HARRO

The Customer Magazine
by Harro Höfliger

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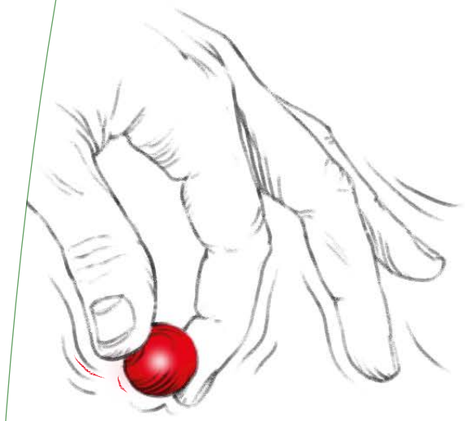
Cool ...

... when excessive heat should be avoided. Aseptic filling and sealing machine for IV bags using completely sterile processes.

Harro Höfliger



We set ideas in motion

Harro Höfliger now also supports customers in the development of new and improved devices.
Page 16

“This product is a real stroke of luck”

Fritz Major presents an ingenious “find” that waits for a resourceful discoverer.
Page 22

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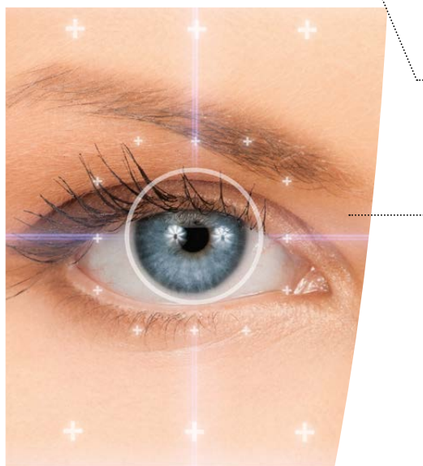

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Dear Readers,
dear Business Associates,

in addition to the continuing evolution of our technology, the demands for more enhanced services is also a growing trend and focus at Harro Höfliger. Therefore, great importance is given to expanding our range of services to meet your needs and to adapt our services to the life cycle of your product.

Since mid-2017 our service units Pharma Services, Engineering & Innovation Services, Device Services and Validation Services have been working under the common umbrella of Process Services, which are directly linked to the Executive Management. This is how we ensure continuity to the operations and procedures within your company. It is the prerequisite for understanding, transferring and implementing your processes in a targeted manner.

This example of Device Services shows how new service offerings are developing at our company. The process-related adaptation of customer devices has always been part of our consulting services. The experience gathered from countless customer projects in addition to our own developments, such as the XStraw®, an oral administration device in straw format, form the basis of our growing expertise. Discussions with customers repeatedly confirm that this know-how is an important factor in minimizing their risks. Therefore, at our customers’ request, we now include devices to an even larger extent in the overall development process. To put it simply, we implement and/or optimize your ideas.

Active ingredient, device and industrial manufacturing options undergo perfectly coordinated optimization processes until they are tested on trial machines. Up-scalable, of course! This means that the path to series production is always open for you. No stumbling blocks, no risk. We look forward to accompanying you.

Your

Thomas Weller,
CEO at Harro Höfliger

New cleanroom facilities

At the Allmersbach im Tal site, ten ultra-modern ISO class 8 cleanrooms offer customers additional capacity for testing originator products with an optimum of practical relevance, and for machine acceptance tests (FATs). Two of the rooms have special air locks and are therefore also suited for certain highly potent substances. Throughout the entire system, ventilation technology allows individual control of temperature and humidity conditions in accordance with the latest standards. A new laboratory has also been installed – giving Harro Höfliger 60 square meters of laboratory space.

Substantial

10

From four to ten: Expansion in several construction phases.

Ultra-modern

60 m²

More space for product studies and tests thanks to a new laboratory equipped to the latest standards.

Large-scale

500 m²

Several hundred square meters of cleanroom space for the processing of active substances and sensitive products.

Printing instead of heat sealing

Harro Höfliger has developed a completely new process for the water sealing of water-soluble pouches filled with cleaning agents. Print heads, such as those used in ink jet printers, with pinpoint accuracy and in a controlled manner moisten the film made from polyvinyl alcohol (PVOH) with water to begin to dissolve it. Contact with the second film produces a very homogeneous, dense and extremely resilient sealing seam, which is significantly narrower than with conventional heat sealing. The same film width allows more packs to be produced with any desired contour and with shorter production times. Cameras continuously monitor all processes and provide 100% quality control of all pouches. The contactless water application does not cause any contamination and thus reduces the cleaning and maintenance efforts and expenses for the system.

