

HARRO

The Customer Magazine
by Harro Höfliger

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Give me five!

Intelligent system solutions
for processing different types
of autoinjectors and devices



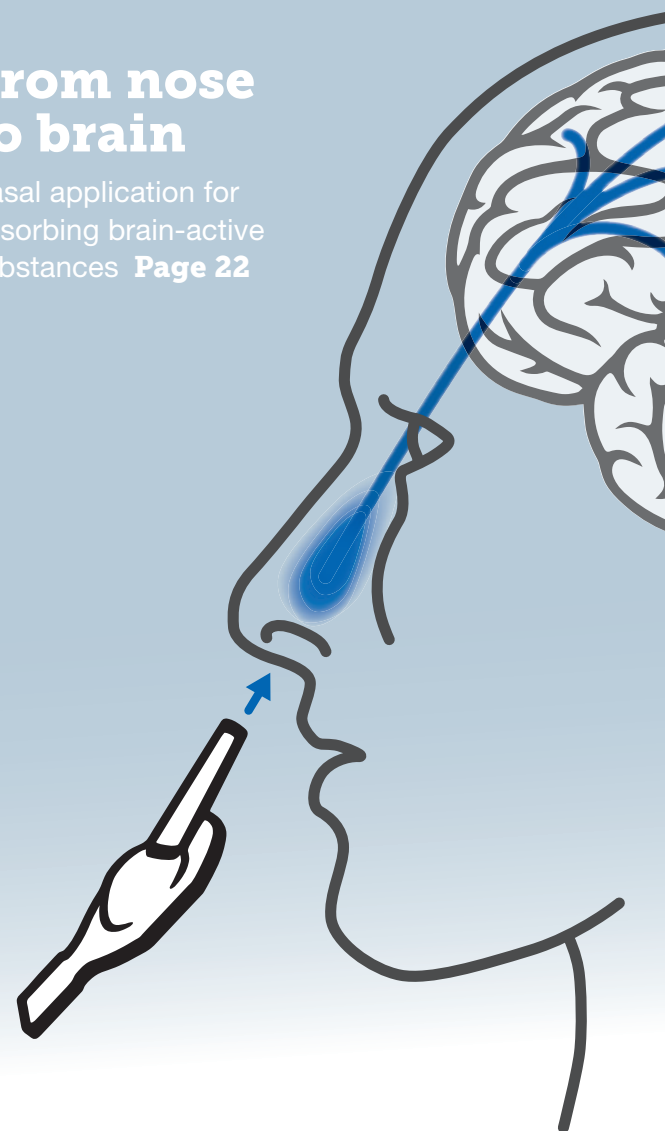
Shaping the future

The new technology center in Backnang **Page 14**



From nose to brain

Nasal application for absorbing brain-active substances **Page 22**



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Intelligent system solutions for processing different types of autoinjectors and devices





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Dear Readers and Business Associates
When our one thousandth employee recently signed on the dotted line, Harro Höfliger officially entered a new league. We have a good line-up, our thinking and actions focus on customer centricity and are the basis for our success. And we're a little bit proud of the fact that we've doubled all our KPIs in the space of just five years. That is both an incentive and commitment to remain true to our promise [ALL YOU NEED].

We aim to put all our efforts and passion into addressing new goals and tasks in the upcoming years, while continuing to clearly focus on our customers. We will be increasing dynamics and reaction speed with higher throughput rates and optimized processes. Based on our high quality standards, we offer solutions with a technical edge. All of this is at the heart of our strategy 2020.

In this second issue of the Harro magazine, we give you a preview of the measures we intend to implement as part of this strategic plan. We are also opening our factory store to you at our new production facilities in Backnang. Visit us there and see how we are already setting our course for the future. Our China representative, Daning Zhao, reports on how current and future market success can only be achieved through sustained global commitment.

Welcome to the second issue of our magazine. We hope it makes inspiring reading.

Best regards

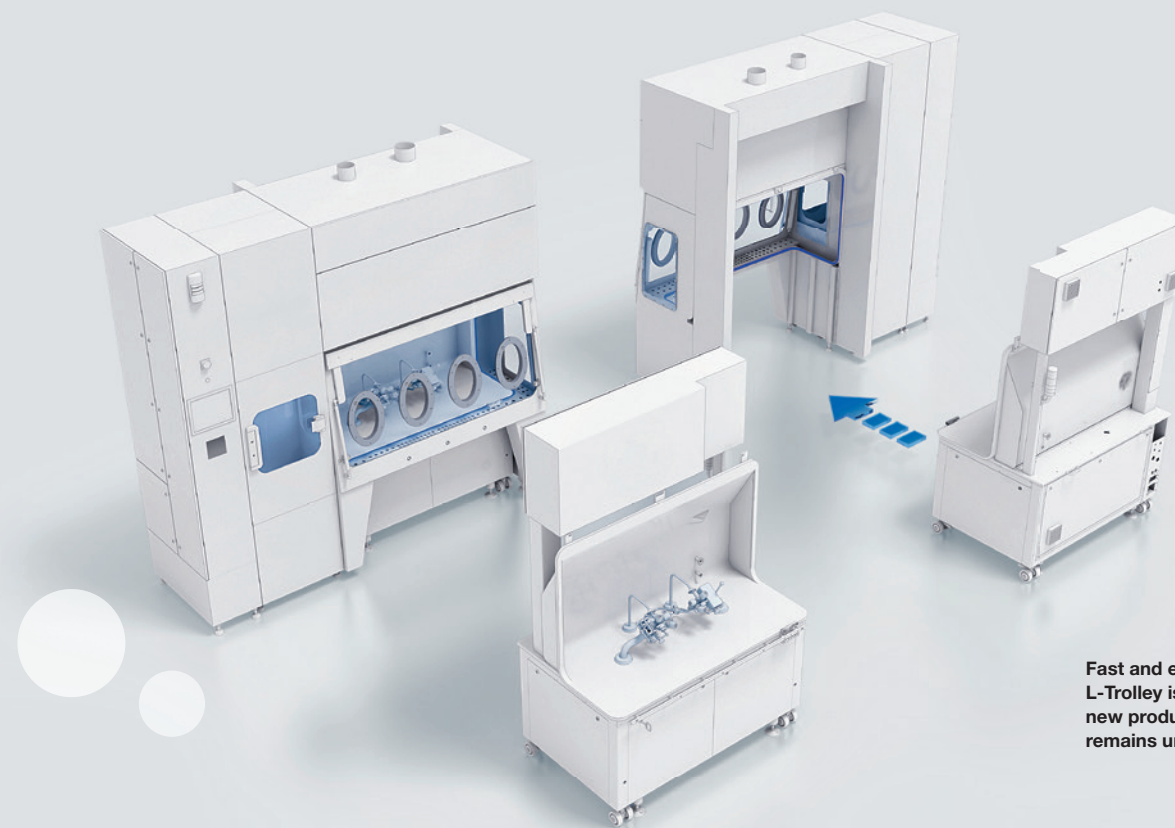
Thomas Weller
Chief Executive Officer
Harro Höfliger Verpackungsmaschinen GmbH

