HARRO

The Customer Magazine by Harro Höfliger **Edition 13 | 2022**

A new kind of freedom

Lightweight, discreet, reliable: CeQur's mealtime insulin patch could change the lives of type 2 diabetes patients.

CONTENT

EDITORIAL

Dear Readers,
dear Business Associates,

Standstill is not an option, or as Greek philosopher Socrates put it 2,500 years ago: "Stagnation is the beginning of the end". Since the company was founded, Harro Höfliger has continuously pursued further development in order to enable growth and to pave the way for innovation together with our customers.

In line with this tradition, in 2022 we have also initiated changes for the future success of our company. For instance, we were able to expand to three new company locations which provide us now with the necessary space for the implementation of the next corporate goals. With our corporate start-up PYNR, we are focusing on digital solutions in the IIoT context to ensure quality, transparency and efficiency of industrial processes, and to create sustainable added value for our customers.

The articles in this issue of HARRO magazine also show that we like to break new ground with our customers and partners – be it a new business card-sized inhaler in which a breathable membrane stores the active ingredient powder, or a special insulin patch that makes the lives of type 2 diabetes patients easier. In cooperation with our partner leon-nanodrugs we develop new technologies in the area of nanomedicine. One thing is certain: We will continue to have a lot of innovative topics and exciting stories in the future!

I hope this magazine meets your interest and you can enjoy reading it.

Your

Thomas Weller,
CEO at Harro Höfliger

3 new sites

Harro Höfliger has expanded its presence in Baden-Württemberg with three new locations in 2022. By taking over the business operations of Widmann Maschinen in Schlierbach, an additional 5,500 sqm of commercial space is available. The strongly growing Assembly Technologies technology division has a second production and assembly site there. In Oppenweiler near Backnang, the former ContiTech site offers the necessary space specifically for large lines, as well as for storing customer sample material. Harro Höfliger's first corporate start-up PYNR began operations in Rommelshausen just outside of Stuttgart in May. With the sites in Schlierbach, Oppenweiler and Rommelshausen, the number of locations in Germany has risen to seven.

Trade fairs 2023

In 2023, we will again be represented at trade fairs around the globe. To name a few, you can find us at

ARAB HEALTH, Dubai
January 30 to February 2, 2023

PHARMAPACK, Paris
February 1 to 2, 2023

ATX West, Anaheim
February 7 to 9, 2023

ICE, Munich
March 14 to 16, 2023

INTERPACK, Düsseldorf
May 4 to 10, 2023

Our customer magazine is also available online:

www.harro-magazine.com

Innovative transport system

For their assembly platform MOT Flex, Harro Höfliger banks on an innovative, highly flexible transport system. Transport from station to station is carried out via individual shuttles, powered by magnetic linear drives. This approach allows to vary transport speed as well as acceleration between process stations. Hence, it is possible to accumulate multiple shuttles for time consuming processes, while less complex tasks such as presence checks can be executed simultaneously. Another advantage is that tray loaders and palletizers for product feeding can be connected directly to the system without using pucks. By working closely with a wide range of development teams, the new transport system was adapted to the needs of the medical and pharmaceutical industries and integrated into the machine platform MOT in a very short time.

All in one

PrestigeFilm, Helmar Lünig, Illustration: vladwel/Adobe Stock

These stainless steel pins serve as both capsule ejectors and segment cleaners. This is how it works: Within the capsule filling machine, the capsules are transported from station to station in special bores of the so-called capsule segments. The pins move into these segments at the end of the filling process and the capsules are pushed out. Immediately afterwards, air flows out of the slots; powder particles are ejected and extracted within the same station. Beginning on page 19, you can read more about the platform where this solution is in use.

A NEW KIND OF FREEDOM

With their unique mealtime insulin patch Simplicity™, the Swiss company CeQur could be changing the lives of millions of type 2 diabetes patients. The device is amazingly simple to use but highly complex in design. Just like the giant production line that Harro Höfliger developed for this product.

A casual meal with friends, an after-work drink served with appetizers, a quick stop at a snack bar: Most people take it for granted. For type 2 diabetes patients who in addition to long-acting sustained-release insulin also require mealtime insulin, it is often a challenge. Especially for these patients the new mealtime insulin patch CeQur Simplicity™ is expected to make life easier in the future. It is thin and invisible under clothes. It is lightweight and you hardly feel that it is there. Once attached to your body, it stays securely and discreetly in place, covering your mealtime insulin needs for around three days. While eating, a short click is all it takes and two doses of rapid-acting insulin enter the body via a soft and flexible cannula. The 2-button dosing mechanism prevents accidental dispensing of the drug. An audible and perceptible "click" gives wearers the assurance that the dose was administered correctly. "This device is unique. There is nothing comparable on the market," enthuses Douglas Gunthardt, Executive Vice President at CeQur. "And it is so easy to use that patients can handle it within a few minutes."

"In the US alone, there are about 27 million people diagnosed with diabetes."

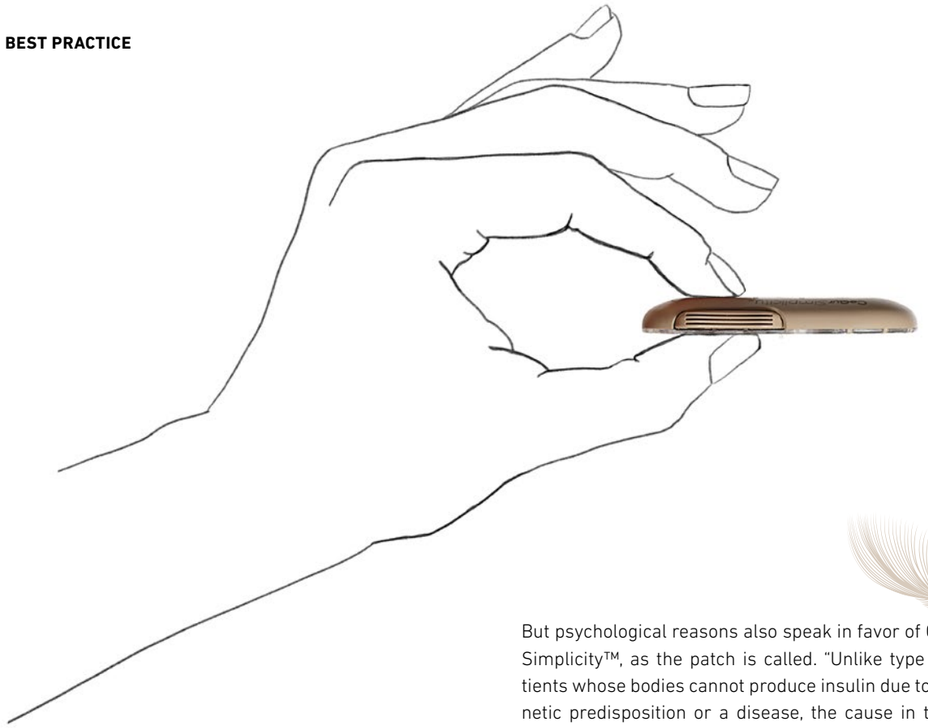
Douglas Gunthardt
Executive Vice President, CeQur

SUDDEN HALT ON THE HOME STRETCH

The idea for this trend setting solution has been existing for a long time. Originally developed by a start-up, a global healthcare player acquired that company in 2012 and invested in the device's Design for Manufacturing. It also conducted one of the most extensive clinical trials at that time for a diabetes med-tech product, with 278 patients. After FDA approval, the company commissioned Harro Höfliger to build a semi-automatic pilot production line. In Puerto Rico the group initially installed the pilot line capable of producing devices for up to 10,000 patients. A high-volume line to supply treatment for 80,000 patients was already under design and construction at Harro Höfliger and another machine manufacturer when in 2018 the customer decided to divest themselves from their entire diabetes med-tech business. The project came to a standstill and, for the time being, the gigantic, almost completed machine slumbered, a true Sleeping Beauty.