Andreas Dalferth, Janine Kyofsky, istock.com/fazon1

"Providing proximity"

Since May 2017, Harro Höfliger has been operating a branch office in Singapore. Simone Stoiber, Regional Marketing Director, and Zein Albahar, Regional Sales Director, explain the added value for customers.

Why did Harro Höfliger decide to establish a branch office in Southeast Asia?
Albahar: Southeast Asia is one of the so-called "Pharmerging Markets", the emerging markets for pharmaceutical and medical products. Countries such as Indonesia, Malaysia or Thailand are going through a phase of industrialization. This is why the demand for machines is rising, also in pharmaceutical and medical technology. Workers used to pack medicines by hand, but more and more frequently automated cartoning machines are taking over this task, just to name one example. We want to be a part of this growth and are therefore expanding our activities in Southeast Asia.
Stoiber: In the past, our colleagues in Germany were responsible for this market, but due to the distance and time difference, it took longer to respond to inquiries. Now we can look after our customers much more thoroughly and quickly, both on the phone or directly on site. Customers are very relationship-oriented here and appreciate us being close by for consultations.

Which technologies are in demand in the Southeast Asian market?
Stoiber: Web converting machines are very popular. They can be used to manufacture traditional medical products, such as heat therapy patches with herbal ingredients to relieve muscle tension. Assembly and packaging technologies for insulin pen systems are also in great demand, since diabetes is on the rise in Southeast Asia. Innovative products such as the XStraw® are also very well received. In addition to existing solutions, we also offer new ideas for niche applications.

Why did you choose Singapore?
Albahar: Singapore has an ideal geographical location. Our markets are only one to three hours away by plane. In addition, we work closely with colleagues from our Excellence United partners Uhlmann and Fette Compacting, with whom we share an office. Together we can offer our customers complete turnkey solutions from a single source that cover all their needs; with blister machines from Uhlmann, tablet presses from Fette and capsule filling machines from us.

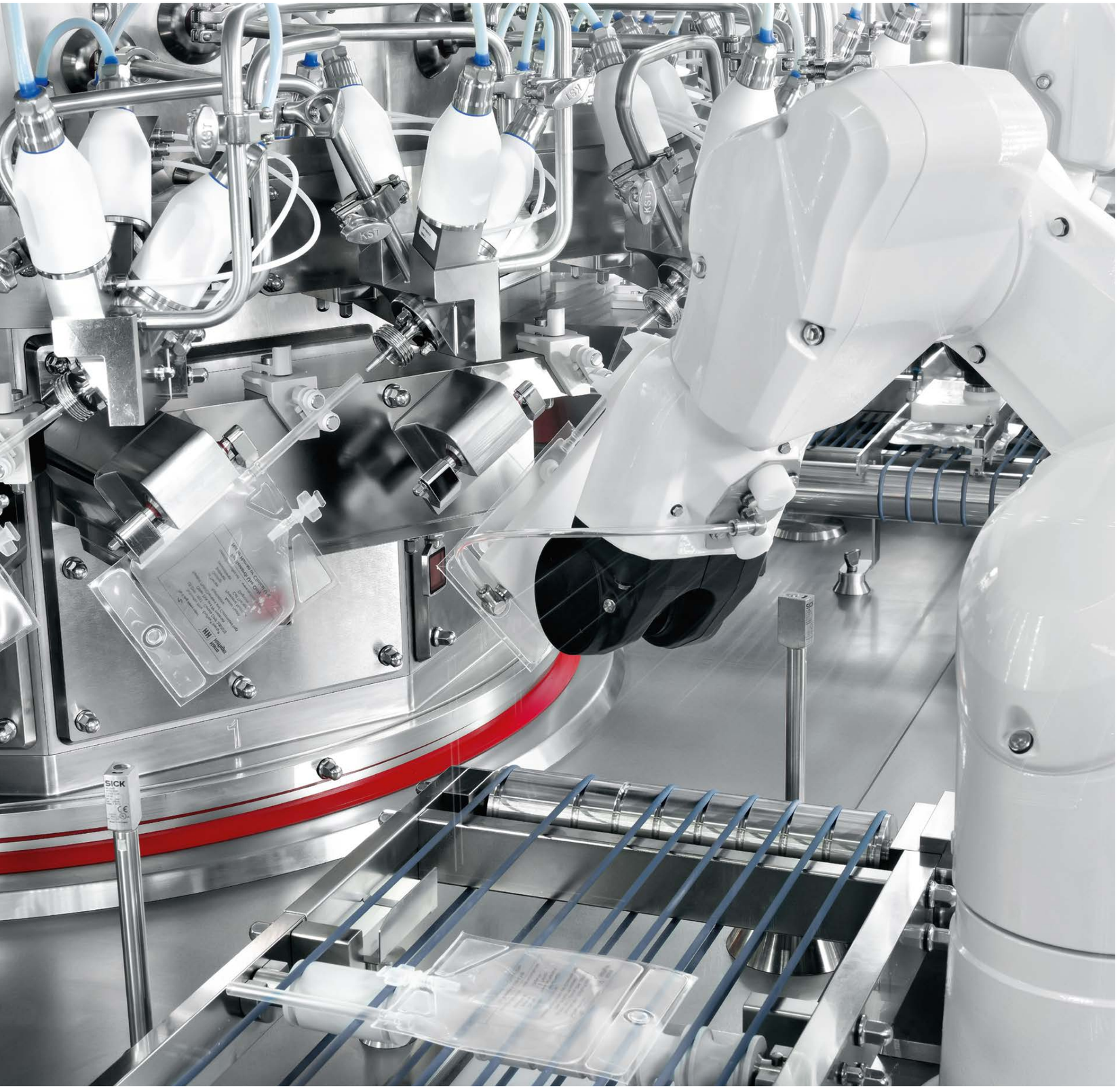
"Now we can look after our customers much more thoroughly and quickly."