Flexible aseptic filling

Model cooperation: Excellence United partners Bausch+Ströbel and Harro Höfliger have developed a flexible production solution for the L-Trolley with VarioSys®.



Short retooling times: IV bags, ampules and vials can be filled quickly and flexibly over the modular system



Fast and easy: only the L-Trolley is swapped for a new product – the isolator remains unchanged

Aseptic work stages in sterile conditions are a common feature in the production of hospital samples, filling active agents for study purposes and comparative studies. The VarioSys® system and L-Trolley create flexible production possibilities in a standard isolator. The requirements are clear: pharmacists need a compact system in which differing volumes are filled into a wide range of dos-

age forms in an isolator. The solution was developed by Excellence United partners Bausch+Ströbel and Harro Höfliger in cooperation with the Swiss isolator specialist Skan: a modular flexible system for filling ampules, vials, syringes or IV bags with active agents.

Many different packaging materials and batches can be processed in an isolator thanks to short retooling times. If another

product is to be filled, the VarioSys® trolley is simply swapped. The isolator remains unchanged. A surrounding inflatable gas-ket system guarantees sterile conditions inside the isolator. The customer thus only invests once in a standard isolator and first trolley. Further trolleys can be added to the existing isolator at any time. Both standard and non-standard receptacles can be filled and sealed. ■

Bausch+Ströbel, Harro Höfliger, Stoll von Gattl



Excellence United member

Bausch+Ströbel designs, builds and sells packing and production systems for the pharmaceutical industry. Products in both liquid and powder form can be reliably and carefully processed on the systems. The Bausch+Ströbel portfolio ranges from semi-automatic equipment for laboratories and medium performance machines to very complex high performance systems – precision in primary packaging.

40 Years of Success

The Harro Höfliger success story spans four decades. Selected milestones illustrate the company's dynamic development from used machinery trader to global supplier of customized system solutions. All-round partner for the pharmaceutical, medical, consumer goods, cosmetic and chemical engineering industry.

1975-79

Company foundation, trading in reconditioned cartoning machines. Four years later: the factory moves to Allmersbach im Tal.



1987-90

Development of a standard machine program. 1990: For the first time more machines are built for the pharmaceutical industry than for other sectors.



1991-98

Beginning of international expansion. Introduction of a quality management system to DIN ISO 9001. 1998: Harro Höfliger employs 200 people.



2008

Extension of the development center to create additional system design capacity. Around 500 employees generate revenues of € 90 million.

2010

Foundation of the Excellence United cooperation between Fette Compacting, Bausch+Ströbel, Uhlmann Pac-Systeme, Glatt and Harro Höfliger.

2015

All relevant KPIs doubled within five years. Revenue of € 200 million. The one thousandth employee is in sight.



Smart hybrid solution

Harro Höfliger teamed up with a well-known Swiss pharmacist on a project for separating and labeling of autoinjectors and devices. Arthur Fabian, Principal Engineer Device Technology, reports on the challenges of the project and process.



Mr. Fabian, what exactly do you process on the line?

The machine was planned and developed at our request to separate, label and check autoinjectors, needle safety and self-injection devices, supplied in tray stacks. These devices are part of a combination product, a handling device with the relevant active agent in liquid form. What's special is that we're talking about chilled products that have to be processed and then shipped in a fixed cold chain at temperatures from +2°C to +8°C. The system is part of an overall line with top loader and end packaging machine, which has been online since November 2015 five days a week, in three-shift operation. It operates at a rate of 15 to 40 devices per minute, depending on the shape of the device. Changing products is easy for us thanks to fast retooling.

What challenges did you have to take on together?

The tight schedule was a very critical aspect of the project. Nevertheless we decided to give the suppliers the time they needed for development and implementation at their own sites and not move one of these phases to our factory. And that was absolutely the right decision. The system was commissioned, successfully qualified and validated without a hitch. The factory acceptance test was also conducted at the supplier's factory, so we stayed on schedule and went into operation in November 2015 according to plan.

"Changing products is easy for us thanks to fast retooling."



Arthur Fabian,
Principal Engineer Device Technology

Does linkage to the downstream system work?

The Harro Höfliger team defined interfacing with the downstream system, a top loader-cartoning machine. Together with the two suppliers a detailed interface description was drafted and implemented without any problem.

Did the project pose any special technical issues or obstacles?

Some technical aspects were completely new, both to Harro Höfliger and ourselves. Making the right decisions was important, based on correct on-site analysis and input from our in-house experts. Experience gained in the course of the project was used to further optimize the machine, update requirements in the URS (User Requirement Specification) and improve packing material in two cases. The effort paid off. What was initially planned as a semi-automatic solution turned out to be a flexible fully automated hybrid system.