An innovative lighting concept provides an overview of the huge system: machine components illuminated in green are working properly, red indicates a need for action, and unlit machines are out of operation.

CeQur SA, raff digital gmbh, Illustration: ilonitta/Freepik



NEW HOPE FOR MILLIONS

CeQur, a start-up founded in 2008 with headquarters in Horw, Switzerland, recognized the opportunity that the patch offered. In mid-2018 the company secured the worldwide license for this product. "A look at the figures in the US shows the potential of this solution," explains Douglas Gunthardt: "In the US alone, there are about 27 million people diagnosed with diabetes and the number is rising. Approximately 24.5 million people suffer from type 2 diabetes and about two million need to provide mealtime insulin to their bodies in addition to long-acting insulin." When Bradley Paddock joined CeQur mid-2019 as CEO, he quickly focused all the company's efforts on bringing this product to market.

But psychological reasons also speak in favor of CeQur Simplicity™, as the patch is called. "Unlike type 1 patients whose bodies cannot produce insulin due to a genetic predisposition or a disease, the cause in type 2 patients can be a poor diet, being overweight and lack of exercise in addition to hereditary predisposition," explains Gunthardt and continues: "These patients often find it difficult to deal openly with their disease. Wearing a pump or handling syringes and pens when having meals is therefore often met with skepticism and rejection by those affected." As a result, more than half of the patients admit that they regularly skip insulin doses for a variety of reasons, which can lead to serious health complications. "This gap is filled by Simplicity™. It is so discreet that patients quickly learn to embrace it," says Gunthardt. The pilot launch of CeQur Simplicity™ in three US states already showed that 95 percent of users were very satisfied with the patch and 93 percent prefer it to pens and syringes.

The flat patch disappears discreetly under clothing and stays in place for up to three days.

A PRODUCTION SYSTEM OF SUPERLATIVES

In 2021, CeQur gave Harro Höfliger the go-ahead for the completion of the stored, fully automatic high-volume line. It comprises a grouping of 30 machines, 28 are from Harro Höfliger. A blister forming and punching machine and a leak test machine come from two partner companies.

"In addition to its size, a special feature of the line is the intelligent conveyor belt system," explains Gunthardt. "It advances the workpiece carriers through the line at two meters per second and enables the production of up to 40 devices per minute."

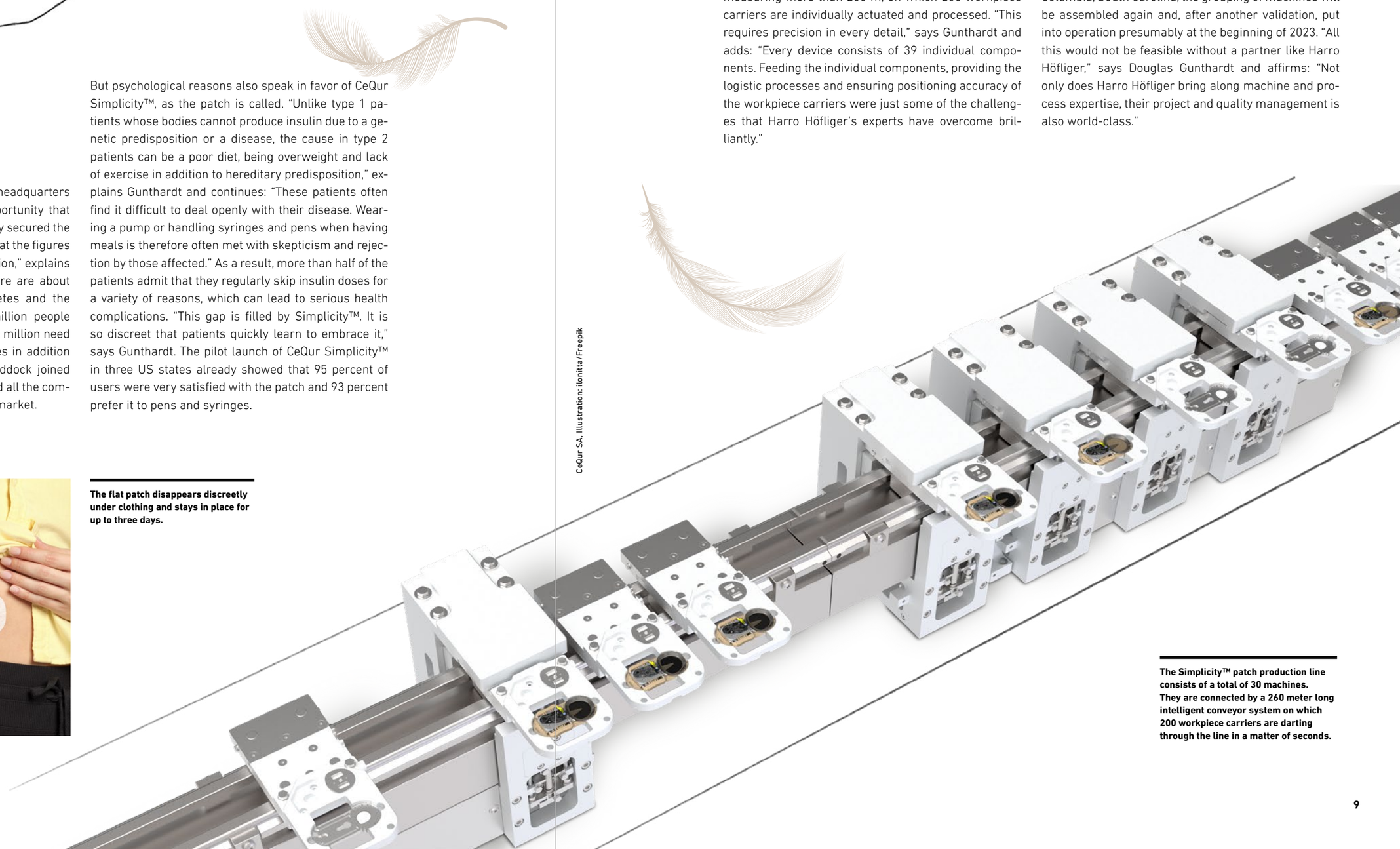
The 30 machines are connected by a conveyor line measuring more than 260 m, on which 200 workpiece carriers are individually actuated and processed. "This requires precision in every detail," says Gunthardt and adds: "Every device consists of 39 individual components. Feeding the individual components, providing the logistic processes and ensuring positioning accuracy of the workpiece carriers were just some of the challenges that Harro Höfliger's experts have overcome brilliantly."

Some of the processes were deliberately implemented redundantly so that the line can continue production in case of a partial failure or during maintenance activities. In addition, space capacities have been provided so that the system can be expanded to 80 devices per minute.

