White Paper

Dry Powder Inhalers on the rise

Boosting treatment adherence with new developments and processes

The market for drug device combination products supporting the treatment of respiratory illnesses is growing at a rapid pace. While the reasons for this growth are multifold, manufacturers of respiratory inhalers are constantly working on innovative solutions for more precise drug administration. They are supported by dedicated CDMOs who have the expertise and the capabilities in both development and production of these urgently needed devices.

According to a recent market report by Market Research Future, the market for respiratory inhalers is predicted to grow at 4.9 % CAGR during the forecast period 2022-2030 and to reach 41.4 billion USD by 2030 globally, with North America being the strongest growth region, followed by Asia-Pacific, Europe and the rest of the world. Among the most prominent respiratory illnesses, asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF) are boosting the need for respiratory inhalers.

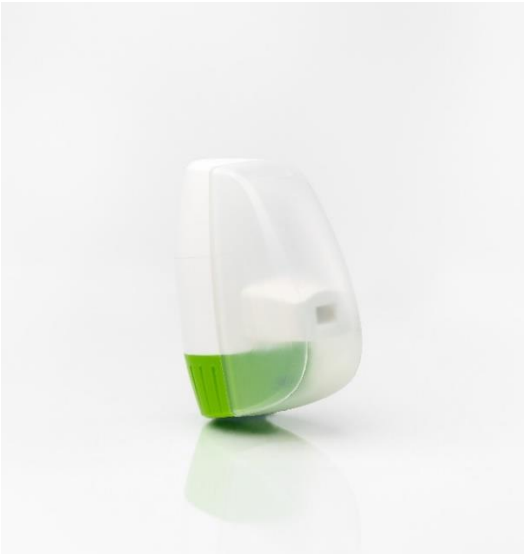
According to the World Health Organization (WHO), COPD is the third leading cause of death worldwide, causing 3.23 million deaths in 2019 alone. Asthma, on the other hand, affected an estimated 262 million people in 2019 and caused 455,000 deaths. Around 105,000 people have been diagnosed with CF across 94 countries, according to the statistics from the Cystic Fibrosis Foundation. The number of cases is predicted to increase during the coming years, amongst others due to increased air pollution, the rising emissions of greenhouse gases, but also the long-term effects of active and passive smoking, as well as the exposure to occupational dust and chemicals in some regions. Moreover, the ageing population will further promote the need for treatment.

Challenge number one: higher treatment adherence

What all these diseases have in common is the need for exact medication. Unfortunately, the medication non-adherence rate is still very high – in the case of asthma, it ranges between 25 and 75 percent, according to the National Council Medical Director Institute. While respiratory inhalers are considered the most effective way to administer the required medicine, many

patients are still reluctant and uncertain of how to use them. They either don't follow the prescribed regimen, or – the majority with inhalation – they misuse the device. Combined with high prices, the acceptance is still not as high as it could be. However, new easy-to-use drug delivery devices and the programs of many governments to provide patients with affordable medical equipment will positively impact market growth. When used in the correct way, respiratory inhalers can provide highly effective treatment and can also promote the use of combination therapies.

The advantages of DPIs



The delivery of a dry powder formulation to the lungs for a local or systemic drug effect is achieved by using specific devices known as dry powder inhalers (DPIs). They are the fastest-growing segment in the asthma and COPD devices market and the foreseeable phasing down of hydrofluoroalkane propellants due to climatic changes is expected to further boost their development. Compared to pressurized metered dose inhalers (pMDIs), DPIs do not require a propellant to deliver a specific amount of drug and do not need to synchronize inhalation with actuation. DPIs are easier to use due to the breath-actuated release of medication in dry powder form. Dry powder aerosols are created by directing air through an aliquot of loose powder.

Basically, there are three types of DPIs: (1) unit-dose devices, in which an individual dose in a gelatin capsule or blister is loaded by the patient immediately before use; (2) multiple unit-dose devices, which contain a series of blisters or capsules; and (3) reservoir devices, where powder is metered from a storage unit of drug powder in bulk by the patient before inhalation. All DPIs require the patient to prepare a dose before inhalation. The appropriate procedure is described in the package insert or patient information leaflet. Patients who do not perform these procedures correctly may receive no dose, irrespective of the inhalation maneuver they adopt – a critical error that occurs frequently.

