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Scaling Capabilities in Nasal Drug Delivery

Nasal drug delivery has traditionally been used for local, inflammatory conditions within the sinus cavity, such as rhinitis and nasal congestion. In recent years however, it has evolved into a versatile route for systemic drug uptake via the nasal epithelium, intranasal vaccination and even emerging nose-to-brain delivery. This evolution has made nasal administration a promising route for both new chemical entities (NCEs) and reformulated therapies with patent-expired formulations.[1]

As applications grow, so does complexity. Every nasal product is unique, defined by where it needs to act, how quickly it needs to work and how it needs to be delivered. Developers must navigate formulation and device challenges, from mucosal clearance to bioavailability, whilst meeting stringent manufacturing and regulatory demands. These factors are driving more innovators to partner with specialist contract development and manufacturing organisations (CDMOs) with the expertise, technology and facilities to help scale their bespoke nasal drug-device combination products to the clinic and beyond.

Next-Generation Nasal Applications

As a route of drug administration, the nasal cavity offers several advantages over oral, intravenous and even pulmonary delivery. Its highly vascularised epithelium allows for rapid drug uptake. Additionally, bypassing first-pass metabolism can enhance the bioavailability of certain therapies. Intranasal delivery can also generate strong immune responses, making intranasal vaccination particularly attractive. Beyond this, nasal administration can offer improved patient experience and compliance through non-invasive, needle-free delivery.

These benefits have led to the successful emergence of nasal systemic therapies that reach the bloodstream, such as naloxone nasal sprays for opioid overdose, dihydroergotamine (DHE) for acute migraine and epinephrine for anaphylaxis. Ongoing research is also exploring direct nose-to-brain delivery through the olfactory epithelium, bypassing the blood-brain barrier.

One of the most promising frontiers for nasal delivery is biologics, such as peptides, monoclonal antibodies (mAbs) and stem cells. Unlike small molecules, however, biologics are larger and more susceptible to stability issues due to factors like pH, osmolality and enzyme activity in the nasal mucosa. Delivering these molecules therefore requires precise formulation development and targeted device technologies which do not destabilise the biomolecules.

Challenges in Formulation and Device Development

Nasal products are drug-device combination products, meaning the drug and delivery system must be developed in parallel to ensure optimal performance. Targeting the

correct site of action, whether local, systemic or nose-to-brain, dictates requirements for other factors, such as droplet size, spray pattern and plume velocity.

Formulations themselves vary in complexity, from aqueous solutions and suspensions to powders, each with specific storage, stability, dosing, and delivery considerations. Biologics, in particular, demand delicate handling, and traditional formulation components, such as preservatives, can be detrimental. While the nasal route offers a gentle delivery environment that can handle these larger, more sensitive molecules, it does not come without challenges. For example, the nasal cavity is designed to protect against pathogens and debris, and so leaves only a short residence time before a drug is cleared. This makes mucosal clearance a critical factor for advanced therapies. One solution to this challenge is targeted deposition using delivery devices that aim for the olfactory region of the upper nasal cavity, where mucosal clearance is slower and epithelial permeability is higher.

Soft mist nasal devices, such as those developed by Resyca®, a joint venture between Bespak® and Medspray®, are designed to address many of these challenges. The unique Resyca nozzle, which creates precise droplet size with low shear forces and delivers them with a lower spray velocity, has been demonstrated to protect fragile molecules.[3] Furthermore, precision targeting allows enhanced delivery to specific regions and slower, longer-duration sprays improve coverage of the nasal epithelium.[4] These features open opportunities to deliver fragile molecules, higher drug loads and improved access to hard-to-reach regions of the nasal cavity, like the olfactory region. For therapies where consistent dosing and molecular stability are critical, this soft plume technology shows promise.

Manufacturing Complex Products

Manufacturing challenges are equally significant when looking to take a product to clinical and commercial scales. Standard multi-dose lines can accommodate many products, but next-generation nasal therapies often require bespoke solutions to support patient safety, product efficacy and regulatory approval. To solve these challenges, developers are increasingly partnering with CDMOs that have expertise and experience in nasal drug delivery.

Early engagement with a CDMO can help smooth the journey to commercialisation and reduce costly delays. In nasal drug delivery, where formulation and device development are tightly linked, early collaboration helps ensure that technical, regulatory and manufacturing considerations are understood. Choosing a CDMO that has been manufacturing nasal drug-device combination products for many years means gaining insight into optimal devices and access to a ready network of specialist partners.

Bespak, a specialist inhalation CDMO, offers decades of expertise in multi dose aqueous nasal sprays and has expanded into nasal powder systems for systemic applications, soft mist technology for the delivery of fragile molecules, and has a novel unit dose delivery device in development.[2] At its Holmes Chapel site, Bespak provides customised manufacturing for complex nasal products, with flexible clinical suites, bespoke equipment validation and seamless scale-up to commercial supply. This expertise is especially valuable for late-stage clinical candidates with unique dosage forms, non-standard devices or challenging delivery needs, helping to shorten timelines and reduce risk.

These site capabilities have been proven through recent customer experiences. Bespak recently partnered with a late-stage biopharmaceutical company to support the scale-up and commercial manufacture of an innovative intranasal migraine treatment. Another recent project demonstrated the site's capability to scale complex nasal therapies from early clinical supply to full commercial readiness. With these bespoke services, Bespak offers a flexible, future-ready partnership for even the most demanding and unique projects.

Capabilities for Bespoke Nasal Drug Delivery

Nasal drug delivery is not one-size-fits-all and, as the field continues to evolve, the need for manufacturing flexibility will only increase. The pipeline for nasal therapies is expanding, driving demand for CDMOs capable of bridging the gap from clinical development to commercial supply.

Bespak, with its proprietary device technologies, adaptable facilities, custom equipment capability and proven scaling experience, is positioned as a trusted partner for developers seeking to bring innovative nasal therapies to patients.

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Joe DePalo

Joseph DePalo is a Director of Business Development at Bespak, with 13 years of experience delivering pharmaceutical drug products to the U.S. market. Over the past four years, he has leveraged his foundation in biomechanical engineering, medical device development, and pharmaceutical expertise to support the unique challenges of combination drug products for inhalation and nasal delivery. He earned his Bachelor of Science in Biomechanical Engineering from Marquette University.