A CHALLENGING RELOCATION

Handling of the giga line is a demanding task too: The first validation and startup operations took place at the Harro Höfliger production site in Satteldorf. In the next step, the complete line will be disassembled and shipped to the USA. At the CeQur production site in Columbia, South Carolina, the grouping of machines will be assembled again and, after another validation, put into operation presumably at the beginning of 2023. "All this would not be feasible without a partner like Harro Höfliger," says Douglas Gunthardt and affirms: "Not only does Harro Höfliger bring along machine and process expertise, their project and quality management is also world-class."

CeQur SA, Illustration: ilonitta/Freepik



The Simplicity™ patch production line consists of a total of 30 machines. They are connected by a 260 meter long intelligent conveyor system on which 200 workpiece carriers are darting through the line in a matter of seconds.

The development of dry powder inhalers is complex. The new alliance INTO aims to simplify these projects. To this end, it combines expertise gained in previously often separate fields of formulation development.

For the treatment of pulmonary diseases, countless people all over the world rely on inhalers. A large part of them are dry powder inhalers (DPIs), where the active ingredient is provided in a powder formulation.

However, it is a long road with numerous obstacles before the devices can actually help patients. Powder development in particular presents many challenges. The active ingredient, excipient, mixing process, filling process or the device itself – all these aspects, and especially the interactions between them, need to be well-balanced in order to make a formulation effective and robust.

At the same time, pharmaceutical companies often outsource the individual development steps to other companies. This is why different parties are responsible for aspects such as development of the active ingredient, selection of the excipient and the appropriate dosing technology. However, their focus is often limited to their specific expertise in the overall project. Upstream or downstream processes may only be partially taken into account and possible repercussions may simply be condoned. Failed development projects or subsequent problems during production can be the result.

It is against this background that INTO (Inhalation Together) was born. INTO is a strategic cooperation between the active ingredient manufacturer Sterling S.P.A., the expert for excipients DFE Pharma and Harro Höfliger who is responsible for the appropriate dosing technology. Each of the companies has decades of experience in the inhalation field. The alliance helps pharmaceutical companies to make formulation development for dry powder inhalers faster, safer and more efficient.

From the very first moment, INTO can see the entire development trajectory, from the active ingredient particle to the filling line. The specialists know where the obstacles are, how to overcome them, and how to, as quickly as possible, achieve the ultimate goal – a perfect powder formulation.

Who is Danny/Adobe Stock

"Pharmaceutical companies benefit from our decades of experience."

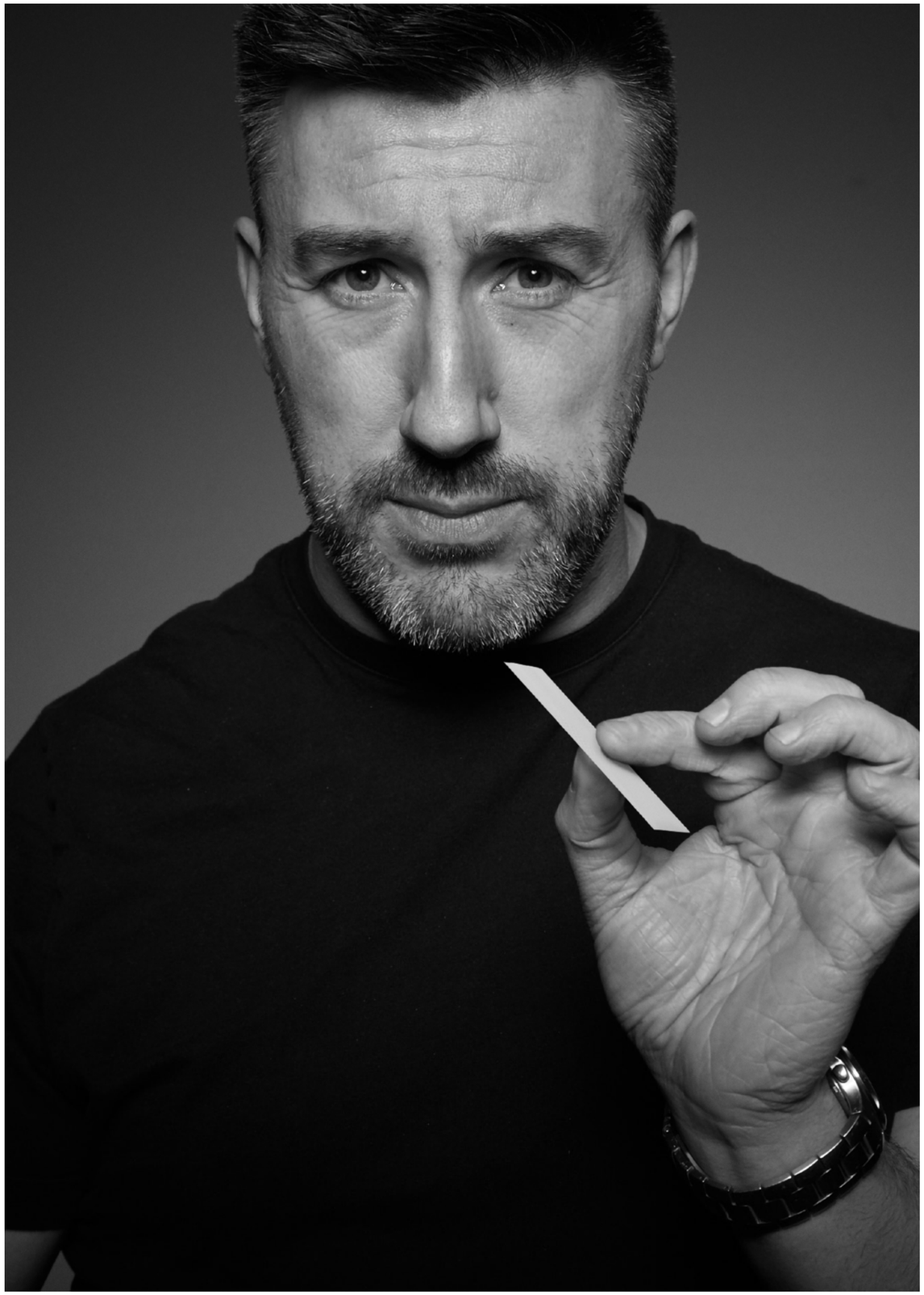
Olga Urazova, Chief Business Development Officer at Sterling S.P.A.

"Our services cover all critical steps involved in DPI development."

Xander van Leeuwen, Sales Director Inhalation at DFE Pharma

"With INTO, our focus is always on the interactions between powder, filling process and inhaler."

Marco Laackmann, Director Inhalation Technology at Harro Höfliger



Considering common inhalers too large, unwieldy and indiscreet, Don Smith went ahead and invented his own device: The 1nhaler. But it was a long road from the initial idea to the groundbreaking concept. The inventor‘s creativity, optimism and ability to inspire others kept him going.

PASSION AND PATIENCE

In his capacity as a successful creative director, Don Smith was solving the design and communication problems of numerous customers for years. In 2016, however, this was no longer enough for him: He quit his job and became an inventor. The idea for his first invention, the 1nhaler, occurred to him when his physician offered him the opportunity to test a new inhaler. Smith is asthmatic and has long been frustrated by the size and bulkiness of current devices.

