

Plastic in the Service of Medicine

Glittenberg Supplies Tools for Vital Medical Devices to Celon Pharma

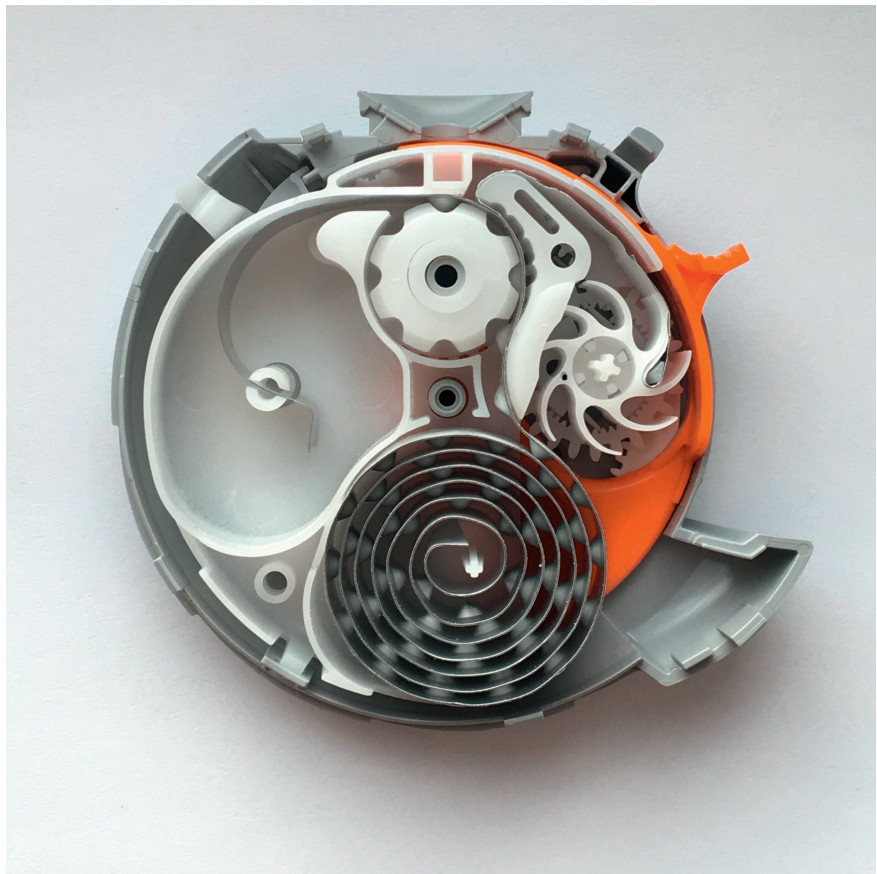
A Polish pharmaceutical company is developing inhalation therapy for the treatment of lung disease and the appropriate drug delivery drug. The inhaler has a complex interior and consists of 14 components. In order to be able to produce these with the required precision, Celon Pharma has formed a partnership with the mold making company Glittenberg and its hot runner sister Witosia.

Mostly detached from developments in other industrial sectors, medical technology continues to be a rapidly growing industry with great innovative strength. Diverse new products with new types of materials for a wide variety of applications offer a wide range of applications, in particular for the field of injection molding technology. Anyone who wants to play here, however, faces great challenges, and not only in terms of quality, innovation and cost efficiency. More than anything, the rules and regulations applicable in this sector must also be mastered.

Compared to other industries, the quality requirements are very high. The documentation requirements are extensive. Production in accordance with GMP (Good Manufacturing Practice) is mandatory. This requires permanent monitoring and compliance with hygiene regulations and complete documentation of all process data over many years. Entry into the medical technology industry as a supplier is therefore difficult and requires a great deal of effort.

Development of an Inhaler for an Enzyme Inhibitor

The Celon Pharma S.A. is a still young pharmaceutical company based in Kielpin near Warsaw, Poland. It was founded in 2002 by Marciej Wieczorek. Today, the company employs 400 people in Poland, including 70 scientists, and distributes medicines in more than 50 countries around the world. The great strengths of Celon Pharma are their extensive re-



For its complex functional mechanism, the inhaler requires 14 components (© Witosia)

search and development facilities. The company has two fully equipped laboratories that develop pharmaceutical products for the treatment of cancer, neurological disorders, diabetes and other metabolic disorders. Another focus is on the development, manufacture and distribution of specialized generics.

The production sites of Celon Pharma have attained appropriate GMP appro-

vals. The GMP certificate enables the company to obtain authorizations for sales and marketing of drugs in all EU countries. Existing quality standards for production are thereby guaranteed.

Celon Pharma launched the PIKCell project in 2014 as part of the EU funding program "European Regional Development Fund". The aim of the project is to use a PI3K inhibitor, which is used to treat

various types of cancer, also for the treatment of lung diseases such as asthma or COPD (chronic obstructive pulmonary disease). The method of administering this medicine is inhalation.

Sophisticated Mechanics with 14 Interrelating Components

As part of this project, Celon Pharma faced the challenge of developing and producing a fully functional discus inhaler (**Title figure**). The customer was requiring from the outset that all parts for the inhaler be manufactured with the highest precision and accuracy in order to ensure a completely reliable functionality. Deviations from the required dimensions and the maximum tolerance of ± 0.02 mm at the individual components of the inhaler are not permitted, since otherwise the function is impaired.

