

# HARRO

The Customer Magazine  
by Harro Höfliger  
Edition 3 | November 2016

## Multidimensional

Klocke Pharma-Service finds solutions  
for flexible package formats  
with technology by Harro Höfliger







# Multidimensional

Klocke Pharma-Service finds solutions  
for flexible package formats  
with technology by Harro Höfliger





- 4

Successful networking

The strategy of the Shane family
- 6

Securely packaged double bags

Klocke Pharma-Service relies on a proven partnership
- 11

Interlacing customer requirements

Harro Höfliger's new business segment matrix
- 14

The large and fast sister machine

MSP blister machine with a focus on powder filling
- 16

Small disks, big in diagnostics

Lab-on-a-chip, the mini lab in close proximity to the patient
- 18

Gentle handling of cryo pellets

Automated solution for sensitive lyophilisates
- 19

Breathe easy

About the production of RespiMat® inhalers
- 23

Made in Japan

First PMK-line for the production of transdermal patches
- 26

Boost for customer projects

Product consulting accelerates processes
- 28

Trends and traditions

In-house show informs customers
- 5

Harro Höfliger News
- 29

Trade fair calendar

**Imprint HARRO, the magazine for customers, interested parties and friends.** Editor: Harro Höfliger Verpackungsmaschinen GmbH; **Publisher:** Thomas Weller, CEO; **Overall responsibility:** Andreas Streicher, Director Creative Marketing; **Editorial planning & coordination:** Denise Dreher; **Graphic coordination:** Farina Hatami; **Photo editor:** Markus von Mallinckrodt; **Editorial team:** Rosemarie Christ; Oliver Naucke, nokey communication by Oliver Naucke, Laichingen; pr+co GmbH, Stuttgart; Steffen Beck, Tanja Haller, Norbert Hiller, Tina Hofmann; **Editorial assistance:** Stefan Gais, Dieter Haberzettl, Marco Laackmann, Hansjörg Schroeder, Dieter Schüle, Dr. Karlheinz Seyfang, Dr. Elke Sternberger-Rützel, Hartmut Thier, Ute Tils, John Van Tol, Achim Wolf; **Concept and implementation:** pr+co GmbH, Stuttgart; **Translation:** Gabriele Rosenland, Übersetzungen, Auenwald; **Reproduction:** raff digital gmbh, Riederich; **Printing:** Druckhaus Götz GmbH, Ludwigsburg; **Editor's address:** Harro Höfliger Verpackungsmaschinen GmbH, Helmholtzstraße 4, 71573 Allmersbach im Tal, harro.magazine@hoeffliger.de; **Circulation:** 7.700 (2.700 in German, 5.000 in English); **Credits:** Title: raff digital gmbh, Riederich; Page 2/3: Janine Kyofsky, Helmar Lünig, Tom Philippi; Page 32: Janine Kyofsky, Helmar Lünig



Dear Readers,  
dear Business Associates,  
There are at least three good reasons for Harro Höfliger's constant dynamic development: Unconditional customer focus, unbridled ingenuity, and enthusiastic employees form our foundation. In retrospect, we anticipated many developments correctly: In the 1980s, my father recognized that convenience products reflected the zeitgeist of the time, and developed packaging machines for the food market. In the 1990s, our present Chief Executives Peter Claußnitzer and Thomas Weller correctly assessed the potential in the pharmaceutical industry. Since the turn of the millennium, we fully concentrate on the value chain of our customers and offer them complete solutions.  
Today we are able to support our business partners throughout the entire product development process – from the laboratory to high-performance production. We are now preparing for the next decade: Going forward, we will continue to develop the appropriate core technology for every new dosage form, and include trends such as Industry 4.0 in our portfolio.  
In doing so, we are adhering to our virtues. We are not only open, reliable and honest, but remain agile and creative – there is a good reason for once again having been awarded as one of the “TOP 100” most innovative German medium-sized companies this year. We move forward with passion and appreciate the proximity to our customers. Not only in our native Swabia, but in all major markets around the globe.

Yours, Markus Höfliger

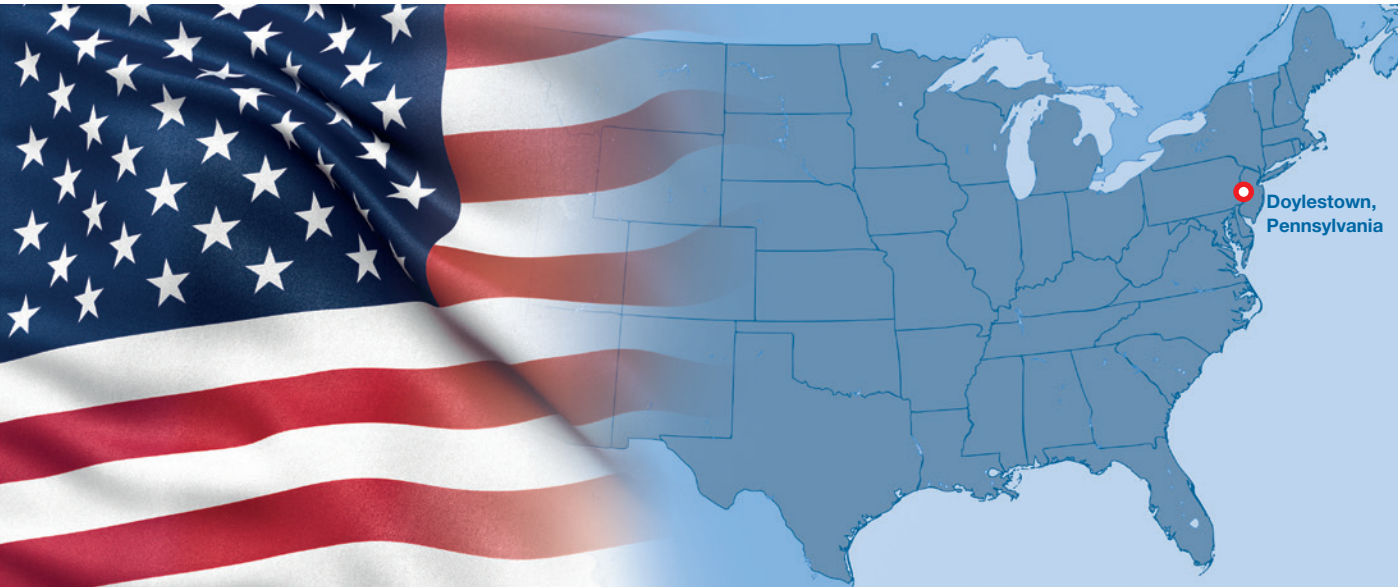


# Successful networking

Since April 1994, pharmaceutical companies in the United States have been a particular focus of the sales and service office Harro Höfliger Packaging Systems Inc. Closely associated with this branch office is the Shane family.

Harro who?” was the counter question when Al Shane introduced his new employer to the US market back in the mid 1990s. Although he had established a strong network of potential customers over a period of three decades in pharmaceutical sales, which helped to open the doors of many companies, establishing the Harro Höfliger name and securing that first deal did not come easily. Only after three years of intensive market cultivation, with the support of Harro Höfliger’s present managing director Thomas Weller, came the breakthrough: A Johnson & Johnson plant in Puerto Rico decided on a special-purpose machine for the packaging of freeze-dried tablets. Ever since, the US branch office with its headquarters in Doylestown, Pennsylvania has been on the road to success. Company founder Al Shane, 80, was followed into the company by his sons Jeffrey, Greg and Michael. His son-in-law Bob and grandson Evan are also now actively involved in the company. In addition to the family-run sales office, six service technicians support customers in the USA. Thomas Weller: “Founding our first foreign branch in the USA attracted worldwide attention to our industry. This positive growth trend has continued since our sales manager Hansjörg Schroeder took over responsibility for the US branch office ensuring streamlined communication and efficient collaboration between the US office and headquarters.”

What makes the “Shane Team” outstanding is the continuity and reliability of a family business combined with an excellent network within the industry. “The turnover of contacts in pharmaceutical companies in the US is rather high. By cultivating personal relationships with customers and prospects, we keep a finger on the pulse and stay connected to changing industry dynamics – even in a new market niche,” Vice President Greg Shane so describes the company’s relationship management approach. Also in North America, Harro Höfliger scores



*“You have to know your customer. Not only their title or work responsibilities but their character. And that requires time and the ability to listen and understand.”*

Al Shane, founder und former President of Harro Höfliger Packaging Systems Inc.

points for its expertise along the value chain of products. President Jeffrey Shane: “What matters most is what the customer needs. We are the experts and provide a complete solution for all the complex production and packaging requirements when no standard processes exist.”