Many companies are further incorporating digital technology into their inhaler devices, such as sensors and connectivity features, to help patients track their medication usage and improve adherence. They support patients with certain functions, such as reminders or dosage information. The collected data can be stored on the device or transferred to a cloud-based platform. A connection to digital interfaces enables direct data analyses. In addition, smart inhalers can support telemedicine, make it easier to evaluate clinical studies, and facilitate traceability.

Working together for optimum results

In all regions worldwide, medtech companies are working on new inhalation solutions for better patient adherence. While Asia, and especially China, faces the challenges of intellectual property protection and very time-consuming approval of inhalation devices, all manufacturers worldwide need to differentiate themselves and find means of achieving a sustainable business model. If they want their inhalation devices to be accepted by patients, user-friendliness and an ergonomic design are highly important quality features. They make a decisive contribution to correct use and acceptance, which ultimately improves therapeutic success.

Hence, it is crucial to pay special attention to these factors in the earliest stages of the development process. This requires a specific process that enables not only detailed product specification, conception, and development of individual solutions, but also does this under competitive conditions. How can all these requirements be reconciled? Which characteristics must a new inhaler solution fulfil to support treatment adherence with convenient and efficient handling? The answer lies in a holistic development process that encompasses several phases – from the development of a first idea through product design to large-scale serial production.

The Sanner Group supports clients all over the world with its holistic six-step Sanner IDP Process® for customized solutions, as well as contract design and manufacturing for drug delivery, medtech and diagnostic projects. The process already starts in the concept and design phase where the processability of the device and the tool development are considered. From rapid prototyping through efficient industrialization to commercialization, this holistic process ensures validated and qualified development.

Best practice example: reservoir type DPI

Especially in China, Sanner has supported clients with the development and optimization of DPIs for several years. An example is the development of a reservoir type DPI. This type of DPI faces very specific challenges, including the air resistance of the device, a stable dosing weight, the delivery and separation of the API and the carrier substance, as well as meeting the critical internal humidity requirements.

Most powder-dispensing systems require the use of carrier substances. This vehicle substance is mixed with the drug to enable the powder to pass out of the device more readily. The carriers that are used include lactose and glucose. Allergic reactions to the lactose and glucose appear to be fewer than to the surfactants and propellants used in pMDIs, even though the amount of these substances is substantially greater than the drug and can represent 98% or more of the weight per inhaled dose in some blends. The particle size of dry powder particles is between 1 and 2 µm, while the size of the lactose or glucose particles can range from approx. 20 to 65 µm. Consequently, most of the carrier deposits in the oropharynx. Hence, the aerodynamic particle size distribution is a critical quality attribute. It defines how particles behave in a moving air stream, which considers the separation rate of the medicine powder and the carrier and is secured by the channel design.

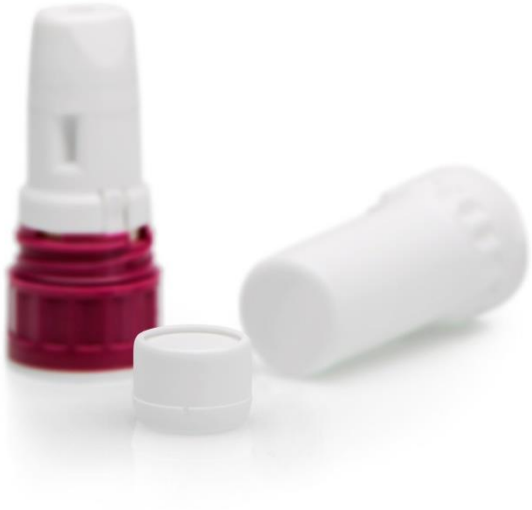
The air resistance and the aerodynamic particle size distribution of the device highly depend on the size and surface characteristics of the particles in the powder blend. The design shape and the geometry of the passage opening of the inhalation channel is crucial to guarantee an optimized “flow” of the formulation out of the device, which must be reflected in the mold configuration. The inhalation channel has to provide an exact dose to the patient during inhalation and therefore ensures the separation of the drug from the carrier in the mouth, with the required dose of API going directly to the lungs, increasing the drug efficacy.