For example, when operating the inhaler, the blister must be transported exactly to the next medication reservoir, opened, the used conveyor belt wound up and the unused stored. The drug must then be completely pulled out of the opened blister and transported through the mouthpiece by a slight negative pressure, as it arises when inhaling a small child. On the other hand, during handling of the inhaler, the drug must not fall out of the reservoir of the blister prior to inhalation.

In this complex mechanism, a total of 14 components work perfectly together to bring the inhaler into the desired function. An absolutely clean and smooth



Fig. 1. The inhalers are fully automatically mounted in the cleanroom (© Witosa)



Fig. 2. Artur Wiczorek (right), Project Manager at Celon Pharma, together with Ravan Graubner, Sales Manager International at Witosa Hot Runner Technology (© Witosa)

functioning of all moving components is a prerequisite. Failures or contamination, for example due to material abrasion, are not permitted.

"The demanded precision for the exact interplay of all parts of the inhaler, which must also remain absolutely constant over a planned serial number of 400 million units per year was one of the yardsticks that we set when choosing a suitable tool manufacturer and hot runner manufacturer," says Artur Wiczorek, Project Manager at Celon Pharma. The fully automatic assembly and assembly of the inhalers in the cleanroom (**Fig. 1**) should not affect product quality.

Narrow Time Frame

The highest uniform quality and hygiene standards based on validated processes and a certified QM system were another basis. In addition, there were the regulations prevailing in medical technology such as the GMP requirements that require the implementation and exact documentation of risk assessments for the injection molding tools. In other words, qualification and process validations must be performed to create and document appropriate process capability certificates.

With this ambitions, Celon Pharma went in search of a suitable partner in Poland and Germany and then approached the Glittenberg Group. Artur Wiczorek

(**Fig. 2**): "The subject of plastic injection molding was completely new to us. We had an inhaler in our hands and in no time needed millions of them. Therefore, short communication channels at this stage were very important to us. We needed a professional partner who could immediately implement our request and offer everything – design, tools, hot runner systems – from a single source."

The time frame for this project was very tight: 14 injection molding tools including the hot runner systems had to be completed in less than a year, based on the article. Added to this were the high quality requirements for the tool surfaces, which are particularly demanded by the US market. "Since we are at home in the medical technology industry, we saw from the outset the enormous effort that we had to put into planning the tools in order to be able to fulfill the guidelines of the industry," says Torsten Glittenberg, Managing Director of the Glittenberg Group.

Go through the Tenth Design Loop

Based on the requirement specifications and the performance specifications of the customer, a corresponding product specification was then drawn up and, in particular, determinations for the cleanroom suitability of the injection molding tools and hot runner systems were made. Among other things, this involved the selection of suitable corrosion-free materi-



Fig. 3. Celon Pharma usually uses DT-16 nozzles with an open nozzle tip or with a needle valve. This series is particularly suitable for products with small shot weights and tools with high numbers (© Witosa)

als for the tools and hot runners. But also maintenance and inspection plans and specifications for cleanroom-compatible cleaning, lubrication and storage of tools were created.

Despite the major hurdles, all deadlines were met and sometimes even undercut. "The design of the article and the documentation were very well prepared by Glittenberg," says Wieczorek. And so already in 2014, the first parts could be produced from the new tools. These were optimized in several design loops and adapted to the required strict article geometries.

The first inhalers were intended for the US market. In 2016, production started for the entire European market with an initial volume of one million units.

Meanwhile, the inhaler has gone through the tenth design loop. "We have grown with the demands of the market. Glittenberg was always open when help was needed and ready for adjustments. The desired changes were implemented in a completely uncomplicated manner", Project Manager Wieczorek assesses the co-operation with his tool supplier.

Meanwhile, 35 injection molds equipped with hot runner systems and over 300 hot runner nozzles from Witosa have been delivered to Celon Pharma (Fig. 3). Under cleanroom conditions, the components for approx. 12 million inhalers per year are manufactured on 16 injection molding machines, then, fully automatically assembled, provided with blisters and tested.

The Next Research Programs Are Running

Celon Pharma is currently running twelve drug development programs funded by the European Union. One special field of research in this program is the administering of the drugs by inhalation. A current program called "Disc" aims to develop this method of administering the drug for treating depression by means of an already known anaesthetic. While currently available depression treatments show therapeutic effects only after a few weeks of regular medication, several clinical studies have demonstrated a direct and long-term antidepressant effect of the anaesthetic. Patients should be able to take the drug themselves and control the dose administered, thanks to the developmental experience of Celon Pharma.

Because of the foreseeable enormous increase in demand of the order of 400 million units per year, Celon Pharma now plans to use further high-cavity tools for very fast cycles. Torsten Glittenberg is confident that "in this case we will be able to meet all the requirements of the medical technology industry. Even though that is sometimes very complex." ■

The Author

Ravan Graubner is Sales Manager International at Witosa GmbH, Hot Runner Technology, Frankenberg, Germany.

Company Profile

The company group Glittenberg, based in Frankenberg in northern Hesse, Germany, was founded in 1990. It consists of the companies Formenbau Glittenberg, Kunststofftechnik Glittenberg and Witosa Heisskanalsysteme. The group now employs over 150 people and is represented worldwide with its products.

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