This happens by working closely with the experts from the German headquarters. “Our German colleagues are always open to new ideas and requirements,” says Greg Shane. “This applies equally to sales, development and service.” Efficient communication is an important prerequisite for successful projects in the New World, because all machines are developed and built at the headquarters in Allmersbach, in accordance with international standards. ■



Successful quartet in the United State (from left): Michael, Greg, Al and Jeff Shane.

# Visit to Tunis

During the Innovation Talks event for the MENA region (see page 29) numerous guests visited one of Harro Höfliger’s first reference customers in North Africa: Médis, based in Nabeul-Hammamet near Tunis. This leading Tunisian pharmaceutical company with around 750 employees specializes in the manufacture and distribution of generic drugs. As a partner for turnkey solutions, Harro Höfliger worked with Médis on the complete product development process of capsules for dry powder inhalers (DPI) and installed one of their high precision Modu-C Mid Speed capsule filling machines for reliable filling of powder.



Experts are discussing the line configuration in the clean room.

# Innovation competition

For the 23rd time, TOP 100 awarded the most innovative German medium-sized companies. Once again, Harro Höfliger participated in the category for companies with over 250 employees – and placed third as a finalist among the innovative elite. This is all the more remarkable given the number of competitors. Out of 366 applicants, 238 leapt into the TOP 100 assessment group. Criteria for the selection of innovators are more than 100 parameters in the following five categories: “Innovation-friendly Senior Management”, “Climate of Innovation”, “Innovative Processes and Organization”, as well as “Innovative Marketing and “Successful Innovations”. The assessment is directed by Professor Dr. Nikolaus Franke from the Chair of Entrepreneurship and Innovation at the Vienna University of Economics and Business. TV presenter Ranga Yogeshwar acts as a mentor of the competition.

TOP 100 mentor Ranga Yogeshwar at the awards ceremony with Innovation Manager Achim Wolf (left) and Managing Director Uwe Amann (right) from Harro Höfliger.





# Securely packaged double bags

Klocke Pharma-Service and Harro Höfliger have been working together for more than a quarter of a century. A few months ago, both enterprises implemented the third line for packaging double bags. A milestone for Klocke in the expansion of their machinery.

**W**hen visiting Klocke in Ap-penweier, their different production lines leave quite an impression: “With twelve lines from Harro Höfliger in operation, we can manage even large orders,” emphasizes Factory Manager Alexander Pergande. This convinces their customers, many of whom are well-known manufacturers of pharmaceuticals.

For example, at Klocke a drug used for the treatment of digestive problems

is filled and packaged into double bags. Eighty percent of all folding cartons are loaded with 15 or 25 double bags. In addition, there are versions with five or ten double bags. Loading the folding cartons with these quantities was a particular challenge in machine processing.

Harro Höfliger drafted several possible machine concepts to address the varying quantities. The first approach, among other solutions, was to process the bags with a toploading cartoner. Stack height

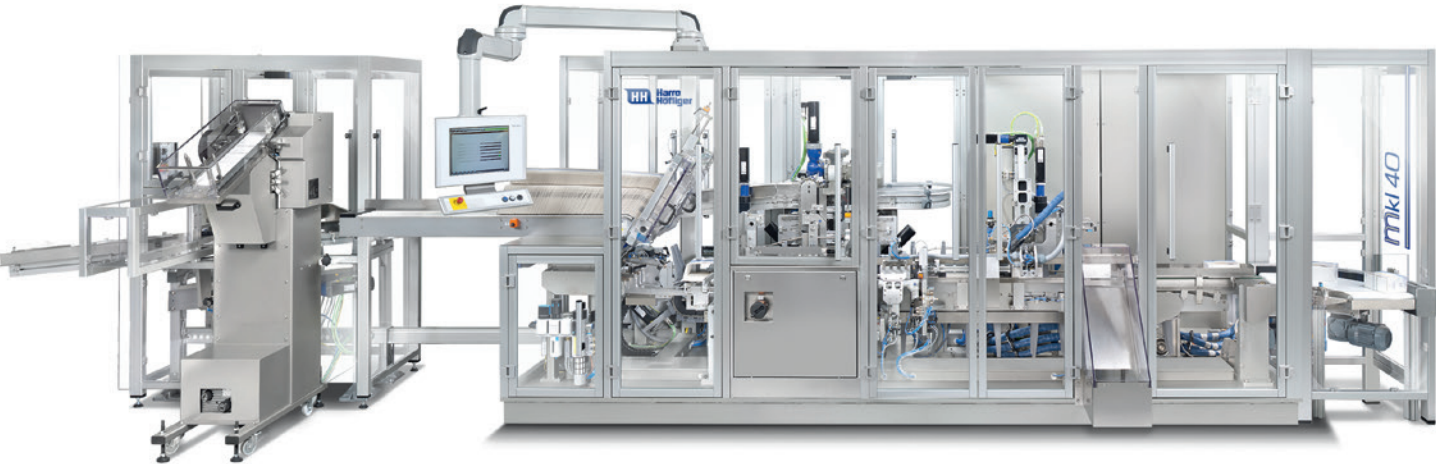
and the handling of 25 bags, however, proved difficult for reliable placement into the folding carton. Pergande: “In addition we wanted to process all pack options at the highest possible speed. With the Toploader, there would have been certain limitations.”

Harro Höfliger provided the right answer and developed a solution using a model MKL horizontal cartoner. In this machine, the bag stacks are held by an insertion and counter-insertion unit. This is





Yearly production  
over 100 million pouches



The new packaging line for double bags with its centerpiece: The MKL Cartoner.



how Klocke can process large-size folding cartons today. “For us, this line is the centerpiece of our packaging lines,” declares Alexander Pergande.

The main processing steps are:

- An instruction leaflet is folded by a folding unit, verified by a code reader and then dispensed onto the topmost double bag in the transport section
- An overhead belt pushes the bag stacks from the workpiece carriers into the stack chain
- The folding carton is erected and verified by a code reader

- In sync with this work step a servo-driven infeed pusher feeds the folding carton with the respective quantity of double bag stacks from the bag chain. Insertion and counter-insertion guides guarantee reliable placement of the products into the folding carton, which is especially important when processing high bag stacks
- In the next step the front flap of the folding carton is closed, while the insertion and counter-insertion guides move back. Next the carton passes a glue station where glue dots can be applied to the bottom flap at the tuck-

in closing stations. After leaving the cartoner, the folding carton is printed with variable data and then wrapped with a stretch bander

- After leaving the cartoner, the folding carton is printed with variable data and then wrapped with a stretch bander.

The cartoner processes folding cartons with a height of up to 165 millimeters. It offers secure processing at all times and highest reliability even at high speeds. ■



Insertion of double bag stacks into folding carton.



**The Klocke Group** is an important service provider for the production and packaging of pharmaceutical and cosmetic products. Klocke employs 2,200 people worldwide at nine sites, 220 at the Appenweier location. Here, Klocke produces and packages solid pharmaceuticals. The product portfolio at this site includes granules, tablets, coated tablets, dragées, hard capsules as well as the filling into sachets and cans. The Group's core activities are:

- Development, manufacturing and packaging of solid drug dosage forms, medical products and dietary supplements
- Manufacture of vaccines
- Manufacture of sterile forms
- Filling of semi-solid and liquid forms in the field of cosmetics, veterinary, OTC, HBA, perfumes, food and chemical-technical products.