The new inhaler also disappointed him. However, he found one detail very promising: The inhaler was a dry powder inhaler. “This technology inspired me to come up with the idea of packing a single powder dose into a completely new kind of small, discreet inhaler,” says the inventor. “It would be capable of releasing the active ingredient in just one breath: a 1nhaler.”

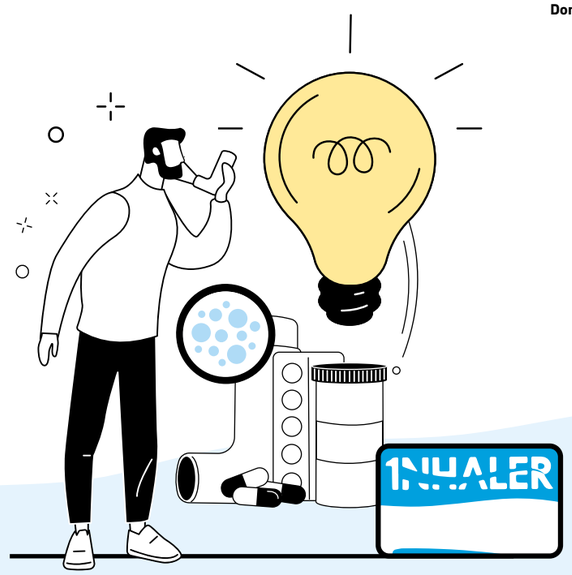
1nhaler Ltd, Illustration: Vectorjuice/Freepik

CHARISMATIC GENERALIST

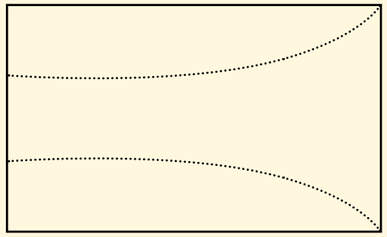
Smith started to read specialist literature about pharmacology, physics and powder processing. He visited pharmaceutical conferences and congresses and talked to experts. “I know a lot about a lot,” he says with a smile. “But I never pretended to be an expert for airways or inhalation. I presented my idea saying that I would appreciate receiving support in the inhaler’s development.” This honesty paid off. “The pharmaceutical industry is full of passionate people who want to keep others healthy,” he says. “Many were inspired by this idea and supported me with their knowledge.”

“Having the idea is the easiest part of any invention. Making it work is the hard part.”

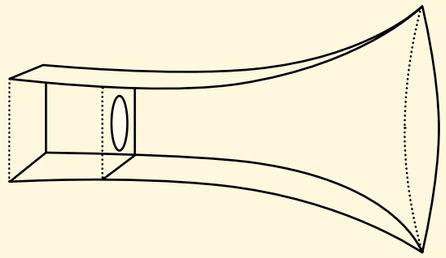
Don Smith



THE DEVICE IN ITS UNOPENED STATE



1NHALER IN 3D STATE



As small and compact as a business card, the 1nhaler is always at hand. One of many potential fields of application is the acute treatment of migraines.

HANDY AND SUSTAINABLE

The core of the single-dose inhaler is a breathable membrane to which a single dose of active ingredient powder is applied. The membrane is embedded between two business-card-sized pieces of cardboard that can be formed into a three-dimensional device when pressure is applied to the two outer edges. With a single breath, the ultra-fine powder penetrates directly into the lungs. "Both the membrane and the sustainable packaging are unique," Don Smith proudly explains.

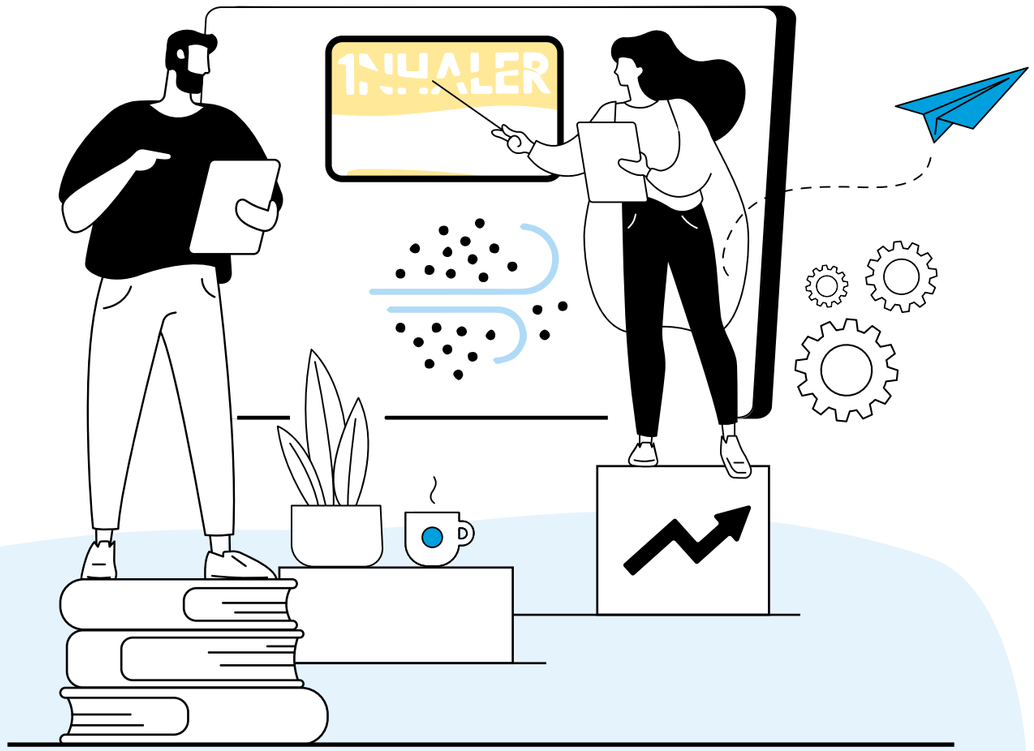
The experts from Harro Höfliger helped him with the technical implementation of his invention. "During my research I met Alan Holmes, a long-standing sales employee of Harro Höfliger in Great Britain. He introduced me to the powder expert Marco Laackmann and his team. Their comprehensive expert knowledge – and even more important – their enthusiasm has pushed the project and made the inhaler's development possible."

Co-Managing Director Lisa McMyn has been helping Don Smith commercialize his invention since 2017.

VISIONARY OUTLOOK

In 2017, Don Smith founded 1nhaler Ltd in Edinburgh, Scotland and started developing the product. He brought in Lisa McMyn, a long time friend and colleague, as his Commercial Director to support him with her natural pragmatism and business acumen. "It is simple to have an idea," he explains. "But it is a challenge to make it work. Financing, establishing partnerships, running a business – this is where Lisa is doing an amazing job."

By developing the 1nhaler, Don Smith has fulfilled a personal dream. "I admire all people who work on solving important issues of mankind. Creative minds who care more about making things better than making a lot of money," Don Smith says and adds: "If the 1nhaler can make breathing easier for people, my work has been worth the effort."



1nhaler Ltd, Illustration: Vectorjuice/Freepik

Freeze-dried beads can be used in many ways. The beads have good storage properties and are used, for example, in lab-on-a-chip systems for diagnostic purposes. Other applications include the life sciences sector and water analysis.

TECHNOLOGY

The Lyo Bead Dispenser TT precisely doses lyophilized beads into different containers.