**Simone Stoiber,
Regional Marketing Director**

What are your goals for the future?
Stoiber: We would like to make Harro Höfliger even more popular in this region, establish new contacts and strengthen the existing ones. The next step is to implement our on-site service in order to provide optimum support for customers in the area. Our colleagues in the sales and service offices in India and China are setting an example for us to follow.

Simone Stoiber and Zein Albahar support our customers in Southeast Asia.

TOP INNOVATION



Helmar Lünig, stock.adobe.com/Sherry Young

Sterile filling of infusion bags

At ACHEMA, all eyes were on the partially automated aseptic filling and sealing line for pre-sterilized infusion bags. New B Innovation Limited (New β Innovation) has now implemented it to produce veterinary infusion products.

It's hard to imagine a doctor's office or clinic anywhere in the world without infusion bags. As with any product administered intravenously, the need to minimize patient risks means that quality requirements for the bag content are especially high. Frequently, after being filled with liquid, infusion bags are terminally sterilized to ensure the vitally important sterility. However, this method is not suitable for active ingredients that are sensitive to heat or gamma radiation, as is the case with the products of the Hong Kong biotechnology company New β Innovation. That's why Harro Höfliger went in a different direction with its first aseptic filling and sealing machine for IV bags. Our experts focused on completely sterile processes and an active open restricted access barrier system (RABS).

In the sterile conditions of the line (EU/GMP Cleanroom Grade A/ISO 5), New β Innovation manufactures IV products at a mid-scale level in its Canadian facility. "We specialize in veterinary products that are used around the world, and which we fill and seal at up to ten bags per minute," says Endre Szilagyi, Senior Manager, Production from New β Innovation. "Of course, the machine can also be used for filling oxygen-sensitive

TOP INNOVATION

1 Glove ports ensure hygienic separation between operator and process.
2 After opening the outer bag, the inner bags are disinfected. They dry on a stainless steel rack.
3 The infusion bags are placed individually on the transfer belt and are automatically fed to the rotary platform via a “mousehole”.
4 A robot which is specially designed for aseptic production environments connects the bags to the filling system.
5 At ten stations the bags are flushed with nitrogen, emptied, filled with the product and sealed.
6 A further robot arm removes the IV bags and separates good and bad parts.

IV products for human use,” notes Christian Kollecker, leader of the Pharma Liquid/Aseptic business unit at Harro Höfliger. “The line takes every necessary hygiene and safety guideline into account. It is suitable for bags with fill volumes of 20 to 250 milliliters, and is a particularly good fit for the ‘low volume-high margin’ sector.”