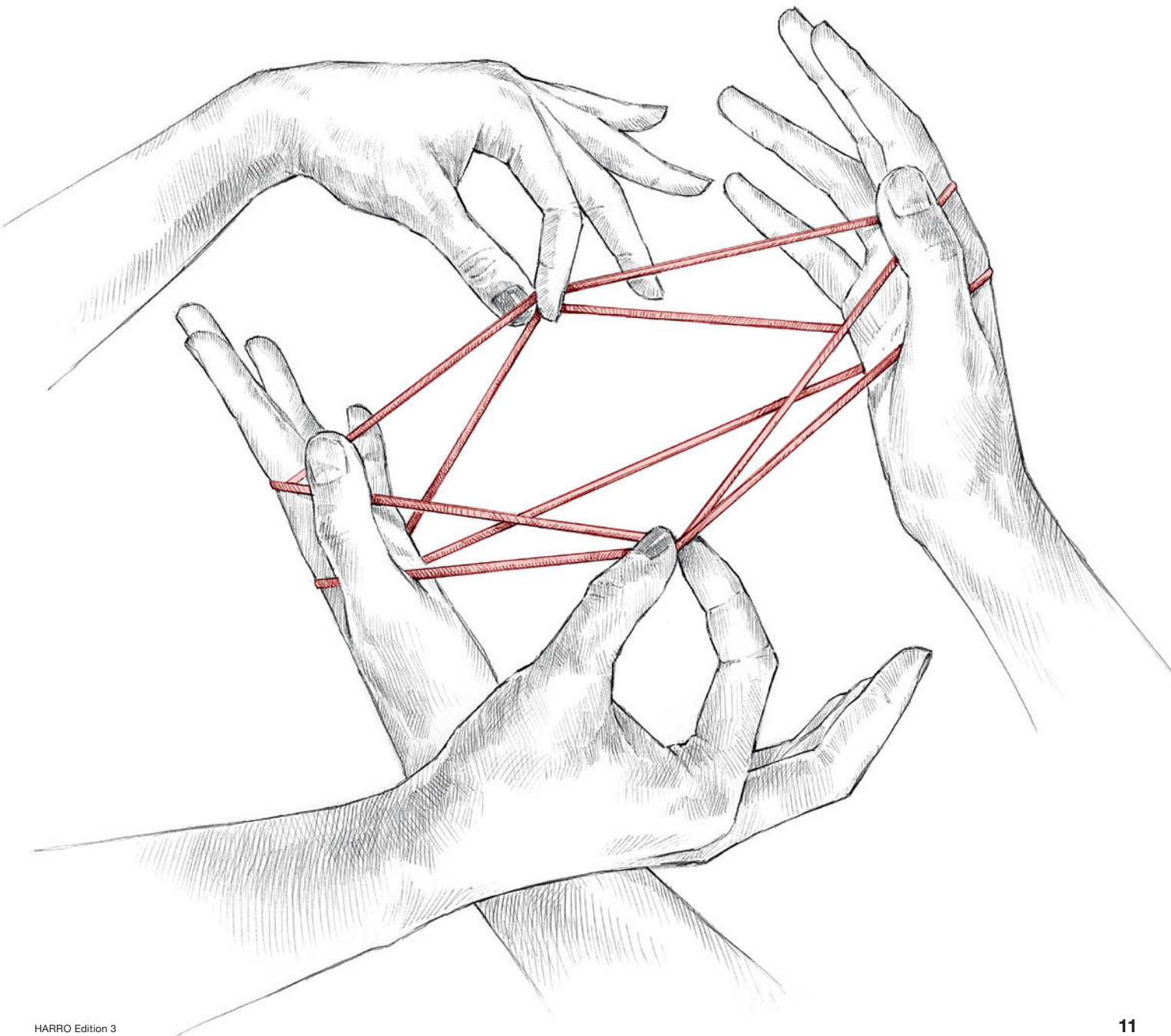
Factory Manager Alexander Pergande in conversation with Simon Mitzel, Manager of Production Technology.

*"The large quantities that Klocke produces nowadays do not allow any unscheduled production downtimes. This is why a partner with high service quality is an absolute must."*

Simon Mitzel,  
Manager of Production Technology  
at Klocke

# Interlacing customer requirements

With a new business segment matrix, Harro Höfliger is preparing for the next step in growth. Chief Executive Officer Thomas Weller comments on the benefits customers receive from the optimized structure. With perfectly coordinated interfaces, the entire range of customer requirements can be incorporated into the design.



Oliver Naucke

Bernd Schifferdecker

## Potentially record-breaking

Alexander Pergande, Factory Manager, and Simon Mitzel, Manager of Production Technology, look back on the successful collaboration between Klocke in Appenweier and Harro Höfliger.

**Working together for a quarter of a century – this is potentially record-breaking. What led to such a long-term relationship?**

*Pergande:* Satisfaction. 25 years ago, Klocke began with a second-hand pouch filling machine. Over the years, machines have become ever more complex and the challenges posed on us increasingly greater. Harro Höfliger met these conditions and consistently faced the challenges with us. Together we developed many different technical solutions. Harro Höfliger convinced us more than

once so that we recently ordered another machine.

**In addition to technology, soft factors also play an important role. What experiences do you share with Harro Höfliger?**

*Pergande:* We maintain an open and trusting partnership. We address problems openly and can therefore quickly search for solutions. The short distances that form an essential part of Harro Höfliger's corporate culture also contribute to the quick identification of solutions. This

is something we appreciate just as much as Harro Höfliger's service and customer orientation. Furthermore, we highly value the employees' ability to think outside the box. They are always open to new ideas, which is extremely important in the problem solving process.

*Mitzel:* The large quantities that we produce nowadays do not allow any unscheduled production downtimes. This is why a partner with high service quality and reliability is an absolute must.





**Almost every turnkey project at Harro Höfliger affects at least two, often three, or even four Business Units. At each point in the value chain the appropriate specialists are involved – precisely when they are needed. Our top priority: The customer product defines the process.**

We achieve interdisciplinary interaction with clearly defined responsibilities and sophisticated interface management. The responsibility rests with the corresponding expert who has mapped the critical core process, because he or she knows the product requirements and challenges. In a structured process, the team relays all relevant information to the next specialist. Each symbolic passing of the baton is documented and is a finely tuned interplay, almost comparable to a Formula 1 pit stop: Concise commands, clear roles, everyone knows what to do.

Essentially, it is easy to have loyal, satisfied customers: Company standards have to be set high, and you have to offer your business partners benefits and services that are optimally tailored to their products. However, this is a rather challenging path. Especially if you, like Harro Höfliger, support your customers throughout the entire product development process – from testing in the laboratory to series production.

Our philosophy: We do not sell machines, but solutions for the processes and core technologies behind the customer's product. Our strategy: Agility in the market with our seven tightly connected expert teams that respond quickly to new products and key technologies, and integrate our expertise in numerous business areas.

Harro Höfliger combines many disciplines, such as engineering, sensors, camera and weighing technology, intelligent control systems, and sophisticated data management. We have created a new map to guide the various

customer options through our seven Business Units – in order to meet the expectations of our business partners at every touch point, and with every customer interaction.

Surgical suture material, for example, clearly illustrates this point. If we are to support the customer product in all phases of development, the first essential step is to swage the often stubborn suture material and wind it. This is a process technology with the highest standards. Then the monitoring of a secure bond – for example, the optical inspection for knots and evaluation of predetermined tensile force limits. Packaging follows – only after these steps have been completed. The project moves from micro process technology, to web forming, to packaging on large machines. Engineers and developers from all these areas need to exchange information, coordinate, and implement the results accordingly. The entire interdisciplinary process should fill the customer with enthusiasm. ■

*"We offer solutions for the entire lifecycle of a customer's product – from the laboratory to series production."*

Thomas Weller,  
Chief Executive Officer,  
Harro Höfliger

Web Converting



Harro Höfliger's core competencies are in intermittent and continuous web converting. This includes the coating and lamination of "delicate" films and substrates, punching, forming and sealing, as well as packaging. When producing medical and pharmaceutical patches, subsequent cartoning is another significant step, where patches are transferred from manufacturing in synchronized processes.

- Laminating, coating, punching, forming and sealing (Web Converting)
- Packaging

Inhalation



Harro Höfliger specializes in liquid and powder filling with different dosing technologies, also under aseptic conditions. This includes film handling, welding and crimping processes, leak and flow measurements, and a complete functional test.

- Pre-assembly (Assembly Automation)
- Dosing (Inhalation or Pharma Liquid)
- Final assembly (Assembly Automation)
- Packaging

Eye Care



For more than 20 years, Harro Höfliger has fully understood the engineering, manufacturing and packaging systems for ophthalmic products. One focus is upon systems for the production and packaging of contact lenses.

