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An Integrated Approach to Inhalation Drug Development

The Inhalation Drug Development Landscape is Expanding

Inhalation drug delivery has traditionally been associated with a familiar set of indications, particularly asthma and chronic obstructive pulmonary disease (COPD). While these conditions continue to represent a major part of the inhalation market, emerging applications are expanding the field. Researchers and developers are increasingly investigating inhalation delivery across a broader range of therapeutic categories and technologies, with particular focus on dry powder systems and other inhaled dosage forms.

Globally, the inhalable drugs sector is projected to grow from roughly $36 billion in 2023 to nearly $60 billion by 2030 as new therapies and delivery approaches emerge.[1] New opportunities are emerging across therapeutic categories including oncology, neuropsychiatric therapies, and advanced biologics. However, these opportunities also bring new challenges.

Some of these programs require devices capable of delivering substantially larger powder payloads than conventional inhaled therapies, which often deliver microgram quantities of active pharmaceutical ingredient (API) through carrier-based systems. This shift means that successful inhalation development increasingly depends on thinking beyond the formulation itself and considering how particle properties, formulation choices, device performance, manufacturing, and clinical supply will ultimately interact.

Modern Inhalation Drugs Require Integrated Development Programs

Emerging applications ranging from oncology to psychedelic compounds illustrate why inhalation development cannot follow a simple formulation-first pathway. The requirements of the eventual product—where it needs to deposit, how much drug it must deliver, which device will administer it, and how it will ultimately be manufactured—can all influence decisions made much earlier in development. Developers therefore need to consider the intended route, deposition profile, device, manufacturing process, and eventual clinical use before committing too far to a formulation strategy.

Particle Properties Determine Lung Deposition

Inhalation therapies rely on precise control of particle properties to determine where a drug deposits in the respiratory tract. Many parameters determine whether particles remain in the upper airway, deposit in the bronchi, or reach the deep lung.[2] Additional parameters, such as device resistance, may also influence how much inspiratory effort is required and how airflow develops through the inhaler, which in turn affects aerosol generation and lung deposition. A device that performs well under laboratory conditions may therefore behave differently when used by patients with varying inhalation profiles.

In addition to standard cascade impactor measurements, developers may use breath simulators and anatomically realistic airway models to replicate patient inhalation profiles and better understand how particle and formulation characteristics translate into aerosol behavior and lung deposition under realistic use conditions. Taken together, these risks highlight the importance of evaluating device performance early and under realistic operating conditions.

Selecting the Right Excipients

Excipient selection presents another potential risk with far-reaching consequences. Often, materials that perform well in oral or parenteral formulations are not automatically suitable for pulmonary delivery. Certain excipients may irritate lung tissue, interfere with aerosolization, or fail to produce particles within the appropriate aerodynamic range. Formulation components therefore need to be considered not only for drug stability and particle formation, but also for compatibility with the lung's physiological environment and the physical requirements of inhalation delivery.

Device Design Influences Powder Dispersion

For inhaled drugs, the choice of delivery device is no simple decision. Device design directly influences powder dispersion and the airflow conditions under which aerosolization occurs. In turn, the aerosol depends on the interaction between formulation properties, device geometry, and airflow. When these factors are poorly matched, powder may not disperse effectively, potentially leading to inconsistent aerosol performance and delivered dose. This mismatch can become significant when developers use simple research devices during early formulation work and later transition to a different device.

Many developers begin inhalation programs using simple capsule-based platforms paired with widely available research devices. These systems are straightforward, commercially accessible, and familiar across the industry. They also provide a practical way to evaluate powder engineering and aerodynamic particle size distribution (APSD) without committing to a proprietary device. However, if the program eventually transitions from a capsule-based platform to a proprietary or bespoke device, this may directly affect the aerosolization mechanism. Relatively small changes in device design can alter particle-size distribution, aerosol performance, or delivered dose. Furthermore, if those changes emerge late in development, they may require additional analytical work or further safety evaluation.

Manufacturing Needs Should be Considered Alongside Aerosolization

A powder that performs well during laboratory aerosol testing may not necessarily be straightforward to manufacture. In fact, the same characteristics that support effective aerosolization can often make a powder difficult to handle, fill, and load. For example, highly micronized or spray-dried particles frequently exhibit poor flowability and strong cohesion unless combined with carrier systems like lactose. Conversely, changes introduced during scale-up, device manufacturing, filling, or packaging can also affect the performance of previously characterized particle-formulation-device systems. To overcome these challenges, these requirements must be considered alongside aerodynamic performance during early stages of development.

Particle Engineering Solutions to Modern Development Challenges

Particle engineering sits at the center of inhalation development because it must balance lung deposition, aerosolization, formulation stability, and manufacturability. The particle's physical characteristics therefore determine how an inhaled formulation performs. Aerodynamic particle size, density, morphology, and surface characteristics all influence how powders disperse and travel through the airways, affecting whether particles deposit in the upper airway, bronchi, or deep lung. These properties must be carefully controlled because changes that improve one aspect of performance can also alter powder handling, formulation stability, or interaction with the delivery device.

Spray drying has become one of the most widely used tools for engineering inhalable particles because it allows developers to control many of these parameters - including particle size, morphology, and surface composition - in ways that improve aerosolization. The technique has also attracted attention for inhalable biologics and other complex molecules that require carefully engineered particles to remain stable and dispersible during delivery.[3]

Electrostatics and Humidity Affect Stability

Even when particle size and morphology are carefully controlled, powders can exhibit other physical behaviors that introduce variability during processing and delivery. Electrostatics and humidity can introduce further sources of variability. Fine powders can accumulate electrostatic charge and adhere to equipment or device surfaces, while humidity can alter particle adhesion and dispersion behavior. After drying, morphology, residual solvent content, and surface energy all influence how powders behave.[4] Furthermore, moisture exposure may further influence stability and aerosol performance over time.