“One-time docking”: a global first

The machine is loaded manually. “The no-touch method proved itself to be the best solution for the continuous transfer of our flexible bags, which can easily stick together,” says Endre Szilagyi. Operators use glove ports to open the pre-sterilized, bagged components, as well as to separate them. A camera records the position of the bag on the transfer belt so that the Stäubli Stericlean robotic arms can precisely place the IV bags on the rotary platform and connect the filling tube to the aseptic triple filling head. The special feature is that the connection to the filling nozzle remains in place through all of the following gas purging, evacuation and filling processes until the transfer from the machine. Harro Höfliger uses this one-time docking principle to minimize the risk of particle entry and keep the residual oxygen content in the bag low.

“The line takes every necessary hygiene and safety guideline into account.”

Christian Kollecker,
Leader Business Unit Pharma Liquid/Aseptic at Harro Höfliger

The amount of nitrogen flushing and the subsequent evacuation of the bag using vacuum can be flexibly adjusted. An integrated, laser-based Wilco HSA (head space analysis) module provides an in-line measurement of the oxygen content, making the quality control results available immediately. If the residual oxygen level is over one percent, the bag is removed and not filled. A high-precision measurement of mass flow using the Coriolis effect is performed by a sensor, which ensures that each infusion bag has been filled to exactly the right amount. An aseptic rotary distribution is used to supply all fill media in a sterile manner.

Quality down to the very last detail

In the next step, paddles “massage” the filled bags so that any trapped gas from the infusion solution rise upwards to the filling tube. The opening is tightly sealed by radio frequency welding to minimize the heat transfer to the active substance. Then, the filling tube is cut off and removed.

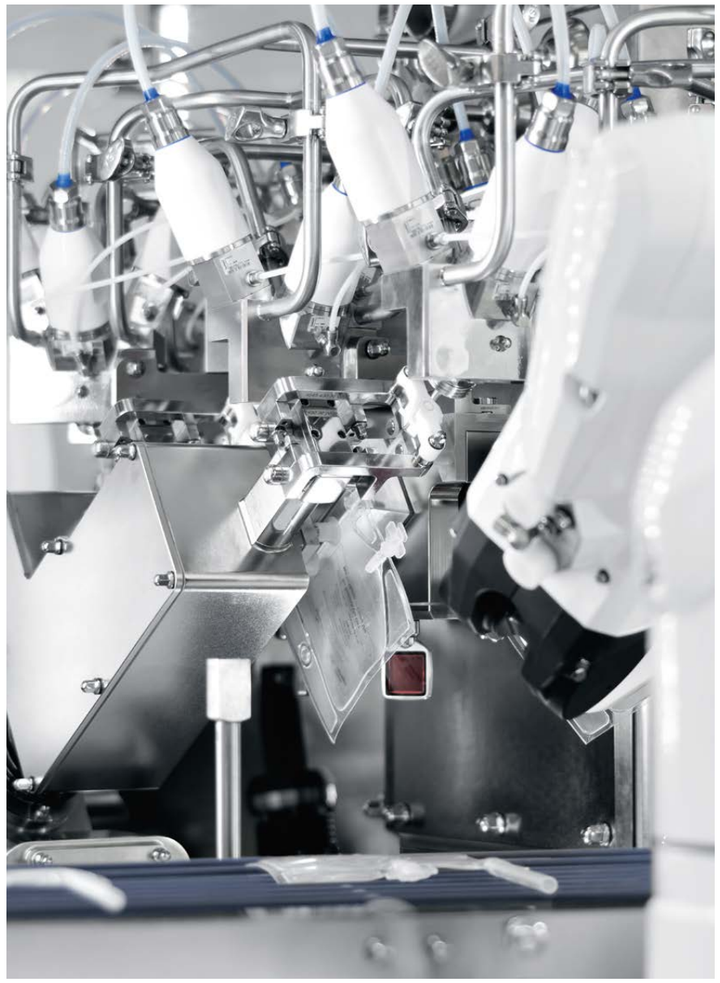
An important component of quality-oriented production is perfect cleaning after each batch using an integrated CIP/SIP (cleaning in place/sterilization in place) system. “The machine’s hygienic design meets the highest pharmaceutical standards,” explains Christian Kollecker. “The complete pipeline system is connected to an automatic CIP/SIP system, making disassembly unnecessary for cleaning. Furthermore, the entire line is optimized for decontamination using hydrogen peroxide based dry fog.”