Highly precise component parts

The exact dosing of the powder at a constant weight must correspond to the requirements of DIN ISO 20072, in this special case the deviation between the first and last dose should be within a range of +/-15%. Another important part of the design consists in preventing powder leakage and ensuring the highest dosing accuracy. Comparable to a mechanical watch, all component parts must fit precisely. This also applies to counting accuracy: only if the counting plate has the correct rotation function, the numbers will be fully visible and exactly printed.

To master all these challenges, the choice of the right material according to the shape and function of each part is crucial. All materials must comply with FDA and NMPA regulations and standards. Moreover, they need to pass compatibility tests with the respective medicine powders. Moreover, the definition of the assembly steps is essential for the production layout of a DPI. They must be efficient but above all they require the highest precision when assembling a DPI with 16 component parts or more.

Desiccant expertise as advantage



The water content of the medicine powder is as crucial as the ambient humidity that can affect drug powders delivered from DPIs. Both must be reflected in the type and amount of integrated desiccant, otherwise the powder cannot move in the inhalation channel and will not be separated from the carrier in an ideal way. Also, the humidity adsorption speed needs to be defined depending on the dry powder properties. The paper board separating the desiccant must be molded ideally with the plastic parts to prevent the desiccant from leaking and contaminating the medicine. By working with a device CDMO like Sanner who has expertise in both areas – drug device combination product development and desiccant manufacturing – suppliers of DPIs have a decisive advantage.

Significantly more space for DPI and MDI projects

Sanner is continuing to prepare itself for further growth in both Asia and Europe. In China, Sanner will start production in a new facility in summer 2023. 4,000 additional square meters of production space are currently being built, including grade D or class 8 clean rooms for GMP-compliant production of pharmaceutical and medical packaging solutions. The site will further comprise a warehouse, a mold workshop, and office areas. A high degree of automation and energy-saving peripheral systems will secure highly efficient production. Altogether, Sanner will be able to increase production capacities in China by around 80 percent.

The new facility in Bensheim, Germany with its 30,000 square meters will allow Sanner to double its German production floor by September 2024. State-of-the-art and highly automated equipment will expand the production capacity by even more than 100 percent. 300 square meters are reserved for the technology and innovation center, where customer-specific solutions and prototypes will be developed. The main production floor for molding and assembly is kept flexible to adapt to customer needs in both the packaging and device CDMO areas. Clean room capacity is ISO class 7 and 8 incl. ESD floors for the production of electronic medical device components will also increase significantly. This way, Sanner will offer customers the highest possible flexibility and automation in both regions – and the space to cater to all needs of device manufacturers.

Towards better treatment adherence

By knowing market demands, trends, regulatory and processing requirements, CDMOs such as Sanner can be invaluable partners to medtech device manufacturers. High transparency and open communication in all project phases is key to keep everyone informed about the current status at any time. Thanks to professional project management and profound expertise, a multi-stage process facilitates the development of new inhalation devices, which will enable device manufacturers to expand their share in the growing inhaler market. But most importantly, both parties will jointly contribute to patients' wellbeing around the world by increasing the ease-of-use of inhalation devices and thus ensuring higher treatment adherence.

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About Sanner

Sanner was founded in 1894. Headquartered in Germany and leveraging its best-in-class manufacturing facilities across Germany, France, Hungary, and China, Sanner has developed from a global market leader for desiccant closures and effervescent tablet packaging into a sought-after provider of customized solutions in the areas of medical devices and diagnostics, pharmaceuticals, and consumer healthcare. Today, Sanner supplies its products to more than 150 countries globally and has over 600 employees. Since November 2021, GHO Capital Partners LLP, a leading specialist healthcare investment advisor, holds the majority shares of Sanner. Together, GHO and the fourth generation of the Sanner family will continue the successful growth and create intelligent healthcare solutions for a better quality of life.