constantly. Although a large proportion of commercial vaccines target airborne pathogens, only a small number are designed to activate mucosal immunity directly. By relying on systemic injections, we might lose the opportunity to generate a strong and localised mucosal immune response that is often obtained using nasal and lung vaccination.

THERAPEUTIC ADVANTAGES OF DIRECT RESPIRATORY DELIVERY OF BIOLOGICS

A key advantage of delivering biotherapeutics to the lungs is the ability to achieve local targeting at the site of action. When treating a lung condition, administering the therapy straight to the affected organ offers clear benefits compared with a general systemic approach.

There are also additional opportunities linked to respiratory delivery that are worth noting. The lungs provide a surface area of nearly 100 m² with an air

blood barrier that is only 1 µm thick. This delicate membrane allows the absorption of certain small molecules and also enables certain small biotherapeutics, including small peptides, to reach the systemic circulation. This supports rapid absorption and a fast onset of action, as seen with inhaled insulin. Although insulin bioavailability is lower than with subcutaneous administration, inhaled insulin remains a reliable and clinically valuable option that provides rapid therapeutic effect without the need for a needle.

Further respiratory advantages may be achieved through nasal delivery. This route is well established for the treatment of conditions such as allergies, congestion and rhinitis. It is also used for systemic peptide administration, particularly for hormones, and interest in this approach continues to expand. Pathways that connect the nasal cavity to the brain and bypass the blood brain barrier are becoming increasingly relevant as scientific understanding in this area expands.

INHALATION FORMULATION AND MODERN DEVICE TECHNOLOGIES ENABLING RESPIRATORY DELIVERY

Inhalation formulation science and device engineering have advanced considerably, yet important questions remain. A central challenge is how to deliver a large and fragile biologic, through a highly turbulent and humid environment during manufacturing or administration, while still ensuring that it remains bioavailable at the intended site of action.

For liquid formulations, a

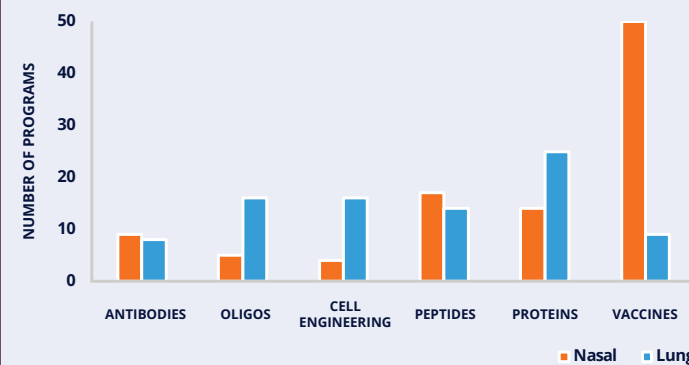
common approach is the use of a vibrating mesh nebuliser, particularly a smart- and breath-actuated design. Devices in this category, including the Phillips Medisize FOX Vibrating Mesh Nebulizer, are gentle on the biologic and provide efficient delivery with minimal residual loss of high-cost materials.

Solid-state formulations are also increasingly used because they offer meaningful advantages, including the removal of cold chain requirements. Particle engineering through spray drying allows liquid biotherapeutics to be transformed into stable inhalable powders. The powder can be delivered by a range of dry-powder inhaler designs, such as the Phillips Medisize O1 unit dose disposable dry powder inhaler concept device. Spray drying helps stabilise the biologic, producing particles with low moisture content and aerodynamic size suitable for deep lung or nasal deposition.

A GROWING CLINICAL PIPELINE OF RESPIRATORY BIOTHERAPEUTICS

Marketed inhaled biotherapeutics remain limited. One enzyme (dornase alpha) widely used for local treatment of cystic fibrosis, along with biosimilar forms, and one recombinant peptide (insulin) represent the current landscape for pulmonary biologic delivery. Nasal biologic products include synthetic peptides intended for systemic use, such as hormones, as well as vaccines for respiratory infections including influenza.

However, close to 100 inhaled biologic programmes and a similar number of nasal programmes are now progressing through clinical development. These include antibodies delivered nasally to prevent COVID by creating an immune shield at the initial entry point; oligonucleotides such as mRNA for cystic fibrosis treatment to encode the full-length CFTR protein; bacteriophages investigated for drug-resistant infections; peptides and proteins assessed for respiratory infections; and nasal influenza vaccines and inhaled tuberculosis vaccines developed with viral vector technologies. Together, these advances signal growing clinical activity in biotherapeutics respiratory innovation.



CASE STUDIES DEMONSTRATING PROGRESS IN RESPIRATORY BIOLOGIC DELIVERY

There are several ways to deliver biologic molecules to the

respiratory tract, ranging from delivering complex liquid formulations using a vibrating-mesh nebuliser to stable solid particles designed for inhalation.

One in-house example involved a nebulised recombinant protein developed for the treatment of idiopathic pulmonary fibrosis with the FOX nebuliser. A lead formulation originally intended for injectable use was adapted for pulmonary delivery by replacing injectable excipients with those that have established precedent in respiratory applications. The viscosity of the liquid was adjusted for efficient vibrating mesh nebulisation, and the amount of surfactant was carefully optimised. Achieving the right surfactant level supported effective drug delivery rates and helped reduce treatment times for patients. Comprehensive evaluation of protein structure, aggregation and potency before and after nebulisation confirmed that the molecule could be redirected to lung delivery and supported early clinical evaluation without compromising performance.

Another example was a monoclonal antibody fragment for severe asthma, initially designed for nebulisation but later transformed into a dry powder inhaler to remove the need for cold chain storage and to enable single inhalation dosing. Particles smaller than 5 µm were produced through spray drying with stabilising sugars and a shell forming agent. After spray drying, testing showed minimal aggregation and preserved biological activity. The powder was filled into a Phillips Medisize blister device and



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demonstrated excellent lung dose delivery. The formulation supported clinical studies and remained stable at 30°C for more than 2 years.

A more general example: lipid nanoparticles (LNPs) and their diverse cargo also hold considerable promise for lung delivery. Their ability to carry many types of genetic payloads has the potential to reshape the treatment landscape for respiratory diseases and support the development of mucosal vaccines. These formulations are delicate, however, and the choice of respiratory delivery system requires careful consideration. Encapsulating nm sized LNP into respirable microparticles offers a successful approach for directing them to the

respiratory tract. This strategy could strengthen preparedness for future pandemics by enabling rapidly produced mRNA therapies to be engineered for aerosol delivery in a dry state, reducing reliance on the cold chain and targeting the mucosal immune system before pathogens can take hold. Such therapies could be administered through a single self-administered dose at home leading to improvements for patients and increasing efficiencies within healthcare systems.

INHALED BIOLOGICS AREN'T JUST A POSSIBILITY, THEY ARE THE FUTURE

It is increasingly clear that systemic injections provide limited lung targeting and do not activate mucosal immunity,

while the lungs and nose present powerful biological opportunities that merit greater attention. Advances in respiratory formulation together with modern inhalation devices offer a clear and lower-risk approach for delivering biologic therapies directly to their intended site of action. The complexity of respiratory delivery can be managed effectively, and the associated risks can be significantly reduced. As inhaled biotherapeutics become part of standard medical practice, patients will be able to treat themselves rapidly at home, therapies will reach global populations without reliance on the cold chain, and mucosal immunity will help prevent diseases before they establish infection.