Helnar Lünig, stock.adobe.com/Sherry Young

"The filling system is one of a kind, only the team at Harro Höfliger can make it happen."

Benjamin Wai, Director of New B Innovation Limited

Benjamin Wai, Director of New β Innovation, is very satisfied with the filling machine – a second line for the Chinese production facility was ordered quickly. "When we first contacted Harro Höfliger, we were looking for laboratory equipment for aseptic liquid filling," says Benjamin Wai. "Because the processes have worked perfectly, Harro Höfliger has scaled from tabletop devices to the semi-automatic production line. In close coordination, we have jointly developed a compact machine layout that meets all of our requirements and takes into consideration the spatial conditions in the cleanroom of our production facility down to the smallest detail."



The filling tube and the filling nozzle remain connected until the IV bags are transfered from the machine. This one-time docking principle minimizes the risk of particle entry.

Helmar Lünig, New β Innovation, stock.adobe.com/Sherry Young

About New β Innovation

New B Innovation Limited, established in 2007, is a dedicated player in the global medical biotechnology market. With headquarters in Hong Kong, the company employs the latest technologies and innovative approaches to deliver health care products that bring better quality of life and address unmet medical needs.

Strong team

The Ypsomed and Harro Höfliger network provides know-how, consulting and technology for injection pens and autoinjectors from a single source.

Ypsomed
Development of device and pre-assembly

Harro Höfliger
Assembly and packaging technology

Customer
Drug development and pen production

Pharmaceutical companies who want to launch an injection pen or an autoinjector are faced with several challenges. Once the active ingredient has been developed and is undergoing trials, the appropriate injection device has to be identified and market approval obtained. On the way to the finished product, pharmaceutical companies not only have to deal with approval authorities but also with various companies: the device manufacturer, the manufacturer of the filling machine as well as one or more manufacturers of assembly and packaging machines. This involves a great deal of coordination. Harro Höfliger recognized this challenge at an early stage and has continuously expanded its service and consulting offerings.

Close partnership
A few years ago, the Swiss device manufacturer Ypsomed also responded to the need for comprehensive customer support by establishing a joint production network with Harro Höfliger. In the development of injection pens and auto-injectors, the device and machine manufacturer work hand in hand with pharmaceutical companies in order to address individual wishes and at the same time ensure rapid market launch. “For both the pharmaceutical customer and Ypsomed, reliable and timely cooperation with the machine supplier is essential in order to adhere to strict schedules,” says Orfeo Niedermann, Business Development Director at Ypsomed. While dosage, shape and color of the device can be adjusted at the customer’s option, the functional components are based on standardized platforms – both in the layout of the Ypsomed device and in the design of the assembly machines.

Expertise
With their consulting services, Ypsomed and Harro Höfliger facilitate the entry into pen and autoinjector production and support companies in the expansion of their portfolios. Harro Höfliger’s Process Services, such as Engineering & Innovation Services, also play a helpful role. The experts in this special development department focus on careful and precise handling. They test material properties and optimize manufacturing processes with the aim of meeting the required quality standards even at high production speeds.

Allotted tasks
The complex pre-assembly of the injection devices takes place directly at Ypsomed. The device manufacturer can guarantee its consistently high quality through high-precision assembly and control processes. The pre-assembled devices are assembled with the syringes or cartridges and packaged at the pharmaceutical company or contract manufacturer. Filling of the active ingredient takes place at the pharmaceutical company or contract manufacturer on a special filling machine. This is where a specialist for the filling of liquids such as Bausch+Ströbel comes into play. Due to the long-standing cooperation within the Excellence United network, the production lines of Bausch+Ströbel can be easily integrated into the lines of Harro Höfliger.

The benefits of this close cooperation are also reflected in the project flow, thanks to reduced interfaces and collective expertise. Harro Höfliger offers tailor-made machine platforms from laboratory to full-scale production for both the final assembly and the subsequent packaging tasks of the devices.

“A strong partner who understands the device and the processes is extremely important. With their competence and experience in the field of semi-automatic pen assembly, we felt comfortable that the required quality would be met.“

Kristen D’Urso,
Project Manager, Ambio, Inc.

The Assembly Lab is a semi-automatic assembly machine for injection pens and auto-injectors. It is used for the final assembly of devices for small series and clinical studies.