SMALL BEAD, LARGE POTENTIAL

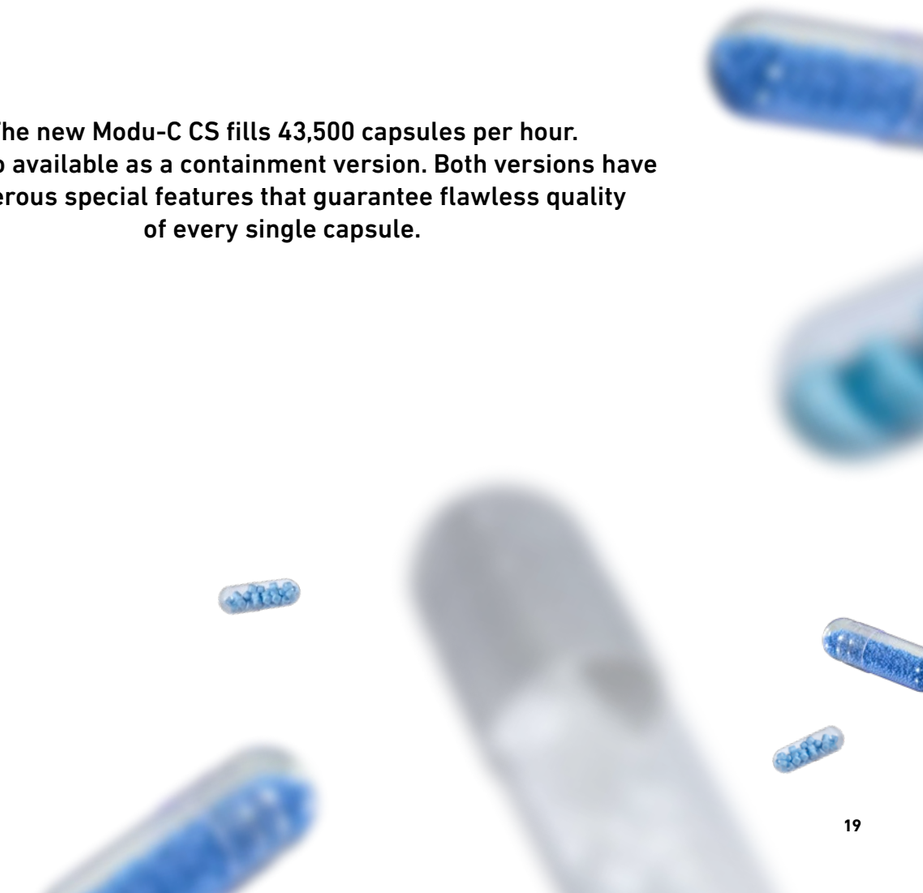
Lyophilized beads have great potential for modern medicine. The versatile granules provide numerous benefits, for example in diagnostic agents.

Small, round, freeze-dried. That is how lyo beads – also known as cryo pellets – can be described. While the beads are rather inconspicuous, they nevertheless provide almost unlimited possibilities. Dieter Haberzettl, Director of the Diagnostic Technologies division at Harro Höfliger: "The field of application depends entirely on the starting material. Many beads are sized between 1.8 mm and 6 mm. They are produced using a dripping or spraying process, flash frozen (for example with liquid nitrogen) and subsequently freeze-dried. They are used, for example, in various rapid diagnostic tests. The smaller microspheres, lyophilized pellets with a diameter of up to 0.5 mm, are primarily used in the life sciences sector. The advantage lies in the storage stability of the active ingredients at room temperature." But the excellent stability of the beads is not their only strength, explains the expert: "They are easy to store and transport in bulk, which further simplifies logistical processes. In addition, the production chain for rapid tests does not have to be interrupted. There is no drying time required, unlike when liquid reagents are being placed into the test kits."

For companies who want to benefit from the potential of the small spheres, Harro Höfliger provides the apppropriate solution. Dieter Haberzettl: "The Lyo Bead Dispenser TT is space saving, easy to operate and thus ideally suited for product development. It doses the beads individually by air flow. Unique throughout the world: The electrostatic charge is very well controllable during this process. The same principle and the same dispenser can be used later in fully automatic production."

EVERY CAPSULE COUNTS

The new Modu-C CS fills 43,500 capsules per hour. It is also available as a containment version. Both versions have numerous special features that guarantee flawless quality of every single capsule.



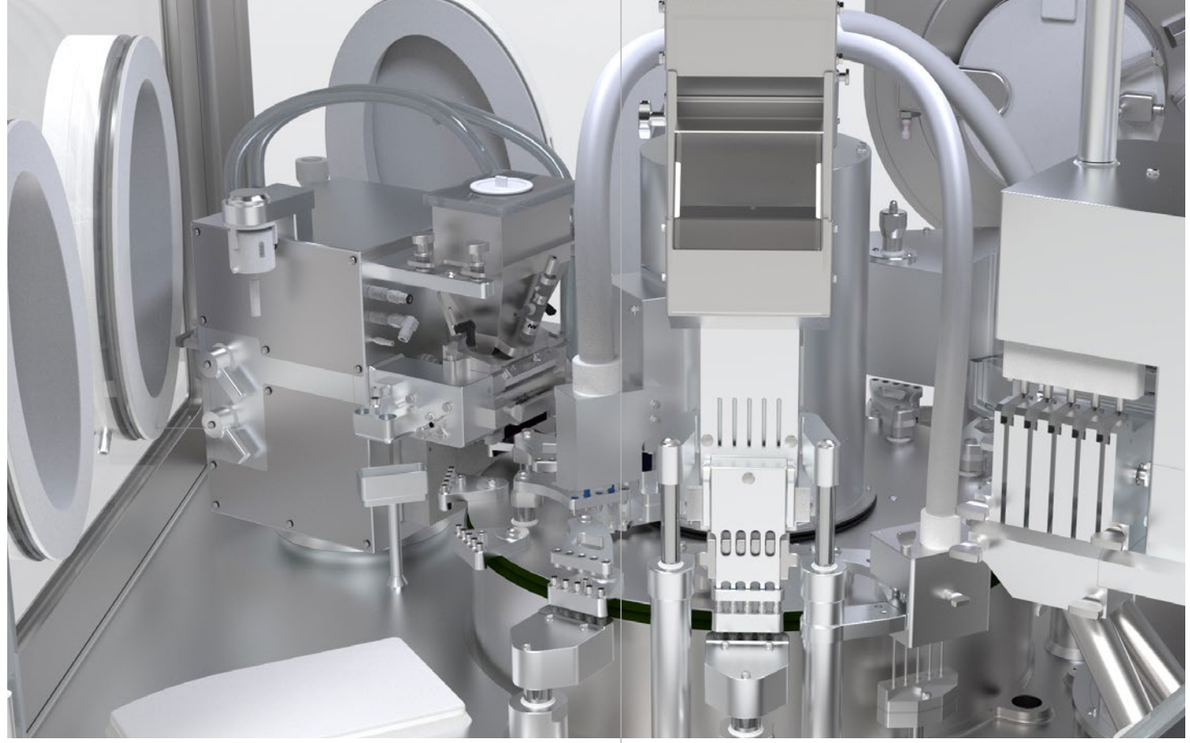
Janine Kyofsky. Helmar Lünig

Daniel Müller is Sales Director in the Capsule Technologies division at Harro Höfliger. In an interview he talks about the development of the new capsule filling machine and explains its unique features.