What does hybrid mean in this context?

It points to the fact that all the different workpiece receivers are already integrated into the system. This idea and solution is a masterpiece on the part of the engineers. We can now convey and label all five differently contoured devices in the system with no need for retooling. The system automatically conveys the different devices to the right receiver in



The flexible hybrid system in action



Fully automated product handling for pen labeling



Delighted with
the successful
production flow

"The idea of preinstalling all the necessary workpiece receivers is a masterpiece on the part of the engineers."

Arthur Fabian

the right position, so there is no need for manual retooling. Automated product changing saves us a huge amount of time and of course dramatically increases the efficiency of the whole production process. The tray loader and rotary indexing assembly machine were also combined on one platform to take up less space.

Can you describe the production flow in the machine for us?

The stack of trays with the devices is inserted into the system manually. The system collects a tray, conveys it to the pick-up point for the robot, which carefully places the device in the right receiver. The device is then transported through the system and labeled at a station, where both label placement

and imprint are checked. The robot then collects the device and places it on the belt for conveying to the top loader. The empty trays are stacked and conveyed to the discharge point for manual removal. A special feature of the system is monitoring via motion sensor. It detects whether a person is reaching into the machine so we can protect operators from potential injury.

How did you feel about the cooperation?

Harro Höfliger was always very fast and to the point. Everything went very quickly from taking stock of the situation, analysis and the drafting and implementation of a solution proposal. That's why we look forward to working with Harro Höfliger on further projects. ■

About the user

The Swiss company has belonged to a large American group since 1959. It focuses on the aseptic production and packing of parenteral products (pre-filled syringes and vials) and associated combination products. With around 1,200 employees the pharmaceutical company is the largest employer in Schaffhausen canton.

5 wins

A program consisting of five palletizing systems enables flexible handling of product components in trays.



One of five tray
loader versions:
Classic model

In response to the rising level of automation in the pharmaceutical industry Harro Höfliger launched development of palletizing systems, resulting today in a formidable line-up of five different palletizing systems. Customized solutions can thus be configured to permit easy flexible loading and unloading of product components onto and off trays. For inhalators, pens or autoinjectors it is no longer a matter of purely plastic product components that require assembly. Now highly sensitive pharmaceutical components like ampoules or pre-filled syringes are processed in the final assembly of the finished products. The tray loaders are equipped with the same control system and proven user navigation as all other Harro Höfliger systems – and of course come in a GMP-compliant design. Interfaces are clearly defined, the customer only has one point of contact, and in the event of a service deployment everything is provided from a single source – quickly and professionally. Distinguishing the various palletizing systems is less a matter of the technology inside than the implementation of systems and devices to meet the project requirements. Camera systems, marking stations and other accessories can thus be ideally complemented. Suddenly completely new solution approaches can now be realized, as illustrated by the examples of the hybrid version described in greater detail in the overleaf. Widely known and proven in many completed projects are the three classic palletizing types for tray sizes up to 400 mm x 600 mm.

Tray loader versions

1

Classic

Optimally combines a compact design with high processing rates and product handling times of up to three seconds.

2

Speed

Always the first choice when speed is of the essence. With tray changing times of under four seconds this version is frequently found in high speed systems.

3

Smart

A very flexible machine type, which can be customized to suit specific material and tray flows. It is very well suited in cramped conditions.

4

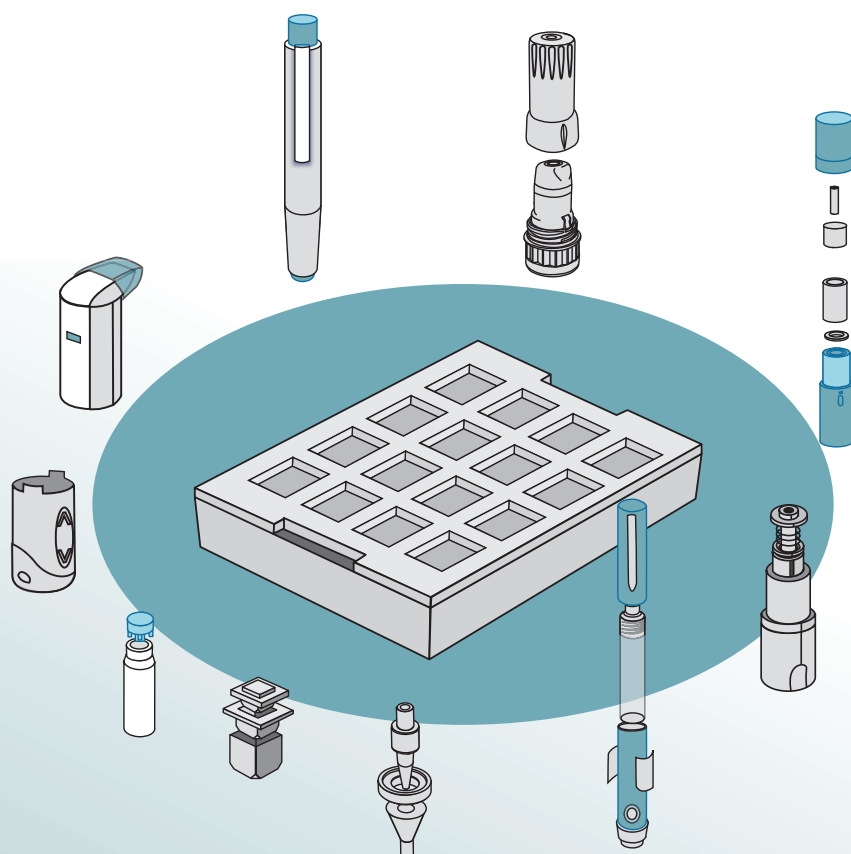
Hybrid

As the name indicates, this version combines a tray loader with flexible assembly and inspection processes in one machine. Benefit: minimum space requirement and reduced complexity. This version is directly integrated into the machine frame and forms a highly flexible effective unit when equipped with a servo axle or robotic system.