- Dosing of monomer and saline solution (Aseptic/Pharma Liquid)
- Preparation of lens (Assembly Automation)
- Foil packaging (Web Forming)
- Packaging



# The large and fast sister machine

MSP – Mid Speed Production: The blister machine with a focus on powder filling is suited for commercial production of inhalation blister strips. It hardly requires more room than its sister SSP2 for smaller scale production, however, it is three times as efficient.



## Easy integration of operator protection

A space-saving containment can be easily integrated. The containment encloses the production section in which the open active ingredient is processed.



## High output

The MSP produces up to 30 blister strips a minute with 60 individual fills. The filling section is designed in a multi-unit configuration in order to achieve the necessary performance.



## Compact engineering

With a length of almost seven meters, the MSP requires only slightly more installation space than the SSP2 which was conceived for smaller series. Due to its balcony design with a separate production section, the MSP is easy to operate and maintain.



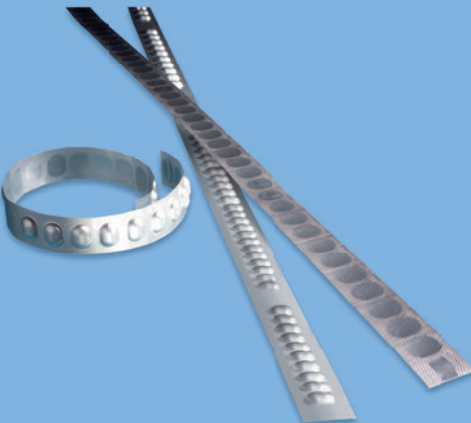
## Continuous inspection of product quality

A camera system is used for continuous quality inspection of the product. In the future, a new inline inspection system will verify the blister strips during production using x-ray technology. The x-ray control could reduce the previously necessary separate destructive test process significantly.



## Perfect connection

The MSP produces aluminium blisters in endless rolls. As a turnkey solution, Harro Höfliger offers downstream machines for the cutting and winding of the strips, for cutting to size to fit the inhalation device, as well as for the final assembly of the inhaler.



Membrane filling  
100% filled



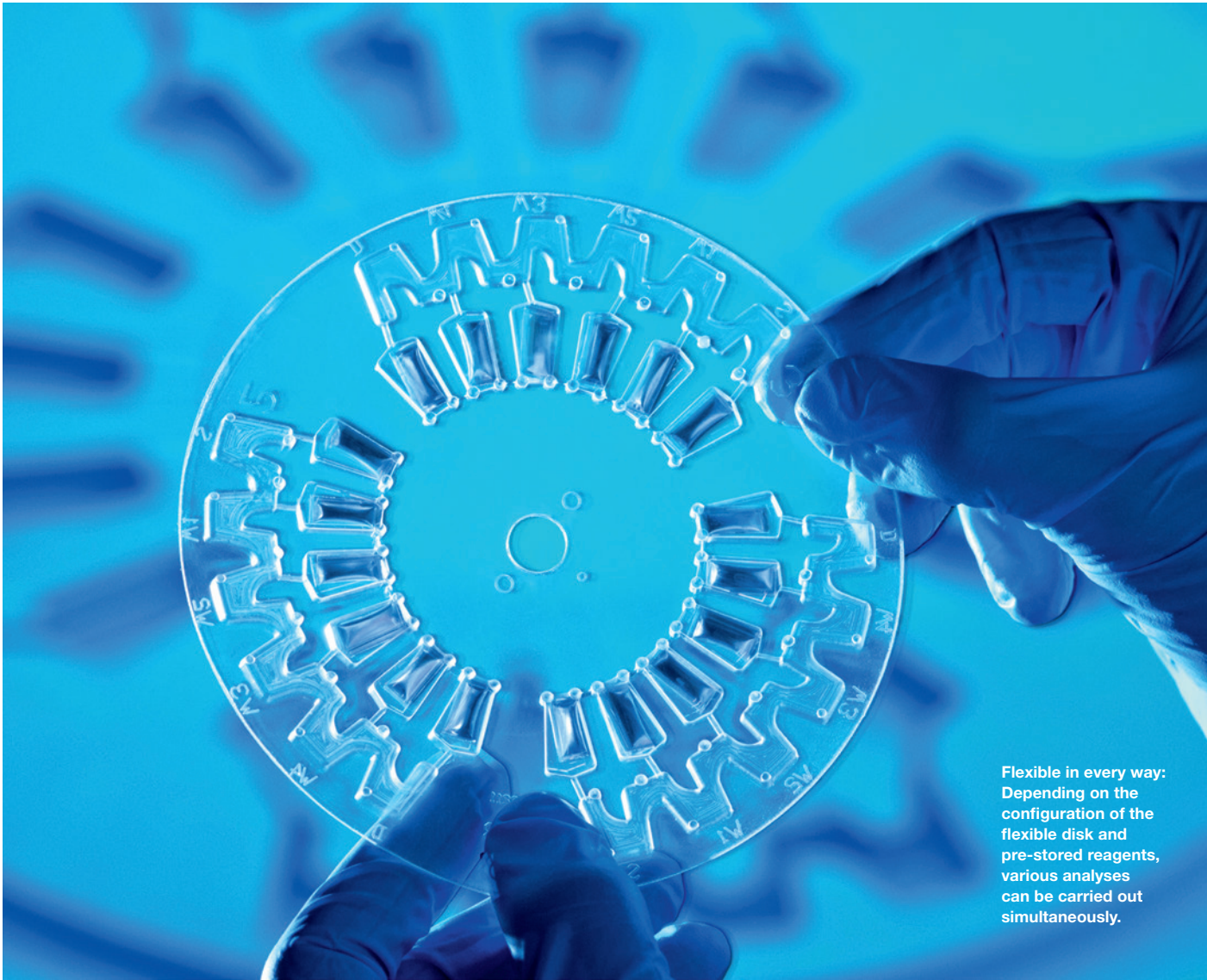
Drum filling  
partially filled



## Two dosing systems

The completely integrated powder filling module offers two principles for micro-dosing of powder into blisters: The drum filler and membrane filler technology. During drum dosing, the cavities are partially filled. During membrane dosing, the dosing units fill the blister cavities to the brim. The foil material is fed from the roll.





Flexible in every way: Depending on the configuration of the flexible disk and pre-stored reagents, various analyses can be carried out simultaneously.

# Small disks, big in diagnostics

Worldwide research is undertaken on so-called mini labs. They make it possible to prepare and analyze samples in close proximity to the patient, at the “Point-of-Care”, so that early treatment can be initiated. Harro Höfliger supplied the suitable components for a pilot system for the production of test elements at Hahn-Schickard in Freiburg.

The Institut für Mikroanalyse-systeme of the Hahn-Schickard-Gesellschaft für angewandte Forschung e.V. (Institute for Microanalysis Systems of the Hahn-Schickard Association for Applied Research, a registered association) in Freiburg, Germany, developed the “LabDisk” together with the local Albert Ludwig University: A centrifugal microfluidic technology platform for quick tests (see page 18). The centerpiece is a disposable plastic disk the size of a CD. On it are all necessary reagents – in solid or liquid form in aluminum-coated plastic bags (“stick-packs”), or in dried form as cryo pellets. The reagents are released by the rotation of the disk in the “player”, they mix with the test sample, and are distributed through very fine channels into reaction chambers. As a result, in 60 to 90 minutes, for example, infectious diseases such as malaria or multi-resistant germs can be detected.

Until 2015 Hahn-Schickard could only produce test elements in small batches up to 100 pieces. A pilot line, for which Harro Höfliger supplied two machines, now provides more capacity for small series. The Pro-Fill module is based on the flexible automated platform Vario-Flex: A pipetting station doses up to 16 dryable reagents as well as magnetic particles onto the pre-structured disks. After the

*“Feeding other types of disks, programming new coordinates, and loading different reagents – it all works very easily.”*



Dominique Kosse, Head of the Lab-on-a-Chip Prototyping and Production Department, Hahn-Schickard, Freiburg

drying process and the loading of cryo pellets, the test elements are tightly sealed with adhesive-coated or thermal sealing films in the Pro-Seal module.

Dominique Kosse, head of the Lab-on-a-Chip Prototyping and Production Department, responsible for the implementation of microfluidic concepts in test samples and small series, sees the LabDisk pilot line as a technological boost for the market readiness of customer products: “Scalable batch sizes of 1,000 to 10,000 items are a typical size for clinical testing and validation for our customers. Up until now we could not meet their needs.” With this project, Hahn-Schickard wants to provide relief, in particular to small- and medium-sized enterprises, from having to make large capital investments.