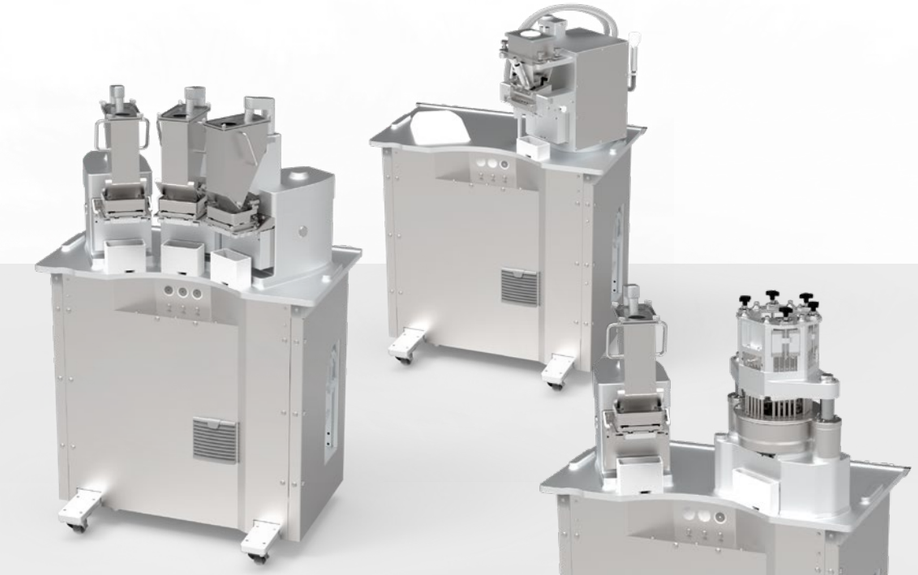
Daniel, the new Modu-C capsule filling machine has the name CS. Why?
So far, the capsule sector has been consisting of three basic machines. The LS (Low Speed), which is mainly suited for development purposes with 25,000 capsules per hour. Then there are two machine types used for production: The MS which stands for Mid Speed with an output of 100,000 capsules per hour, and the HS – High Speed – with an output of 200,000 capsules. With 43,500 capsules per hour, the new machine ranks right between our LS and MS models. This is where CS comes from: Cross Speed.

Who was the target audience for the development of this machine?
Generally speaking, every company in the capsule sector that finds itself in this output segment. All common powders and pellets can be filled on it; and the machine can be used for both R&D and commercial production.

Due to working very efficiently with small residual powder quantities, it is also ideally suited for high-priced drugs. In addition, pharmaceutical development departments are dealing with increasingly complex powders, such as freeze-dried powders or pure active ingredients, which are usually very cohesive. Even such demanding powders can be safely dosed with the CS model.



The patented segment turret reliably conveys the capsules through the system. In the containment version, a milled tabletop facilitates easy cleaning.



The dosing systems are mounted on easily changeable mobile trolleys. That way completely different capsules can be produced with just one machine.

A unique feature is that we can install two drum stations on one dosing trolley at the same time. This enables the filling of two separate powder types into one capsule. Furthermore, the drum filler technology is used for the dosing of tiny quantities or of material with very low density.

Not least, we are also addressing contract manufacturers with the CS because, among other things, it offers the Modu-C series' famous flexibility.

"100 % weighing of capsules in a closed containment is a real revolution."

Daniel Müller,
Sales Director Capsule Technologies at Harro Höfliger

What does flexibility mean here?
Theoretically, it means that hundreds of different products can be produced on one single machine. This is due to our trolley concept: The dosing systems are located on a mobile trolley which can be rapidly and easily moved out of the machine and replaced by another one. In addition, our exchangeable format parts cover the entire dosing range. By the way, one and the same trolley can be used in the non-containment and in the containment version.

Why is there a containment version?
Many ingredients which are filled into capsules nowadays are highly active. This is why we generate negative pressure in the machine so that the particles cannot escape. The active ingredient shall reach the patient but not the operator. We can integrate a deduster to clean the shell of every capsule. An external deduster is no longer necessary, which reduces space requirements. In addition, we have developed a special cleaning system with spray mist for additional operator safety. Moreover, the fact that 100 % weighing can also be implemented in the closed containment, is a real revolution in the capsule sector.

What makes this weighing method so special in your eyes?
We check the weight of every individual filled capsule gravimetrically – and this is done completely inside the system, which is something that does not exist in any other containment capsule filling machine. Weigh cells are very sensitive and weight determination can be disturbed by air flows and vibrations. In order to prevent this, our engineers have developed a special technical solution.

In addition to 100 % weighing, we can integrate an IPC station, which stands for in-process control. The system then checks the net weight, i.e. only the filling material of, for example, 20 capsules every half hour. We also use that station to adjust and calibrate the AMV sensor for the capacitive inline control of the filling quantity.

Hence the motto "Every capsule counts"?
Capsule weighing and many other additional features make it possible to ensure high capsule quality. Whether we are talking about a patient who needs a medication for treating a disease, or a pharmaceutical company who fills high-priced powders – both depend on flawless processing and in both cases this means: "Every capsule counts". Therefore, this motto was at the heart of developing the CS.

Helmar Lünig

MODU-C CS

The Modu-C CS can be individually configured according to customer requirements. All functions are available in both the containment and the non-containment version.

Modularity

Thanks to the patented trolley system, numerous products can be filled on just one machine – including a wide range of powders, pellets and liquids.

HMI

Full HD Display with sophisticated design and user-friendly navigation structures.

IPC station

The system weighs capsules during ongoing operation with an accuracy of +/- 0.1 mg. Quantity and frequency can be easily adjusted according to individual requirements.

100% gross control

Every filled capsule is weighed during ongoing operation. The weighing accuracy is +/- 2 mg.

Containment

The system provides protection concepts for every field of application, even for powder OEL < 1 µg/OEB 5. This guarantees the highest operator protection.

Deduster

An integrated deduster removes even very small residual powder quantities from the capsule shell. An external deduster is not required and the footprint is considerably reduced.

Helmar Lünig

Wet-in-Place

Special technology enables safe cleaning of the interior. This involves the use of spray mist from up to 10 l of water per passage.

STAYING IN FLOW

Auger dosers are suited for the dosing of a wide range of powders. Thanks to a special closing mechanism, technology from Harro Höfliger also reliably fills extremely free-flowing powders.