5

Rondo

Specially designed for the standardized Rondo tray in combination with cylinder ampules and is used for instance in assembly systems for insulin pens. It is designed for the medium output range and thanks to its slimline format, also takes up very little space. As an alternative to the Rondo tray, syringes in tubs can also be reliably handled.



The trays can take both individual components or pre-assembled units of inhalators, pens or injectors ready for assembly

New drive: Harro 2020

Passionate – close – inventive – reliable

What a development: in the space of five years Harro Höfliger has doubled its revenues, and the workforce record of 1,000 employees has been surpassed. Capitalizing on the dynamics generated by growth, Harro Höfliger aims to continue ensuring customer satisfaction and top quality as part of its Strategy 2020. Despite its new size, the company intends to take up the future challenge of preserving flexibility and customer closeness. As CEO Thomas Weller admits: “We are conscious of the fact that we have to manage growth and our new size. We will have to take a closer look at many routine processes. It’s the only way to increase customer satisfaction and loyalty.” For Harro

Höfliger intends to continue offering everything from a single source and always set the benchmark in international comparisons. Thomas Weller continues: “We aim to increase our dynamism and speed of reaction and thus preserve our flexibility. Market managers and business units are to be incorporated into an interdisciplinary organization structure in the future. Our new structure is based on a 3D matrix.”

To ensure that projects run smoothly, Harro Höfliger offers over-arching shared services, for instance in Global Sales, Pharma Service or Controlling.



At Backnang efficiency is guaranteed by organization and optimized intralogistics

Harro Höfliger

Tom Philippi



"We aim to increase our dynamism and speed of reaction. We're never more than a call away."

Thomas Weller,
Chief Executive Officer,
Harro Höfliger

On the horizon: the new Structure 2020

Harro Höfliger is steadily adapting its organization to accommodate growth and increased size. Already launched, the process is due to reach completion in 2020 to preserve the company's dynamism, speed of reaction and customer centricity. The aim is top quality with perceptibly shorter throughput times. As part of Strategy 2020 Harro Höfliger is setting up seven business units, which will operate as independent units within the company. Thomas Weller: "We need agile expert teams that act with purpose in their core business and respond promptly to changes." In large-scale turnkey projects the competence of the individual units can be called upon as required in multidisciplinary efforts.

Process-optimized. Process optimization models will be the norm in all seven units. However, the individuality that makes Harro Höfliger so special will be preserved. Harro Höfliger is aiming for less red tape, optimized material supplying and the best possible assembly processes.

Consolidated. The business units will gradually grow together. The interaction between developers, control engineers, project managers and assembly planners will be intensified, thus improving and speeding up communication and boosting team spirit.

The focus, however, remains on the customer's product. Every solution is geared towards specific requirements, true to the motto: [ALL YOU NEED]. ■

Unchanging: the values of Harro Höfliger

[ALL YOU NEED]. As Thomas Weller emphasizes: "Harro Höfliger's key qualities, the core competencies that made us what we are today, a successful major player, remain unchanged." This also applies to continued efforts to support business partners as far as possible across their process and value chain. The customer's product determines the production process and machine design concept. Precisely customized product solutions are the result.

Passion for the job. Unconventional ideas, getting down to work and making what seemed absolutely impossible, possible are qualities that have always put Harro Höfliger in a league of its own. Harro Höfliger continues to pursue this passion and accepts no compromises.

Customer closeness. The global network of around 150 sales advisors and key account managers gives the company a leading edge in the market. In close contact with customers these experts ensure that only the best solutions are implemented to meet requirements.

Inventive. Swabian inventors with a bold unconventional spirit will continue to create unique solutions in the future. Harro Höfliger engineers set benchmarks for the industry. The unique interaction of engineering and pharmaceutical experts remains one of the company's key USPs.



The new Factory 5 in the 'Pharma Solid' business unit serves as the prototype for the new organization. Thomas Weller comments: "We're working here on how the entire company is going to be organized in the future. If you like, it's a true test run that is going to set benchmarks."



Welcome to Backnang



Felix Nink (second on right) and his team in Backnang depart from well-trodden paths to pioneer new ground and thus achieve optimum efficiency

Shaping the future

At the new Backnang technology center Harro Höfliger optimizes the production and assembly of capsule filling machines.

All sectors of the Pharma Solid business unit are combined in 3,500 square meters of production and office space. Development, design, production and assembly departments work in concert with sales, project and product management and customer service under one roof. The goal is clear: to achieve greater efficiency and customer closeness. An ambitious objective: lead times at Pharma Solid are to be reduced by half within the year. Unit manager Felix Nink and his team plan to achieve this in small steps, with an on-going improvement process. As Mr. Nink remarks enthusiastically: "Now we have all departments close together under one roof, making it easier for us to identify improvement potentials."

Following the move in May 2015 many measures in the assembly area were successfully implemented during the first few months. The central warehouse and implementation of pre-picked subassemblies in material shuttles speed up internal logistics. Newly defined assembly flows minimize error rates and short distances facilitate communication. Since the move, team spirit among the approximately 80 employees in the business unit has improved perceptibly. Ideas can be exchanged very quickly when the Design Department is right next door to Control Engineering. Harro Höfliger regards the Backnang site as a pilot project for future company restructuring. ■





Fabian Elsässer (on right) and his colleague are pleased with the operating terminal they developed together

Tom Philipp, Harro Höfliger

Transparency for operators

Harro Höfliger's HMI interface has long been regarded as a benchmark. Development of a new user interface began back in 2013 to guarantee that competitive edge. Currently all new machines and systems are equipped with it.