Harro Höfliger’s system concept focuses on a variable and scalable lab-on-a-chip production. “The extraordinarily rapid changeover to new products was a major reason for choosing this system design. Feeding other types of disks, programming new coordinates, and loading different reagents – it all works very easily with Pro-Fill,” says Kosse.

Currently, the cryo pellets are still inserted manually. However, with an annual capacity of up to 200,000 test elements, an additional automation step has not been ruled out. ■



Operation of the pilot line in the clean room guarantees the highest quality of the test elements produced.

The Hahn-Schickard-Gesellschaft für angewandte Forschung e.V. with 180 employees at locations in Stuttgart, Villingen-Schwenningen and Freiburg is a non-profit association of industrial enterprises. As an innovation partner for small and medium-sized companies, Hahn-Schickard conducts research and development in the fields of life sciences and medical technology, sustainability, energy and the environment, Industry 4.0, mobility and movement, as well as in other fields.



On-site diagnostics

Diagnostic procedures at the so-called Point-of-Care (POC) or Point-of-Need (PON) are not performed in a central laboratory, but in proximity to the patient, for example in medical practices. Diagnostic procedures such as glucose and pregnancy tests are well established, and even a medical layperson can use them reliably. Automated lab-on-a-chip systems are significantly more efficient: They integrate various laboratory diagnostic procedures in the smallest space, and enable parallel analysis of materials, including nucleic acids or proteins. In addition to speed, these mini laboratories score with simple operation, requiring only small sample volumes and reagents. They offer process precision and clean analysis due to the use of disposable test elements. This is what makes them attractive for countries with a weak infrastructure. But they are also useful at airports during epidemics, in forensic science, aerospace, as well as personalized medicine of the future.



Fast diagnosis at the push of a button: Evaluation of the analysis is fully automatic as seen here with the LabDisk player.

Gentle handling of cryo pellets

For sensitive lyophilisates, Harro Höfliger offers a unique automated solution with gentle transport and dosage via air flow: the Cryo Pellet Dispenser.

There are many active ingredients which can only be preserved in aqueous solutions for a short time. Particularly with thermally sensitive materials, freeze-drying (lyophilization) into pellets is a method used to achieve storable formulations. After flash freezing and dehydration under high negative pressure, a spherical, porous framework of active ingredients and excipients remains – with low density and a large, highly hygroscopic surface by comparison.

Cryo pellets are well suited for parenteral products such as vaccines due to their high rate of dissolution. Even for new diagnostic tools, such as lab-on-a-chip systems, they are ideal

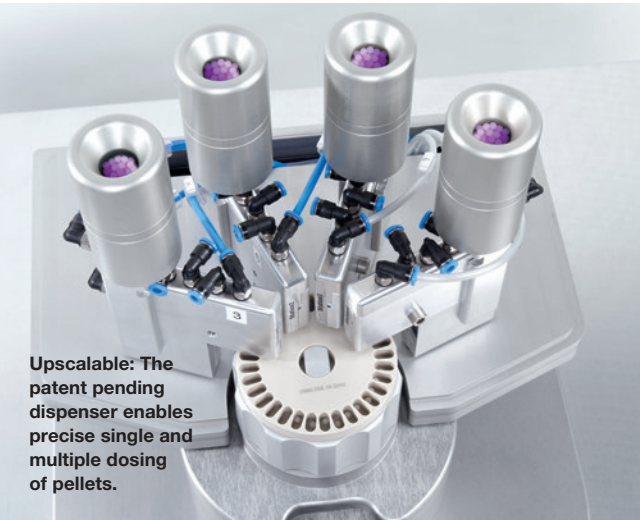
due to their storage stability. However, the fragile structure of the lyophilisates requires a great deal of dexterity in handling: Typical 0.5 to two-millimeter pellets are prone to mechanical abrasion and compression, become electrostatically charged, and must be processed at low humidity. Moreover, the small dosing amounts usually don't allow volumetric dosing.

Flexible and gentle product treatment

Harro Höfliger's entirely pneumatic Cryo-Pellet Dispenser can handle pellets with these properties. The pellets are fed in bulk, then separated non-destructively by dry air, precisely counted, and gently placed in the container. By eliminating mechanical transport solutions, the lyophilisates are safely conveyed and accurately dosed.

In addition to gentle processing, flexibility is a top priority. Depending on the degree of automation and number of dosing stations, single and multiple dosing is possible – including combinations of products into a variety of containers. The most common include vials, discs, cartridges or titer plates. The dosing speed per station is up to 30 pellets per minute, depending on the product properties.

Further benefits of the compact, low-maintenance dispenser are its ease of use and cleaning, as well as good integration capabilities in lines. An upstream sorting station rejects damaged pellets or pellet conglomerates, guaranteeing the highest product quality. ■



Upscalable: The patent pending dispenser enables precise single and multiple dosing of pellets.



Breathe easy

The Respimat® by Boehringer Ingelheim is a successful product for the treatment of respiratory diseases, entirely without propellants and especially patient-friendly.

At the Ingelheim site, the pharmaceutical company has considerably expanded filling and packaging capacities for the inhaler. Together with Harro Höfliger, partner companies from Excellence United are a part of this project.

For their blockbuster Respimat®, Boehringer Ingelheim invested on a massive scale at several sites. The main production sites are located in Ingelheim and Dortmund. In Ingelheim, the cartridges are filled under sterile conditions with active pharmaceutical ingredients on high-tech equipment. Together with the inhalers that are produced in Dortmund, the cartridges are packaged and distributed worldwide. In line with the investments, many new jobs

were created at both sites to safeguard production. Harro Höfliger, Uhlmann Pac-Systeme and Bausch+Ströbel supplied the production lines.

With this investment, Boehringer Ingelheim ensures the world market supply with their innovative respiratory product for the treatment of chronic obstructive pulmonary disease (COPD) and asthma. Respimat®'s secret of success lies in its advanced technology that has benefited patients and the environment. With-

out the use of propellants, it generates a long lasting fine mist that allows the active ingredient to effectively reach the lungs during normal inhalation. The patient can breathe better again, climb stairs and participate in life.

Boehringer Ingelheim developed a mechanical pump which allows the active ingredient to escape slowly. This provides an ideal droplet distribution when inhaling. With Respimat® it takes about 1.5 seconds to expel the dose of active



ingredient – thus making inhalation very effective. Respimat® also facilitates patient coordination of the application.

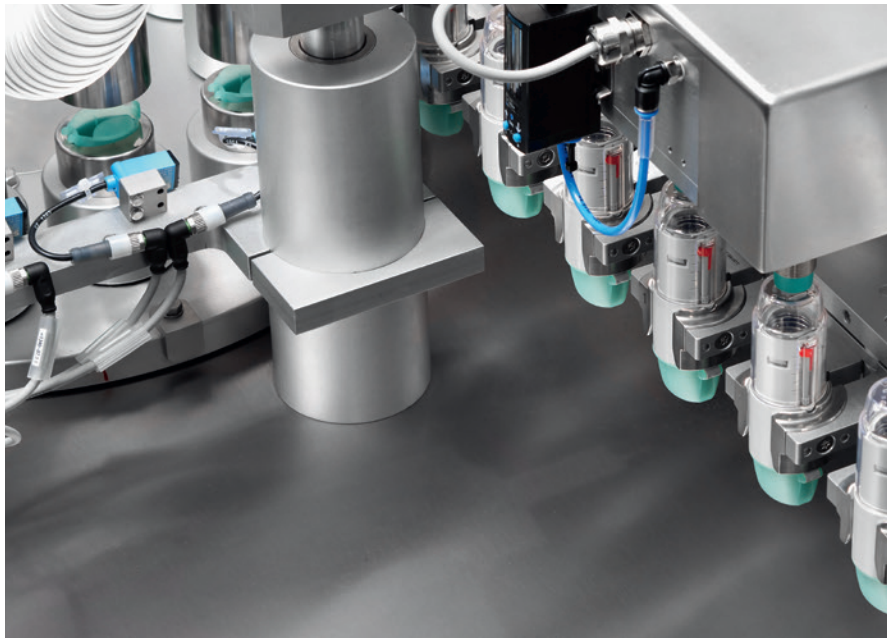
Gerald Mathe, Head of Process Management Bulk Production at Boehringer Ingelheim, gives an insight into production.