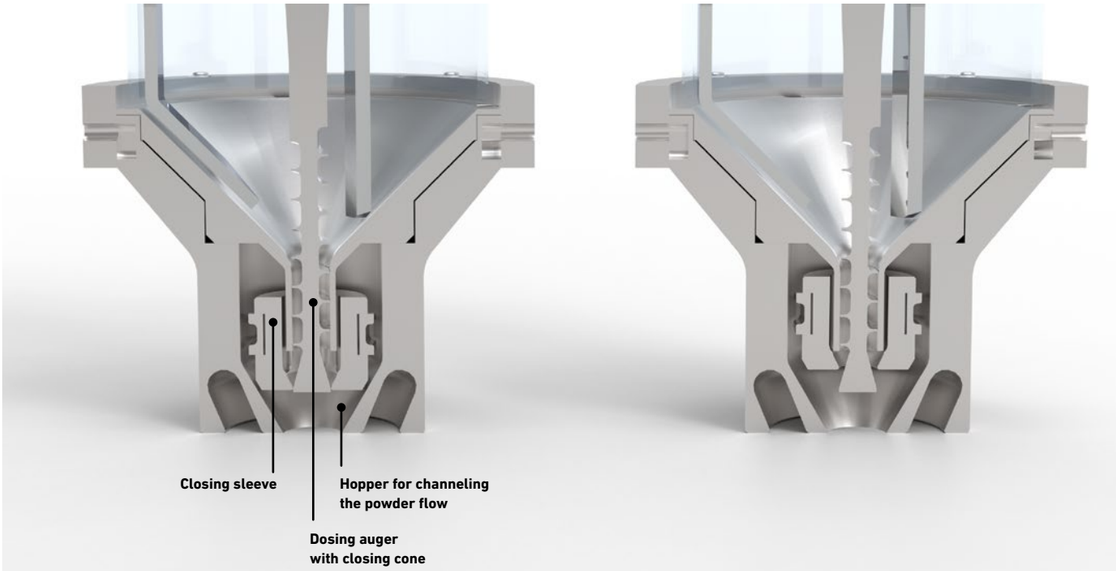
Sometimes you are completely absorbed in your tasks. Everything is easy and seems to flow by itself – you are "in the flow". Those who have ever dealt with the filling of powders can even better understand the metaphor behind this term. In order to make sure that the powder can be dosed at all, it must flow or be prepared to flow. Frequently, this is not an easy task, because as diverse as powders are, as different are their flow properties. Dosing systems have to be designed and adapted accordingly.

A suitable solution for many powders is the auger doser from Harro Höfliger. It provides precision, flexibility and is even capable of reliably advancing cohesive powders: Initially, it is located in a container, with the dosing unit – the eponymous auger – positioned in the center. Rotating movements convey the material to its destination, for example the reservoir of an inhaler.

In order to keep the powder moving, the hopper has a special stirrer for powder fluidization. Stirrer and auger have separate drives so that the powder can be better controlled during dosing stops. However, especially with very well flowing powders, such dosing stops are a real challenge for quite a few auger dosers; the powder may continue to trickle, causing contamination and inaccurate dosing results.

Therefore, for more than ten years, Harro Höfliger's system has included a special locking mechanism. The discharge opening of the dispensing cylinder is open during dosing and will close automatically when dosing stops. This is done by means of a sleeve which, when closed, rests on the closing cone of the dosing auger so that the powder cannot escape. That way, the powder is kept flowing when – and only when – it is desired.

CLOSING MECHANISM OF THE AUGER DOSER



Closing sleeve lowered, discharge opening closed, no powder flow

Closing sleeve lifted, discharge opening open, powder flow is released

AUGER DOSER SDM

In the auger doser, the powder is stored in a container. The eponymous auger transports it from there to its destination with rotational movements. The principle is suitable, for example, for filling dry powder inhalers.

Helmar Lünig

INTERVIEW

5 QUESTIONS FOR CHRISTIAN KOLLECKER

In August, Harro Höfliger's new platform for aseptic bag filling was launched. Christian Kollecker, Director Aseptic Technologies, answers the questions about "baXeptic".

1

Aseptic machine engineering is nothing new at Harro Höfliger. What makes baXeptic special?

The new word mark baXeptic is made up of the words "bags" and "aseptic" and already gives an indication of the two main aspects: The aseptic filling of liquid products into pre-sterilized bags, which must not be contaminated under any circumstances during the filling process. More and more complex pharmaceutical products with large molecules and high filling volumes are administered via infusion. Existing process solutions, however, often do not meet the requirements for flexibility and GMP-compliant hygiene design. With baXeptic, the customer's application determines the technical solution and this is where we come in. We can draw on a wide range of proven technologies and more than 30 years of experience in the design and construction of aseptic production machines.

2

What types of therapy do you have in mind?

Generally speaking, the market for aseptic bag applications is growing worldwide. In particular, we are targeting biopharmaceuticals and new therapies with gene- and cell-based ingredients that have great potential to cure chronic and serious diseases. It is a foregone conclusion that terminal bag sterilization after filling is out of the question for biomolecules and livings cells. Due to the small batch sizes, the production and filling of personalized medicine requires a maximum degree of product and process reliability.

3

Keyword process reliability: How do you ensure it?

First and foremost baXeptic is about meeting customer requirements which are usually determined by the product and the primary packaging material. At the beginning of the technical conception, we are in close contact with the customer, so that we can combine their process experience and knowledge about product and primary packaging material with our expertise in building aseptic bag filling lines. This is the basis for achieving a robust and reliable solution. Not only the filling process itself is important but the overall understanding of processes from bag feeding to handling, filling and sealing, all the way to process analytical testing. This understanding must then be transferred to an aseptic system, taking into account the applicable standards and regulations. In the laboratory of our Pharma Services department, liquid media can be tested in order to find optimal processes at an early stage. Our customers benefit from our philosophy "From lab to production", which means scalable processes. At the same time, baXeptic also enables scaling-out, where multiple small-scale lines lead to increased production capacity.

4

Are there special baXeptic machines?

Invariably, the customer's product determines the design, and the end product of our joint effort is always a tailor-made system. This is also due to the fact that there are hardly any standardized bag applications. baXeptic symbolizes the general method how we develop and implement machines for aseptic bag filling. We use the technology program of Harro Höfliger and integrate aseptic key processes into proven machine platforms that can be flexibly configured. This includes our established rotary and oval motion machines, but also barrier systems with isolators or RABS with glove ports, sophisticated concepts for product and operator protection, the use of robots for bag handling as well as the appropriate processes for cleaning and decontamination.

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What regulations must be observed in aseptic manufacturing processes?

The manufacture of sterile products is subject to strict requirements which ultimately ensure patient safety. The most important regulations are specified in Annex 1 on sterile production of EUDRALEX Volume 4 of the EU GMP Guide. The revised final version was published in August 2022 and will will come into force on August 25, 2023. Harro Höfliger has already devised a detailed concept for GMP-compliant hygiene design, for example about material and surface requirements, cleanability and sterile environments – which was documented in white papers. Companies that take the initiative now to prepare for the new regulatory framework, can gain an important lead in pharmaceutical engineering.

baXeptic

Helmar Lünig

THINK NANO

Nanoparticles can stabilize vaccines and pharmaceuticals, increase the bioavailability of drugs and deliver substances to their target site. With the new technology platform developed by leon-nanodrugs, nanoparticles for healthcare will be produced faster, easier and more economically in the future.

When the first vaccines against Covid-19 based on mRNA were approved for use, nanotechnology also came into the focus of the broader public. Naked mRNA degrades readily. Therefore, in order to stabilize mRNA and deliver it to the target cells to trigger an immune response successfully, it was packed inside nano-sized transport capsules. These capsules, or "lipid nanoparticles" (LNP), act as a vehicle for genetic material or other active pharmaceutical substances. With LNPs, substances can be targeted to specific regions of the body, which is of great advantage in cancer therapy, among others.