The new beginning was the achievement of Fabian Elsässer (see box) and his team along with external partners. As Mr. Elsässer explains: "An outside view broadens your horizon." Harro Höfliger designed and developed the new HMI (Human-Machine Interface) together with CaderaDesign, a specialist in industrial and user interface design, usability and user experience. Mr. Elsässer continues: "The experts at CaderaDesign are by no means impractical creatives, but down-to-earth industrial designers, who understand machines." An important aspect

because the new HMI is not only meant to support operators, but also make things easier for control engineering.

Learning about what matters

The basis for the new user interface was an intensive analysis phase and feedback rounds with users and developers of the existing HMI system. The project members then cataloged the operator tasks, examined the various machine types and jointly rated their functions and benefits.

The next step involved outlining ideas and developing and assessing layout concepts. Mr. Elsässer sums up: "We came up with the first structural designs of the user interface very quickly and fleshed out and honed the drafts step by step in workshops. The basis was of course multi-touch technology, which is common today. Our clear aim was to offer operators maximum user-friendliness and transparency – without incurring additional costs for the customer."

The requirements dictated a navigation structure with as few nesting levels as possible and a standard look and feel on all levels. It was already settled that implementation would be in-house at

User-oriented



Station-oriented



Task-oriented



As intuitive as a smartphone

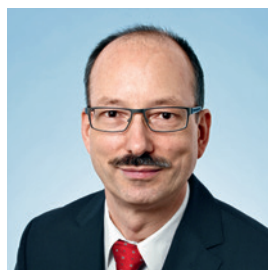
The new operating terminal for all future Harro Höfliger machines and systems impresses with the highest ergonomic standards. All functions can be conveniently controlled from the touch display. Preserving the proven station overview eases transition to the new HMI, along with swipe or zoom functions that are long-familiar from smartphones or tablet PCs.

Harro Höfliger with the existing HMI/SCADA solution zenon by COPA-DATA. As Mr. Elsässer explains: “Only we know our requirements with regard to project planning. And it’s imperative that this know-how stays with the machine builder.”

Combining task and station orientation

In addition to station orientation, which was already familiar from the previous HMI, Harro Höfliger also opted for task orientation as an operating and interaction principle. This was due to the complexity of the machines. Thanks to this task orientation in the HMI the operator is supported in all the activities that he performs on the machine. The HMI therefore prompts the operator situationally, regardless of whether he has to set up a machine or retool, load a new recipe or launch batch recording. The operator is assigned tasks according to the pro-

“Dispensing with the frills, the new HMI focuses on essentials and reliably navigates the operator through the menus.”



Sebastian Rittner,
Project Engineer Assembly,
Boehringer Ingelheim
microParts GmbH

duction mode (set up production, start production, run machine until empty, end production) and depending on the role assigned to him. The user profiles store which actions may be initiated by defined users and which machine function they may use. Preserving the station overview proven in the preceding HMI eases system handling. Operators familiar with the old HMI system therefore intuitively find their way around the new terminal without training.

Customizing for clarity

The new HMI ensures that during production the operator only receives the information he needs for his respective role. Machine data are displayed in widgets on the main screen. Drawing on a machine-specific box, every operator can pick out the widgets relevant to his tasks and thus create a customized home screen. ■

“We don’t sell machines, we generate projects”

Daning Zhao, Chief Representative Officer China at Harro Höfliger, describes how the Swabian mindset copes with Chinese market practices.



Promising future for talent

Careers at Harro Höfliger

He is 27 years old, ambitious and single-minded: Fabian Elsässer has headed strategic planning and development of HMI and SCADA systems at Harro Höfliger since 2013. Experts like Mr. Elsässer are welcome at Harro Höfliger. And it is part of the company’s innovative culture that they quickly gain responsibility, for according to Höfliger, technical progress flourishes best in a climate of trust. In Mr. Elsässer’s case it was the immense task of orienting the Human-Machine Interface (HMI) for all systems even more closely to the operator and his tasks. His original team of three has now



swelled to eight software experts and is still growing. What makes him the man for the job, is not only his dynamism and determination, but also his well-founded experience. Following an integrated degree program in electrical engineering, in the midst of the global financial crisis in 2009, he began his career as a developer of HMI and SCADA systems with a machine builder specializing in the pharmaceutical and cosmetic industry in Crailsheim. In 2013 the man from Backnang took up the challenge at Allmersbach. Back on home ground Fabian Elsässer has found his future.

Boehringer Ingelheim, Tom Philipp

Christoph Kalscheuer, Chunhai Cao/Stockphoto.com

How does a Chinese academic end up in Allmersbach?

Danling Zhao: Through the Steinbeis Foundation. Interested academics were specifically recruited to facilitate SMEs market entry in China. The Steinbeis Foundation arranged an integrated degree program for this purpose in cooperation with Danube University Krems. I seized the opportunity in 1998 and then came to Allmersbach. My technically and pharmaceutically focused biology degree suits Harro Höfliger at least as well as that of a mechanical engineer.

Did you originally come with the intention of staying?

Well, I certainly hoped to forge bridges between Europe and China. Nobody could safely predict that a two-year integrated degree program was going to turn into one-and-a-half decades. At any rate, during my studies I was already working on a concept allowing my employer Harro Höfliger to tap the market in the Middle Kingdom. It went on to become the subject of my Master thesis.

What is the key to business success in China?

The crucial basis for doing business in my country of birth are trust and good personal relationships. And initially, you need patience. You have to invest a lot of time building up networks. In Chinese 'Guanxi' means an established circle whose members are bound by particularly close relationships. Our strength within the team is that we are at home in both cultures. We see ourselves as bridge-builders and relationship managers. Speaking personally, I have long felt at home in Allmersbach. So much so in fact that I don't offer 'Made in Germany' but 'Made in Swabia'. Our business associates regard the industrial belt around Stuttgart as a symbol of German quality and thoroughness. Germany still enjoys an excellent reputation for quality. And it is something we can build on.

What do customers expect of you as machine providers?