**Mr. Mathe, what was special about the layout and configuration of the production line for the Respimat® inhaler?**

*Mathe:* In many sections of the production and assembly process, the production of Respimat® and the cartridge demanded technologies that had previously not been available on the market. This is why, together with Harro Höfliger, we developed specific solutions in the aseptic filling technology and sealing sections, and for the extraordinary drawing and crimping process.

**Why did you decide in favor of Harro Höfliger?**

We do not want to buy machines – we want to buy processes. Harro Höfliger’s

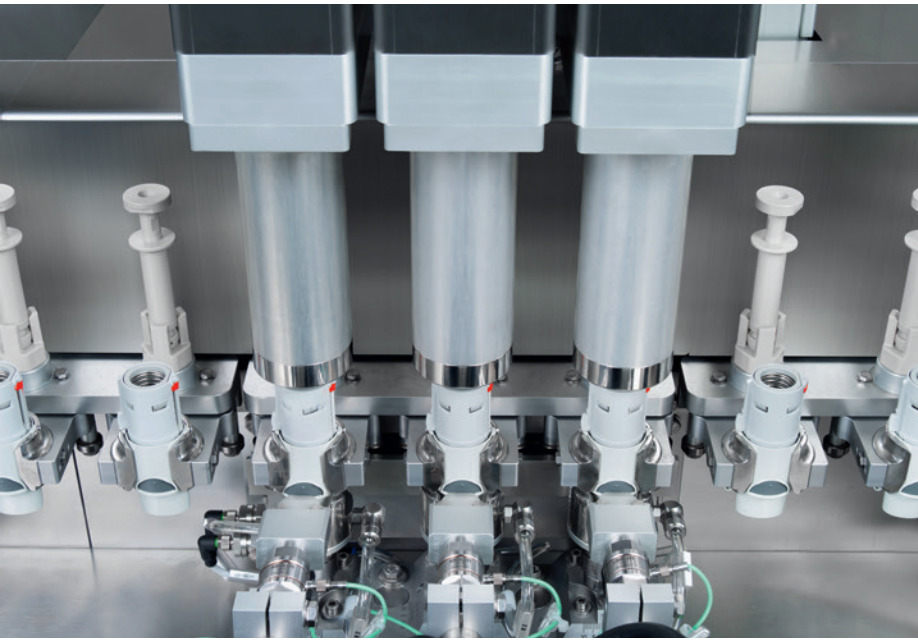


Final assembly of Respimat® inhalers.

advertising slogan is [ALL YOU NEED], a promise that we do make use of. From our experience, the company is well-positioned and reliable, from concept to design to implementation. This applies both to the project phase as well as to subsequent series production, when things need to be changed.

**What role does Excellence United play – the group of companies consisting of Harro Höfliger, Uhlmann Pac-Systeme, Glatt, Bausch+Ströbel and Fette?**

In addition to Harro Höfliger, two more Excellence United members are represented in the production chain for the




Quality assurance by means of operability tests on the device.

Respimat®: Uhlmann for packaging and Bausch+Ströbel for labeling.

**How did you handle unpredictable obstacles and pitfalls?**

We always face unpredictable events with special projects, and we have to be equal to the challenge. To date we have

always been successful in coping with such uncertainties. Situations like this require explicit handling and there has to be a structured approach. It is important that people remain calm and reserve capacities for contingencies. Here, Harro Höfliger distinguishes itself for good teamwork. ■

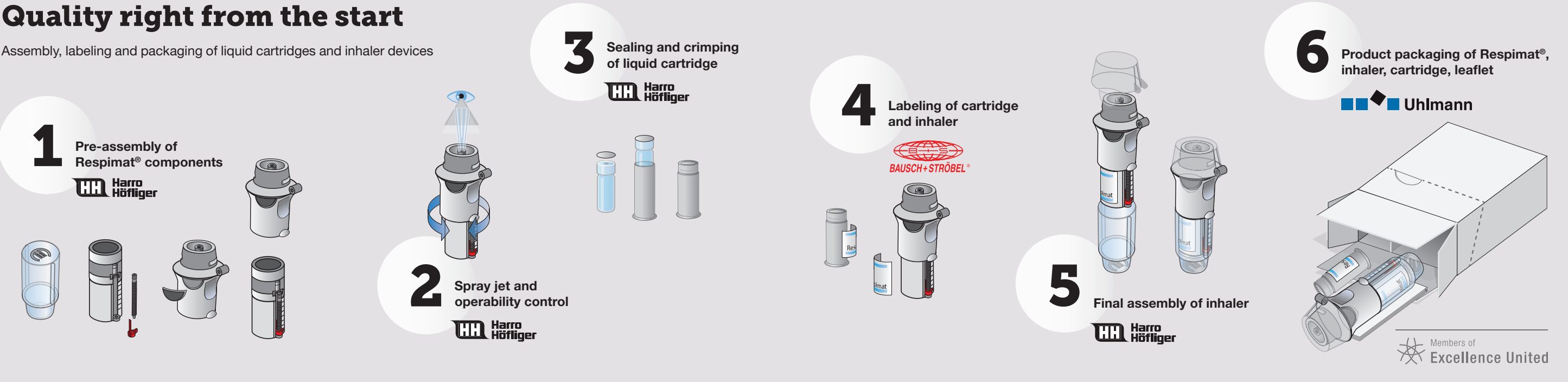


**COPD:**  
**Gasping for air**

Together with bronchial asthma, chronic obstructive pulmonary disease (COPD) is among the most widespread chronic diseases. COPD is a pulmonary disease which mainly affects the gas exchange in the alveoli. Coughing, excess mucus production and inflammation are typical symptoms. Restricted breathing, shortness of breath as well as acute deterioration are indicators for the progression of this chronic disease. Medication by Boehringer Ingelheim that is administered with the Respimat®, helps COPD-patients.

**Quality right from the start**

Assembly, labeling and packaging of liquid cartridges and inhaler devices





# Power pack

Application of a liquid medication under high pressure – a life-sustaining effect for the patient. The Respimat® with its active ingredients for the treatment of COPD and asthma is manufactured with highest quality standards for perfection.

- 1

The reservoirs are closed with a cap. The cap is sealed in order to lock the reservoirs 100% until activation in the inhalation device. The reservoirs are then fed into the transfer system.
- 2

At the same time an aluminum shell is aligned, fed and checked for deformation. In a subsequent process step, the reservoir is removed from the transfer unit and inserted into the aluminum shell.
- 3

The aluminum shell is then pressed to a specific length, so that it protrudes the reservoir's rim.
- 4

In the next step, the protruding aluminum rim is drawn over the reservoir cap in order to close it. Reservoir and shell are firmly joined together to form the completed cartridge.
- 5

The crimping and head seal operations are verified for 100% quality. Only completely round cartridges will continue to be processed.
- 6

In order to ensure the inhaler's mechanical function, the entire geometry of the cartridge is verified once again.
- 7

All good parts pass through a belt weigher, verifying the cartridges are the proper weight. After a pre-set number of cartridges has been checked, they are transferred to the automatic in-process-control. There, a specific number of cartridges is automatically measured, statistically recorded and evaluated. ■



**Uhlmann Pac-Systeme GmbH & Co. KG:** Tablets, capsules, ampoules, syringes – for almost 70 years, the focus at Uhlmann has been on the topic of pharmaceutical packaging and the optimal solution for every customer requirement, no matter how tricky it may be. Whether complete high-end packaging lines for 24/7 production or compact machines for small quantities and frequent format or product changes: As a solution provider, Uhlmann covers the full range of innovative machine technology combined with extensive support and services. At present, more than 8,000 packaging machines in more than 80 countries contribute to the safe and efficient production of medication. The export rate is more than 80 percent. More than 1,800 employees worldwide are responsible for this success.



Transfer of liquid cartridges towards the drawing and crimping system.



Exactly synchronized processes during drawing and crimping of aluminum shells.

Boehringer Ingelheim

istockphoto.com/bledhome, istockphoto.com/Shedevrator, Helmar Lünig



Transdermal patches are popular in Japan and used for many indications.