These effects can become particularly problematic during manufacturing and device filling, where changes in powder behavior may result in inconsistent recovery, filling performance, or delivered dose. Managing these variables requires developers to consider not only the powder's intrinsic properties, but also how those properties may change under the environmental conditions encountered during processing, storage, and use.

Expanding Dose Requirements and Device Risks

Larger Dose Requirements and Device Capacity

Emerging therapeutic applications are expanding expectations around dose capacity. Whereas traditional inhaled therapies typically deliver microgram quantities of active pharmaceutical ingredient, some newer therapeutic classes may require substantially larger powder payloads to achieve clinical activity. Delivering tens of milligrams of finely engineered powder in a single administration is technically feasible but can strain existing device architectures and filling technologies.

This strain is driving demand for innovative inhalation devices that can accommodate larger payloads while maintaining consistent aerosolization and dose delivery. For these devices, the physical interaction between larger powder loads and the device's internal materials and geometry becomes increasingly important. Additionally, materials such as surface finish, polymer composition, and electrostatic properties can influence how powders interact with internal components.

Device Materials and Powder Retention

Material properties can directly contribute to powder retention and inconsistent dose delivery. Capsule-based devices rely on airflow and mechanical puncturing to release powder from the capsule and disperse it into an aerosol. If the powder does not interact effectively with these mechanisms, some may remain in the capsule or device, reducing the delivered dose even when laboratory testing suggests an acceptable aerodynamic particle size distribution.

Materials that accumulate electrostatic charge may promote particle adhesion, while electrostatically dissipative materials can reduce unwanted deposition inside the device. In multi-dose devices, this accumulation can become additive, potentially affecting performance across repeated actuations. Material selection, surface properties, and electrostatic behavior can therefore influence how consistently a device delivers its intended dose.

Dry powder nebulization is an emerging delivery technology that could combine the techniques of conventional nebulizers, potentially enabling controlled aerosol generation while reducing reliance on patient inspiratory effort.

Device Resistance and Patient Use

Unlike nebulizers, dry powder inhalers rely on the patient's inspiratory effort to generate the airflow that disperses and deagglomerates the powder. Device resistance affects the relationship between inspiratory effort and airflow through the device, which can influence aerosol generation and ultimately the delivered dose. If some patients find it difficult to achieve the required inspiratory flow, the device may produce different aerosol performance under actual use conditions than during laboratory testing. Device resistance is therefore both a patient-use consideration and an important component of inhaler performance.

Regulatory Considerations

The consequences of these interconnected design decisions extend beyond technical performance into regulatory requirements. Because inhalation products combine pharmaceutical and device elements, regulators treat them as combination products. During development, developers must therefore evaluate device components not only for extractables and leachables but also for biocompatibility. The wide range of regulatory and performance requirements illustrates why an inhalation product cannot be assessed solely by asking whether the formulation produces an acceptable aerosol. Formulation and device development typically receive the greatest attention during inhalation programs, but clinical supply can become an equally significant constraint as products progress toward human studies.

Clinical Supply Constraints

Clinical supply can become an important constraint as inhalation products move toward human studies. Moving from early development processes toward commercial manufacturing pathways can introduce additional challenges, particularly when laboratory-scale workflows are not sufficiently representative of later-stage manufacturing. Single-dose and bespoke devices may require filling, sealing, forming, and packaging operations that remain partially manual at clinical scale. At the same time, device-based products can create additional packaging and storage requirements. Blinded trials introduce another layer of operational complexity, as pre-packaged units may need to be opened, labeled, and resealed while preserving the blind. Each additional handling step can increase cost and operational risk.

These considerations make early coordination between formulation development, device manufacturing, and clinical supply particularly important. When these activities proceed in isolation, they can lead to inefficient workflows, unnecessary repackaging, and unexpected costs or delays. Inhalation products remain device-driven even after the formulation performs as intended, and the decisions made during particle engineering can affect formulation, device selection, manufacturing, clinical supply, and ultimately patient use. These technical and operational considerations illustrate why inhalation development is difficult to manage through isolated workstreams.

Integrating Expertise Throughout Drug Development

Inhalation development works best as a collaborative, iterative process rather than a series of handoffs. Few teams can cover the full range of expertise required, from particle engineering and formulation through device performance, manufacturing, and clinical supply. With deadlines and budgets pressuring every development program, a problem missed early can quickly become expensive to fix and may ultimately derail a promising therapy. Working closely with an experienced inhalation CDMO can help developers bring these capabilities together, identify potential gaps early, and keep the program moving along the development pathway.

How such collaboration is organized can vary, however, depending on the program's needs and maturity. Some developers want a clearly defined scope, with individual activities planned and priced as discrete work packages. Others prefer a dedicated team that can pursue questions as they emerge and adapt experiments as the development program evolves. Both approaches can work. What matters is having a partner that can adapt its operating model without losing sight of the scientific and development objectives.

Experic's Integrated Capabilities

Experic brings together capabilities across particle engineering, formulation, aerosol performance, and manufacturing. Specializing in advanced powder-handling and inhalation capabilities, we help small, mid-sized, and specialty drug developers address challenges with fine powders and highly potent compounds across the full product lifecycle from particle to patient. Contact us to discuss how we can help support your program.

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