Standards are high in the Chinese pharmaceutical indus-

try. Ultimately, what counts is that a perfect product drops off the production line. Interest in detail is only peripheral. We create a basis for trust with quality and reliability. Once trust is established, we rely on the machine suppliers to do their bit. So actually we don't sell machines, but generate projects.

That sounds like high expectations of consulting expertise?

Absolutely. Know-how transfer is very important. You're not only buying a machine, but expertise. That's why we listen very closely first of all, then discuss the details on a sound technical basis and stake out the technical scope. There is a lively interest in practical tips, market assessment and detailed knowledge, including examples of successes to date. This shows customers that we're not talking through our hats, but really do deliver what we promise. We open up new perspectives to our customers and occasionally new markets as well. For instance, we are assisting Chinese API manufacturer Hisun to develop new dosage forms.

Is it accurate to say that the systems for new dosage forms define your business with China?

That's right. We also aim to stay true to our niche. We have virtually no local competition when it comes to systems for transdermal plaster, orally soluble film, mucoadhesive film strips for mucosal resorption or inhalators. We have the field to ourselves with specialized machines and customized solutions.

What's coming up next on the Chinese market?

We will continue to cooperate with our trade partner Rieckermann as distributor and first-level support and moderately extend our own team in Shanghai. We still see a lot of potential across our portfolio, because we keep the pharmaceutical market moving and help our customers to tap new business fields. After all, Chinese enterprises are always on the look-out for something new. ■

Danling Zhao and his team represent Harro Höfliger in China. From left to right: Frank Zheng, Tony Jing, Daning Zhao, Lily Yao, Yuan Su



Harro Höfliger

Atelier Lüning, Chunhai Cao/Stockphoto.com, Narong Jongsirikul/fotolia.com

Focus on new markets

Hisun aims to extend its market base with new dosage forms. Due to its diversification, the Chinese enterprise has opted specially for Harro Höfliger know-how.

The Chinese pharmaceutical industry is girding itself to make up lost ground. Mainly engaged in producing generics so far, Chinese manufacturers are planning to make a name for themselves with new products and dosage forms in the future. This also applies to Zhejiang Hisun Pharmaceutical (or Hisun for short), China's largest manufacturer of active pharmaceutical ingredients (APIs). In addition to its joint venture with Pfizer in 2012, the blue chip company is also well-known outside the pharmaceutical industry. The pharmaceutical group is working to reposition itself with a meticulously planned strategy. Diversification is Hisun's chosen path to counter the increasing price pressure on the market for pharmaceutical substances. The strategy involves supporting business on

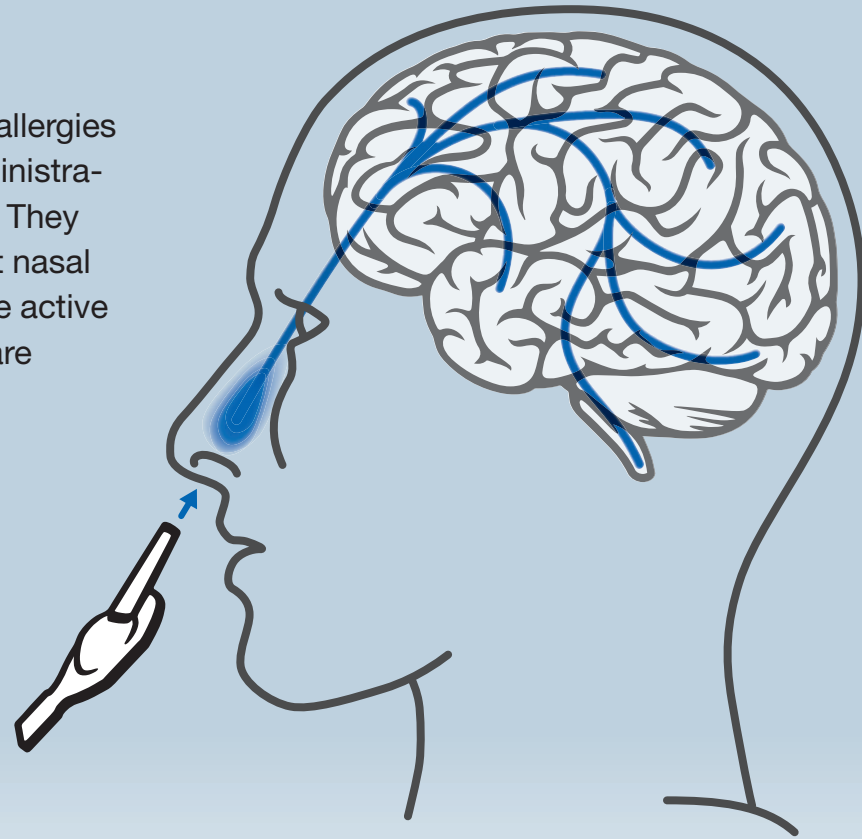
several platforms and developing alternatives to tablets and capsules. The group management is therefore interested in new dosage forms. And indeed 'new drug delivery systems' are deemed to be THE growth market. Products like transdermal plaster, oral or buccal film strips and inhalators are the dosage forms of the future. They make the administration of medicine easier and safer – and thus increase user-friendliness for patients.

Inhalation applications are Hisun's current priority. Ordered in autumn 2014, a production line for inhalers was installed in Fuyang, China in November 2015 – built and assembled by Harro Höfliger. Other lines for producing transdermal plaster, orally soluble film strips and autoinjectors will be delivered step-by-step in 2016. ■



Dosage forms of the future: transdermal plaster, oral and buccal film strips, inhalator DPI blister strips and autoinjectors

Besides local use to treat colds or allergies nasal applications also permit administration of brain-enhancing molecules. They reach the brain directly via different nasal paths. In this case, it is vital that the active agent, formulation and applicator are perfectly matched.