# Made in Japan

Japanese companies have a reputation for high process and quality requirements, as their focus is on delivering a perfect final product to the customer. When it comes to the production of patches for the treatment of asthma and pain Nipro Patch relies on Harro Höfliger's many years of expertise in web converting and confectioning as well as in transdermal systems (TTS/TDS). The result is the delivery of the first PMK-line to Japan.



Due to its long tradition and patients' acceptance of patch treatments, Japan has developed into the second largest market for general transdermal systems in the world, with a sales volume of more than 500 million US dollars per year. In Japan patches are available for a wide variety of applications, for many indications, and with different active ingredients.

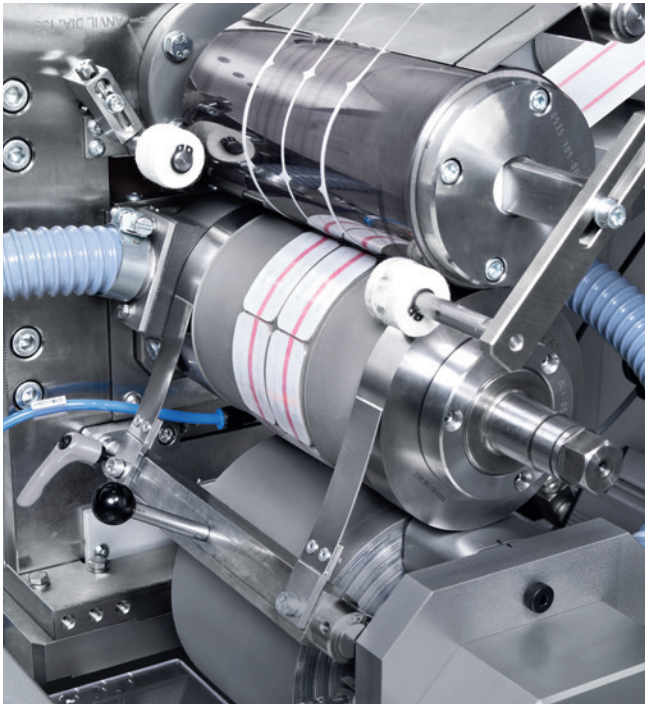
Nipro Patch is one of the biggest players in the country's market for external-use pharmaceuticals and an expert in the field of TTS/TDS products. In addition to Nipro Patch's existing sites in Kasukabe and Hanyu, a new plant for transdermal patches was built in Odate in northern Japan last year, featuring a high output production line including coating, converting, pouching, stacking and bundling.

For Harro Höfliger and partner Mutual Corporation this meant a high-speed turn-key PMK150 line, designed for web converting and primary packing into individual sachets, including stacking, unique sachet stack bundling and secondary packaging into folding cartons. Key elements to consider and integrate included the careful use of resources, minimum waste, high production yield, and flexibility with regard to future market demands and new patch designs.

With the PMK150 – a 2-lane high-speed system – Nipro Patch manufactures both an innovative 24-hour patch containing Tulobuterol for the treatment of asthma and bronchitis, and a Lidocaine patch as a local anesthetic in a twin sachet perforation design. Unique features, such as very small patch sizes without overlapping release liners and clean score cuts for the liners, optimize use of materials. Special backing webs in combination with delicate sachet poly materials and pattern sealing require attention with regard to process and inline registration.

Special features and design elements installed on the machine include:

- Unique auto splicer executions followed by a patch laminate cut & place/slip system to maximize use of the active webs when cutting the individual patch.
- Easy to clean machine parts to factor in the adhesive (PSA) behaviors of the different formulations and the possibility to carry out tooling changeovers within a few minutes in order to keep set-up times and downtimes short.



Material-saving cutting of active ingredient layer using the cut & place/slip system.

Helmar Lüning

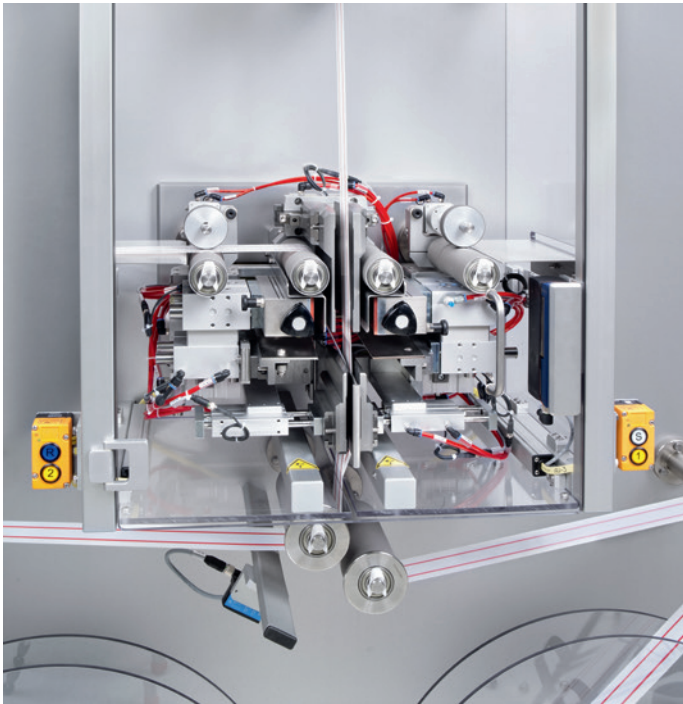
Helmar Lüning

### About TTS/TDS

Transdermal patches or transdermal therapeutic systems (TTS/TDS) are drug delivery systems that are applied directly to the skin. The active substance is absorbed by the skin and distributed through the body via bloodstream. Major benefits of a transdermal drug delivery route are that the patch provides a controlled release of the active ingredient which is not metabolized by the liver ("First-pass effect"). The main disadvantage of transdermal delivery systems is the skin's highly effective barrier property, which means that the drug molecule to be applied should not exceed a certain size. So far, there are only around 20 active substances known to meet this requirement, for instance Fentanyl, Nicotine or hormones.

- Comprehensive camera inspection systems for quality and process monitoring. The recorded data provide transparency in the batch report and in all subsequent operation data systems for continuous product and process improvements.
- Exact placement of the Lidocaine patch and twin sachet filling – including perforation – by means of a flexible and format-free paddle. During high-speed operation, this process is monitored by a vision system.

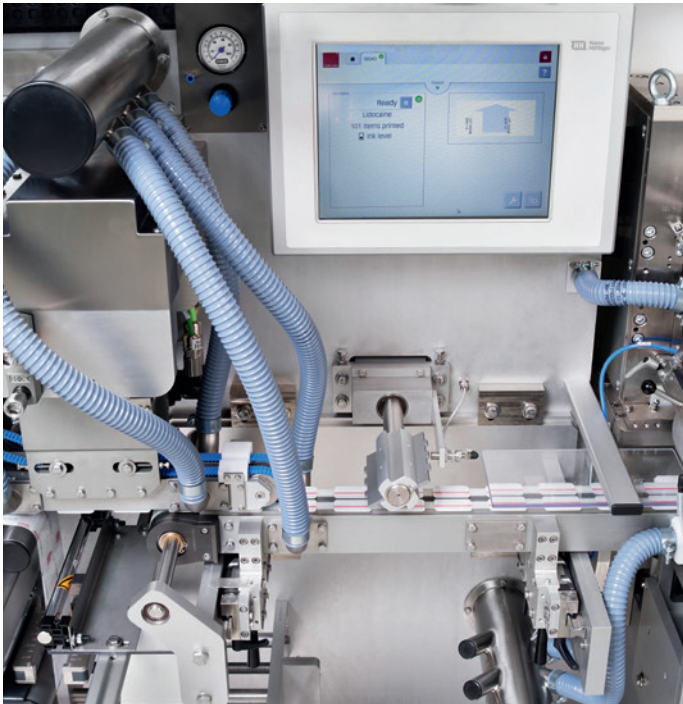
Challenges met by Harro Höfliger were the processing of a full range of format sizes from small patch and sachet size to bigger format ranges, as well as different roll stock materials. In addition, late stage customization was incorporated, i.e. inline printing and vision verification of patch and sachet. Particular attention was paid to details like perfect positioning of the



The auto-splicer enables the processing of roll materials without a machine stop.

tear notches, optimization of the residual oxygen quantity in the sachet by applying nitrogen gas in combination with the accompanying plate sealing unit, and an intuitive "Japanese" operator control. ■

**Nipro Patch** was founded in 1963 as a pharmaceutical company called Shinsen Yakugyo starting with the production of hydrogel patch products. Since 2007 they have been a member of Nipro Corporation Group, and have developed a number of products for external medical treatments and innovative matrix patches. These include the so-called "tape products", such as patches for the treatment of inflammatory diseases. Nipro Patch no longer produces solely for the Japanese market but is extending business globally, also as a partner for developing and manufacturing new products and technologies.



