GERRESHEIMER

DEVELOPMENT AND PRODUCTION OF THE RESPIMAT® REUSABLE INHALER HOUSING MODULE

Here, Josef Schmid, Program Manager, Markus Müller, Development Engineer, and Nina Zielonka, Mould Engineer, all of Gerresheimer, discuss Gerresheimer's recent work on developing the housing module for Boehringer Ingelheim's new version of the Respimat® inhaler, including how design and creation of manufacturing equipment for the industrial scale-up took place in tandem with device design to meet the desired schedule.

Recently, Gerresheimer was commissioned by Boehringer Ingelheim to develop and produce a housing module for the new generation of Respimat® inhalers (Figure 1). The new model is an environmentally friendly successor to the established Respimat® inhaler, which can be successively loaded with up to six active agent cartridges, thus ensuring less waste and a considerably reduced CO_2 footprint over the product lifecycle. Gerresheimer developed the housing module for the new inhaler and built the pre-series and series moulds, as well as the special-purpose machinery, for both pre-series and series production. Gerresheimer is also providing the scaled-up industrial production.

> "One of the challenges Gerresheimer faced during product development and industrialisation was the need for the new inhaler to be immediately available in large numbers for its market launch. Therefore, it was necessary to immediately transition from the development phase to a robust, high-volume series production."

The Respimat® inhaler is a firmly established product in the respiratory drug delivery market. Patients with chronic lung diseases, such as chronic obstructive pulmonary disease (COPD), use bronchodilation drugs on a daily basis to relieve their illnesses. Alongside the

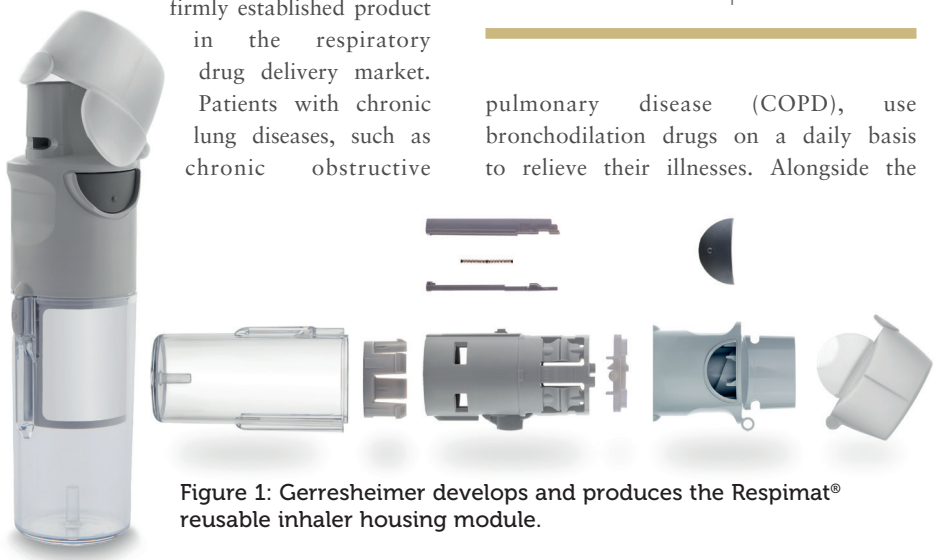

Figure 1: Gerresheimer develops and produces the Respimat® reusable inhaler housing module.

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frequency of required use is a correspondingly high demand for inhalers, which usually need to be replaced once the active agent has been exhausted. To address this, Boehringer Ingelheim decided that the new version of the Respimat® would be reusable. In addition to being more environmentally friendly, the new Respimat® incorporates feedback from patients using the current model, including improving the inhaler's ergonomics, via an extension of the housing, and making the dosage display more readable.

ROBUST DEVELOPMENT FOR A TIGHT PRODUCTION TIMELINE

One of the challenges Gerresheimer faced during product development and industrialisation was the need for the new inhaler to be immediately available in large numbers for its market launch. Therefore, it was necessary to immediately transition from the development phase to a robust, high-volume series production. In technical terms, a reversible blocking mechanism had to be developed for the inhaler, without significantly changing the exterior design of the product and the valuable high level of recognition that goes with it.