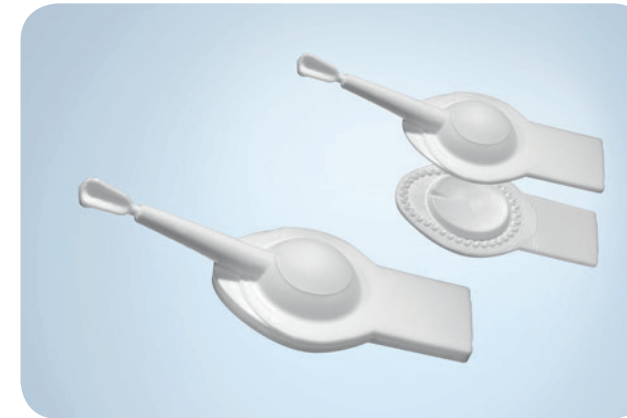
From nose to brain

So far there are very few approved nasal applications for brain-enhancing substances. Despite obvious advantages – easy administration for children instead of parenterals, in emergencies for asthma or epilepsy patients or poor venous access in the case of older patients – nasal application has enjoyed little support thus far. The development of such nasal applications often swings back and forth between optimism and disappointment. M et P has been engaged in the effects of medicine administered over nasal application for many years. This also includes consideration of the optimum application aids. As CSO Dr. Claudia Mattern comments: “Nasal application is the direct way of absorbing brain-enhancing substances. It is the focus of our research.”

The development and successful use of brain-enhancing nasal dosage forms however only works, as noted, when the three factors active agent, formulation and applicator are optimally matched. Newly developed delivery systems and brain research findings make nasal application an increasingly interesting alternative.

Drugs like ‘Tescum/Tescum Junior’ are one example of a new nasal application development of testosterone for men. Like all nasal applications, in its existing formulation ‘Tescum/Tescum Junior’ needs a container to ensure perfect administration. Multi-dose containers for multiple administration do not satisfy these demands. Although most multi-dose containers now operate without preservatives, contamination of the application tip was not taken into account for these containers. At the same time, depending on the formulation, exact dosing is not always guaranteed for multi-dose containers. M et P began development of a suitable solution for this challenging process and chose Harro Höfliger as a competent system builder for filling and sealing their devices.

The nasal device for ‘Tescum/Tescum Junior’ is a unit dose container, whose pin is easily twisted off for application. The product contains no preservatives and features long-term stability. Dosing accuracy is +/- 5 percent. In cooperation with Harro Höfliger, M et P conducted a large-scale trial series. Based on the results, a pilot system was developed at Harro



The new nasal device is a unit dose container with practical pin that simply twists off for application

Properties of ideal containers for nasal administration:

- Easy administration (compliance)
- Exact dosing
- Attractive design
- Protection from external contamination (single-use doser)
- Extractables/leachables* compliance

* satisfies requirements for leaking and extractable substances

Höfliger for M et P. The individual processes for filling the unit dose device were finally optimized in the system at the M et P laboratory. Today the prototype system is used in the lab to produce material for clinical studies and commercial samples. At the same time experience from this system is used in the planning and development of the first production line.

The controlled filling process and reliable sealing of the two-part device with ultrasound fulfills the highest technical standards. Harro Höfliger’s liquid filler successfully fills the thixo-

tropic oil formulation with a viscosity of 3,000 to 10,000 mPa · sec for exact doses. The material composition also posed a challenge for the applicator. A low-density polyethylene enriched with titanium dioxide (TiO₂) as additive was selected.

The prototype system went into operation in 2012. Today the patented line fills and seals around 5,000 applicators daily. An additional commercial scale production system is currently being assembled at Harro Höfliger and is due to go into operation at the end of 2016. ■



Dr. Claudia Mattern

is co-founder of the Swiss M et P Pharma AG, which specializes in nasal application. She has headed Pharmaceutical Development since 1998 and held the scientific chairmanship since 2002. In this capacity she developed a galenic platform for nasal applications. She is responsible for medicine production and implementation of feasibility and pre-clinic studies in humans. Claudia Mattern completed her PhD at the Humboldt University, Berlin on the subject of “Development of stable dosage forms of the coenzyme NADH for peroral and parenteral administration”. In 2013 she was vested with an extraordinary chair at the Oceanographic Center of Nova Southeastern University in Florida. With a track record already including 200 patents, she is a member of several scientific associations, has several publications to her name and is an expert for scientific journals.

The new Modu-C HS (High Speed) enhances the capsule filling machine series in the high speed range. With an output of up to 200,000 capsules per hour the system opens up a new dimension in reliable high efficiency production. With the addition of the Modu-C HS, Harro Höfliger offers capsule filling machines for every requirement from laboratory development to high speed production.

High speed capsule filling

Modu-C family product features

From lab to production

Low speed up to 25,000 capsules/hour
Mid speed up to 100,000 capsules/hour
High speed up to 200,000 capsules/hour

- Flexibility via dosing trolley system
- Precise dosing
- Simple intuitive operation
- 21 CFR Part 11-compliant
- 100% inline control
- Operator protection (containment)
- Full turnkey supplier

For more details of the Modu-C family visit www.hoefliger.com

Perfect combination

Along with the Accura-C capsule weighing machine the Modu-C HS forms the perfect combination for efficient capsule production that meets the highest quality standards. The feedback loop enables automatic trend controlling of the filling weight.

Optimum cleaning

GMP-compliance, an ergonomic design and best accessibility permit optimum ease of cleaning. Filling stations can be prepared in advance on changeover trolleys, thus minimizing tooling and downtimes.

Application diversity



A wide range of filling stations on trolley systems are available to match product requirements: powder, pellets, tablets and capsules. Various filling combinations are of course also possible. Equipped for present and future applications.

Fast and easy

Besides a rugged machine design the main focus is on easy operation and fast format changeover times. Operators quickly find their way around the intuitive menu on the modern HMI (Human-Machine Interface). The machine also offers interfaces for automation concepts along the lines of continuous manufacturing.