Exactly positioned placement of patch and twin sachet filling by means of a format-free paddle.



THE PATH TO PERFECT QUALITY



# Boost for customer projects

Accelerating processes, minimizing project costs and risks – this is what the Harro Höfliger Pharma Service experts specialize in. The basis for our product consulting is a statistical design of experiments and a comprehensive database.

The development of new drugs requires plenty of staying power. According to the Association of Research-Based Pharmaceutical Companies in Germany (Verband der forschenden Pharma-Unternehmen, vfa) the pharmaceutical industry invests an average 13.5 years and up to 1.6 billion US dollars per drug until market approval is granted. These figures factor in failed projects, as well as those which are successfully launched. So it pays off when processes can be shortened en route to commercial production.

This is precisely what pharmacist Dr. Elke Sternberger-Rützel, Head of Pharma Service at Harro Höfliger, and her nine-member team are working on. Besides an extensive test program, they count on a database with the department's pharmaceutical-technological product knowledge. "A true in-house development – implemented across departments by Sabine J. Böhne from Pharma Service and Claudia Schoder from IT", explains Sternberger-Rützel. The advantage: "If we develop processes for a new customer product, we compare its physical properties with already known materials. This way, we



Dr. Elke Sternberger-Rützel, Head of Pharma Service at Harro Höfliger.

can pre-define a product specific process window." Therefore, since we already have the basic parameters, customers can expect a faster transition from manual tests on laboratory equipment to automated project processes. In addition, smaller sample volumes of the precious new product are needed – sometimes only a few hundred grams.

### Data for practical use

Since 2005, the technological characterization and classification of active substance-containing material is a part of Harro Höfliger's service portfolio. On the one hand, this data facilitates the selection of a suitable, scalable method for the production and filling process. On the other hand, it can be incorporated into the modification and optimization of the formulation. For example: Powder is a complex material and its behavior is determined by many factors, such as particle shape, compressibility, cohesiveness and a tendency to be electrostatically charged. In dry powder for inhalation (DPI), the flow characteristics and compressibility of the carrier material – mainly lactose with different amounts of fine particles – are particularly important for clean and consistent filling into blister strips or capsules.

All of these critical characteristics are systematically examined and documented by the specialists of the Pharma Service department. In the in-house laboratory, besides a digital microscope, the team utilizes a powder rheometer, a vibrating sieve machine, a jolting volumeter for the determination of flowability, particle size and density, as well as a moisture meter and other equipment. In addition, drum and membrane fillers in manual and semi-automatic versions are available for filling tests. Very often, optimizations can be achieved rather quickly, when the customer accepts the Pharma Service recommendations and, for instance, uses an alternate lactose, which already proved to be optimal for filling during preliminary tests. This proves to be a convincing benefit that illustrates the value of Harro Höfliger's product database. ■



Alexander Malin, CEO Nativa

*"In the case of our inhalation project with Harro Höfliger, the Pharma Service product database has set the course for our process. With Pharma Service's support, we were able to decisively and quickly identify the appropriate procedure. For future product development, we will also count on Harro Höfliger's pharmaceutical expertise and reliable service. Our partnership has proven successful once again!"*

Founded in 2010 in Moscow, Nativa has specialized in the development and production of generic and import substituting drugs for the Russian market.





200 guests from all over the world came to the Innovation Expo in Allmersbach im Tal.

## Trends and traditions at the Innovation Expo



At their in-house show "Innovation Expo" on April 19 and 20, 2016, Harro Höfliger informed about 200 guests from all over the world about their latest production and packaging technologies. In line with the slogan "Technology and Trends", the enterprise presented a cross section of their extensive machine and service portfolios on 1,000 square meters in Allmersbach im Tal and the new technology center in Backnang.

In addition to inhalation and capsule filling, the focus was also on product assembly and packaging. Furthermore, the special exhibition "40 Years of Success" documented four decades of Harro Höfliger's history. Numerous videos and product exhibits documented the development of the company from a straightforward one-man business to a technological leader with more than 1,000 employees. ■



Harro Höfliger (right) with Siegfried Bullinger (Bausch+Ströbel) at the in-house show of the Excellence United partner Uhlmann.



Expert lectures, for example about the new XStraw® administration form, and discussions rounded off the exhibition program.



The disc filler was one of the exhibits to be experienced in action in different workshops.

Thomas Geffken, Tom Philippi

Haykel Ghennem/Studio BlackBird



The professional framework was provided by lectures and customer presentations about current market developments and innovative drug dosage forms.



The German Ambassador in Tunisia, Dr. Andreas Reinicke, welcomed the participants of the "Innovation Talks".

## Networking in the MENA region



By founding Harro Höfliger MENA S.a.r.l. in 2015, Harro Höfliger is now also represented in the Middle East and North Africa (MENA). The official inauguration of the branch office in Tunis was the reason for the "Innovation Talks" on site. From May 11 to 12, 2016 100 guests from the Arab World and North Africa as well as from India, Pakistan and Iran came together to exchange information and think about the future together. Among the guests were owners, managing directors and business development managers from pharmaceutical companies, the German Ambassador in Tunisia, a representative of the Tunisian Health Ministry as well as the President of the National Chamber of the Pharmaceutical Industry. "The strong customer relationship and trust in Harro Höfliger's technologies was demonstrated by the large number of participants," Fadhel Belaiba, Managing Director HH MENA, summarizes the event. "This is the basis for HH MENA's further growth across the borders." ■

### Visit us:

**Pack Expo/Pharma Expo**  
Chicago, USA,  
06.11. – 09.11.2016

**All4Pack/Salon de l'Emballage**  
Paris, France,  
14.11 – 17.11.2016

**P-Mec India**  
Mumbai, India,  
21.11. – 23.11.2016

**PharmTech**  
Moscow, Russia,  
22.11. – 25.11.2016

**Drug Delivery to the Lungs (DDL 27)**  
Edinburgh, GB,  
07.12. – 09.12.2016

**Arab Health**  
Dubai, United Arab Emirates,  
30.01. – 02.02.2017

**Pharmapack**  
Paris, France,  
01.02. – 02.02.2017

**Interphex**  
New York City, USA,  
21.03. – 23.03.2017

**ICE**  
Munich, Germany,  
21.03. – 23.03.2017

**RDD Europe**  
Nice, France,  
25.03. – 28.03.2017

**INTERPACK**  
Düsseldorf, Germany,  
04.05. – 10.05.2017



# Inventive. Qualified. Reliable.

ARGENTINA  
AUSTRALIA  
AUSTRIA  
BRAZIL  
BULGARIA  
CANADA  
CZECH REPUBLIC  
CHINA  
CROATIA  
EGYPT  
FRANCE  
GERMANY  
GREECE

GREAT BRITAIN  
HONG KONG  
HUNGARY  
INDIA  
IRAN  
ISRAEL  
ITALY  
JORDAN  
MEXICO  
NEW ZEALAND  
PERU  
POLAND  
ROMANIA

RUSSIA  
SLOVAC REPUBLIC  
SINGAPORE  
SOUTH AFRICA  
SOUTH KOREA  
SPAIN  
SWEDEN  
SWITZERLAND  
THAILAND  
TUNISIA  
TURKEY  
UNITED STATES

5 | 2016 | 2017 | 2018 | 2019 | 2020 | 2022 | 2023 | 2024



## Focused on High-Tech Engineering. Anytime, Anywhere.

For more than 40 years we have been a reliable partner for our customers. This is based on innovation, technological expertise, creativity as well as traditional values such as trust, honesty and loyalty. Thanks to mature technology and proven system platforms, Harro Höfliger can fulfill all the requirements of com-

plex manufacturing and packaging lines. Our availability does not end simply with a successfully finished project. As reliable system providers we support our business partners worldwide with ongoing comprehensive service throughout the life of the equipment.