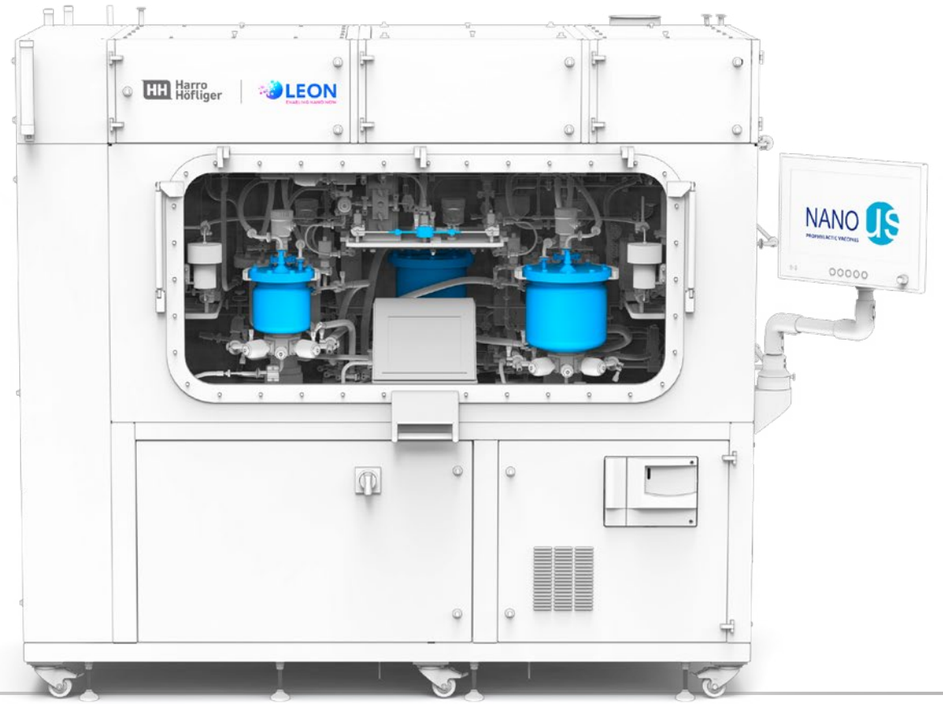
leon-nanodrugs, a Munich-based start-up, has been active in the nanotechnology space since 2011, with a clear goal: to make the production of therapeutics based on nanoparticles easier, more efficient and more economical through fast and seamless scale-up. To this end, leon-nanodrugs has developed the NANOnow technology, with its proprietary jet impinging reactor, in which substances collide at high speed. This patented platform is a breakthrough technology designed for continuous, reliable encapsulation of mRNA, biomolecules or other active pharmaceutical ingredients (API) into lipid nanoparticles with a reproducible size between 10 nanometers and up to 70 micrometers.

NEW POSSIBILITIES

NANOnow has long outgrown the laboratory environment. In cooperation with Harro Höfliger, the assembly of the fully-automated aseptic device, NANOus, for the GMP-compliant nano-encapsulation of APIs on a commercial scale is under way. This manufacturing device is particularly suited for flexible production of LNP-based vaccines, enabling encapsulation of active substance for 6 to 8 million vaccine doses per day. It features an integrated process analysis technology (PAT) that enables real time product release.

"Staying true to our motto 'One process, one reactor', which perfectly complements Harro Höfliger's philosophy 'From Lab to Production', NANOnow can be implemented in various production systems. Scale-up takes place using the same reactor core and therefore is much faster, since new validation of the process is not required," says Dr. Setu Kasera, Head of Science and Engineering at leon-nanodrugs. "This opens up new opportunities to make LNP-based medicines widely available for public healthcare and targets unmet needs of pharmaceutical and biotech industries, as well as contract manufacturers (CDMOs)."

Harro Höfliger is not only responsible for the development and production of NANOus; their Pharma Services department also supports leon-nanodrugs in product development work. Further joint applications of nanotechnology are in the pipeline, for example for personalized medicine, another increasingly important future market.



leon-nanodrugs GmbH

EQUIPPED FOR TOMORROW

Obsolescence management enables Customer Service to let customers know ahead of time when a machine component will be discontinued. This allows to plan with certainty and saves money.

Felix Haberl, Product Manager in the Customer Service department, is responsible for obsolenscence management which he considers a very important tool to prevent, for example, unplanned machine downtimes.

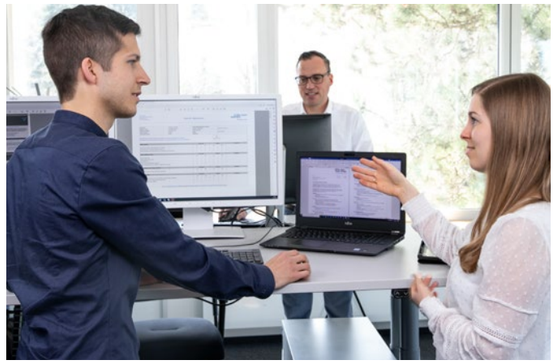
The packaging machine has stopped unexpectedly. A cylinder has broken. The production engineer calls the Customer Service at Harro Höfliger to order the required spare part. But the employee there has bad news: The cylinder no longer exists and the available successor is a few millimeters longer. In order to use it, machine sections have to be converted. This is expensive – and time consuming.

Harro Höfliger wants to protect customers from such scenarios with a new service: The obsolescence management for components that will be discontinued. Felix Haberl, Product Manager Customer Service, explains how it works: "Upon customer request, we will check the entire parts list of a machine for discontinued parts. For each component that is no longer produced, our engineers will search for successor products. The results are classified and categorized accordingly in a table. A basic distinction is made as to whether the parts are still available or can be replaced by a one-to-one successor, or whether minor adjustments or even complete conversions are required."

TAKING ACTION

The big advantage: Thanks to this service, customers can plan and determine the required measures at an early stage. This also became evident in a pilot project with a pharmaceutical company, where Harro Höfliger compiled overview lists for two large lines and then jointly developed the following strategy: It made sense to stockpile individual components that were still available as spare parts. Since other sections of one machine needed to be optimized anyway, a planned conversion with the new product versions was the obvious solution. Felix Haberl summarizes: "This service means an enormous added value for every customer. With this information customers can be proactive and avoid machine downtimes."

The Customer Service team creates a systematic overview of the availability of spare parts.



The corporate startup PYNR develops digital solutions which are precisely tailored to the requirements of the pharmaceutical industry. Their Mission: To increase the quality, transparency and efficiency of industrial processes – always individually adapted to customer needs.

The fusion of know-how in mechanical engineering and digital technology creates sustainable added value. On the basis of a specially developed software kit, digital solutions are created by using agile methods. Connecting machines, services and software via an IIoT platform opens up new possibilities for production, maintenance, and much more.

www.pynr.io

PYNR
BY HARRO

IMPRINT

HARRO, the magazine for customers, interested parties and friends. Editor: Harro Höfliger Verpackungsmaschinen GmbH; **Publisher:** Thomas Weller, CEO; **Editorial team:** Rosemarie Christ, Michael Waghubinger, Markus von Mallinckrodt, Monika Unkelbach (Die Magaziniker GmbH); **Concept & design:** Heike Moll; **Editorial assistance:** Dr. Karlheinz Seyfang; **Translation:** Gabriele Rosenland; **Reproduction:** raff digital gmbh; **Printing:** Druckhaus Götz GmbH; **Editor's address:** Harro Höfliger Verpackungsmaschinen GmbH, Helmholtzstraße 4, 71573 Allmersbach im Tal, harro.magazine@hoefliger.de; **Circulation:** 1,700 (550 in German, 1,150 in English); November 2022; **Credits:** Cover: CeQur SA, Illustration: ilonitta/Freepik; P. 32: gremlin/istockphoto

PEFC
PEFC/04-31-1568