Patented dosing trolley system

Thanks to the trolley system the Modu-C HS achieves maximum flexibility and productivity. The basic machine offers the option – depending on the required filling medium – of deploying the appropriate dosing trolley in a plug & play procedure for short tooling and cleaning times. Additional dosing units can be retrofitted at any time.



The arrangement of the new labeling and packaging line was optimally planned to suit the layout of the new pharmaceutical production line at Pharma Stulln

Fast solution for eye drops

Harro Höfliger produced a labeling and packaging line for Pharma Stulln – a GMP-compliant production line with all components from a single source – within a very tight deadline. The limited space available required special line planning.

Dr. Susanne Koschatzky sits at her desk with the phone in one hand and a pen in the other. Concentrating, she takes down notes on her pad. She explains with a laugh: “Irregularities between different interfaces can be best dealt with over the phone. In-house developed risk assessment for handling good parts in the event of faults provides an additional safeguard, precluding any confusion between good and bad parts.” The Head of Qualification/Validation at Pharma Stulln took on project management for developing a system that produces eye drops in single-dose containers 15 months ago. As central point of contact she has since coordinated internal departments and external suppliers, convened meetings and kept an eye on scheduling. “Holistic project planning is a lot of fun – but also a lot of work.”

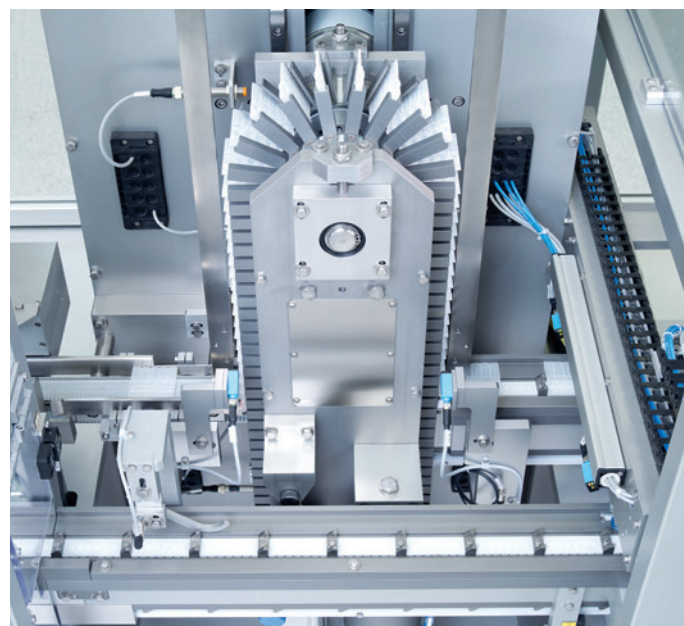
The blow-fill-seal production process has been part of Pharma Stulln’s core business for many years.

What was new to the company was the planning of a fully automated process flow. As Dr. Koschatzky describes the task: “Our requirements could only be satisfied by continuous highly automated line production from sterile filling through to boxing.” And the deadline was extremely tight: just 15 months lay between the initial meeting and system commissioning. As Dr. Koschatzky assumed the role of central coordinator, she was able to smooth the way and clarify matters, for instance when defining product orientation for machine-to-machine conveying.

However every bit as important to success were proven suppliers like Harro Höfliger. “There was no time for experiments”, stresses Dr. Koschatzky, “We have been working with Harro Höfliger for six years, so we knew that we would be getting fast and good solution approaches to state-of-the-art standard.” Their Allmersbach partner was also able to help



State-of-the-art technology: cartoning machine, type MKT



Line balancing belt for synchronizing the blow-fill-seal strips



Closer look: lab inspection

"We had no time to experiment, which was why we opted for a proven partner like Harro Höfliger."



Dr. Susanne Koschatzky,
Head of Qualification/Validation,
Pharma Stulln

Pharma Stulln with the assembly situation. As the existing production facilities were working to full capacity, the warehouse was converted into a clean room area. Harro Höfliger designed several assembly versions for individual machines and thus helped to make the most of available space. Harro Höfliger delivered a complete labeling and packaging line consisting of a high speed labeling machine with camera inspection and picker cell for transferring products to the packaging line. Plus a cartoning machine, serialization device and bulk packer. Dr Koschatzky adds: "That left us with a minimum of interfaces on the packing line – with virtually everything from one supplier." The packaging expert developed the labeling machine specifically for the job. It consists

of a redundant system with two label dispensers connected in parallel. If one label roll is finished, the dispenser switches to the other system. The operation continues while an operator changes the roll for the first dispenser. The bulk packer ensures serialization and identification in the system. Every product can be fully traced over the track & trace process – enhancing forgery protection.

An additional bypass function in front of the labeling machine allows the manual introduction of acceptable parts. The system produces 33,000 ampule strips per hour or 3,300 folding cartons. "Only our own product is produced on the system, our proven Stulln Mono eye drops", comments Dr. Koschatzky. They are used to treat asthenopia, a weakness of the ciliary muscles. ■

Pharma Stulln

Pharma Stulln GmbH has been producing eye drops for more than 60 years. In 1953 it developed its first major eye medication: the Stulln eye tonic for tired eyes that still exists today in a slightly amended form. The company is headquartered in the Upper Palatinate and currently employs 220 people. The eye drops are marketed internationally from this site.



The finished product: folding carton, package leaflet and two blow-fill-seal strips with 5 eye drop ampules each

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Committed to Perfect Process Performance.

Quality can be measured by consistent results. We continuously improve the value added, reliability and quality of your production. Taking a comprehensive view of our customers' products we can develop customized production and packaging processes that are perfectly tailored to each individu-

al product in terms of quality and efficiency. Our values and standards are reflected in our customer-centric approach and activities. At Harro Höfliger interaction with all project stakeholders is characterized by openness and flexibility.