In order to meet such a demanding schedule, both the device-development phase and the creation of equipment for large series production were undertaken simultaneously. Another decisive factor for the success of the project was the availability of Gerresheimer's own cleanroom for small series production, which allowed for prompt testing of prototypes under real conditions (Figure 2).

Figure 2: Cleanroom production in small batch production of Gerresheimer in Wackersdorf, Germany.

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During development, a small-scale production foundation was first established using low-cavity moulds and semi-automated processes. On the basis of this foundation, the development of high-cavity moulds and fully automated processes for high-volume, large series production was undertaken immediately. By doing so, the development of the series equipment could be initiated ten months prior to the planned design verification. A risk-based approach that ensured the systematic mastering of all risks pertaining to the device functions was used for the jump to large series production (Figure 3).

Due to this robust development approach, along with the prescribed high functional density of the device, all functional tests for the design verification of the low-cavity moulds, and later those for the implementation of the high-cavity series moulds, were passed immediately.

Figure 3: High-volume line for the assembly of the Respimat® reusable inhaler housing module in a clean-room ISO class 8 in Pfreimd, Germany.

"The size and complexity of the high-cavity moulds for large series production, which weigh up to three tons, were especially challenging."

MOULDS OF EXTRAORDINARY COMPLEXITY

The moulds for the development phase and series production were developed, produced, and optimised in Gerresheimer's Technical Competence Center in Wackersdorf (Germany), which is home to its own mould-making facility. The size and complexity of the high-cavity moulds for large series production, which weigh up to three tons, were especially challenging. Gerresheimer used mould flow and finite element method calculations during mould development, as well as for the continuous improvement of the mould design and ensuring its long-life fatigue strength.

Verification of the results took place on the basis of real long-life fatigue strength experiments carried out on selected steel types. The start-up management of the moulds was secured with the help of Kepner-Tregoe analyses for the methodological, continuous improvement process. Work is currently being carried out on the creation and qualification of the third generation of successor tools.

INNOVATIVE AUTOMATION CONCEPTS

Gerresheimer used the innovative XTS system from Beckhoff (Verl, Germany) for the first time for automating the module assembly for the reusable Respimat®. Here, products are transported on movers, which are moved across the transport area by freely configurable electromagnetic forces. As a key component of the reusable inhaler, the device block requires a complex assembly process, for which an innovative assembly concept was formulated in a multi-stage process. This assembly process was initially realised in a semi-automatic assembly system and then transferred to an automated high-volume series machine. The immediate success of the acceptance run confirmed the chosen procedure.

ABOUT THE COMPANY

Gerresheimer is a leading international partner to the pharmaceutical and healthcare industries. The company contributes to health and well-being with its range of glass and plastic products. Gerresheimer has a worldwide presence, with around 10,000 employees; locations in Europe, Asia and North and South America; and an annual turnover of around €1.4 billion (£1.3 billion). The company's product offering includes insulin pens, inhalers, micro pumps, pre-fillable syringes, injection vials, ampules, bottles and containers for liquid and solid medications with sealing and safety systems, as well as packaging for the cosmetics industry.

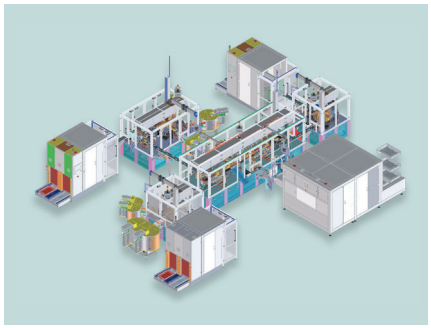
We bring every kind of medicine safely, reliably and conveniently to or into the patient!

Gerresheimer – your one-stop shop for every kind of drug delivery devices

With Gerresheimer Medical Systems as your partner, you profit from more than fourty years of experience in the development, industrialization and contract manufacturing of customized drug delivery systems. Each year, we produce over 150 million inhalers and more than 300 million insulin pens which meet the full requirements of modern pharmaceutical packaging. As a system supplier, Gerresheimer develops patient-friendly products that are easy to use, provide precise dosing, and efficiently transport the active substance to it's target site. Prior to production, we apply demanding quality standards to material selection, assembly technique and device functionality.

Product Development

Industrialization



Manufacturing

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