Orfeo Niedermann, Business Development Director, Ypsomed

Michael Kanzler, Leader Business Unit Assembly Automation, Harro Höfliger

What role does Ypsomed play in the production of injection pens and autoinjectors?
We advise customers on the optimum device for their purposes and recommend the appropriate machine manufacturers. We also support the final assembly at the pharmaceutical company or contract manufacturer by defining all parameters of the final assembly process and working closely with the customer and the machine manufacturer.

Why are Ypsomed platform products for self-injection so successful?
For years, Ypsomed has been investing heavily in patented innovations and pays great attention to the high degree of user-friendliness of their devices. The best technologies are implemented as flexible platform products and manufactured in highly automated processes, which enable high quality at attractive unit costs.

Mr. Kanzler, what opportunities does the Assembly Lab offer for pharmaceutical companies?
On this semi-automatic, validatable laboratory machine, all critical processes can be tested and then transferred to the high-performance assembly machine.

Which areas of pen and autoinjector production can Harro Höfliger cover?
Harro Höfliger supplies assembly machines for the complex pre-assembly of devices. In cooperation with our Excellence United partner Bausch+Ströbel, we offer proven solutions for the filling of cartridges and syringes. In addition, Harro Höfliger also builds customized assembly and packaging machines for the subsequent steps from final device assembly to ready-to-ship packaging. Consulting, development, production and service for the entire project are thus provided from a single source.

Heilmar Lünig, Janine Kyofsky, Ypsomed AG

Service – anytime and anywhere

Customer Service accompanies the customer throughout the entire machine life cycle. The team consults and assists during production start-up, trains users and technicians on site and stands ready to provide worldwide service should a malfunction occur. For years after installation, service employees are still direct contacts when it comes to maintenance, spare parts or machine modifications.

Worldwide service

Customer Service at Harro Höfliger supports our customers all over the world – online, by phone and of course personally on site. Each customer is different and every project has specific requirements. This is why it is important for us that every customer has access to a personal contact person who provides support over a long period of time. These employees are assisted by specialized teams within our organization who are in charge of their respective service products. As a part of our digitization efforts, we are working on smart solutions to make our machines and the associated services as efficient as possible.

Luise Räuchle, Product Manager

Training

At Harro Höfliger almost every machine is unique. Consequently, training courses are tailored to customer requirements. Technical editors compile individual training documents for each machine. The instructor is always a technician from the team who built the machine. Our training courses focus on the safe handling of the machine and the minimization of operating errors. This is how we ensure reliable production. On request, we can also share expert knowledge on integrated devices such as cameras, laser technology, robots or sensors. Depending on the information requirements of your company, we offer different training levels, from operator training and technician and maintenance training to training for electricians. Training courses take place primarily at your location. Upon request, we would also be happy to arrange for instruction at our facilities.

Hergen Wersch, Team Leader Customer Training

Remote maintenance

We find that more than 80 percent of service requests can be solved by remote maintenance. Our team responds within three hours and offers 24/7 support if needed. In most cases, we can solve software problems and identify mechanical malfunctions immediately. If spare parts are needed, we will inform the appropriate colleagues within our organization directly. Remote maintenance preferably takes place via the Excellence United portal, which enables a secure port-to-port connection. The connection for machine access is only established after a service request has been initiated by our customer. Initiation of external access from our side is not possible.

Fabian Schoene, Technical Customer Support

Spare parts

Our top priority is to guarantee the production reliability of our customers' systems and to prevent machine downtime. The initial equipment package that we compile for each machine gives customers an overview of which spare parts they should have on hand. Customers can stock the spare parts packages and have immediate access if required. With each machine we supply a 3D spare parts catalogue, enabling the rapid identification and ordering of parts. Depending on the urgency, the parts are delivered by express or courier service. Of course, we can also assist with identifying parts using a photo or description.

Güldane Gedik, Service Administrator

Maintenance

In order to ensure trouble-free operation of a machine and to keep maintenance costs low, regular inspections and maintenance are required. On request, we will develop an individual maintenance concept for each machine. Our maintenance schedule is based on a FMECA-risk analysis, in which we evaluate the service life of each wear part. With this data, maintenance intervals can be precisely defined and even the duration of a maintenance task planned in advance can be anticipated. Our evaluation and close customer contact make sure that only those parts that are actually worn are replaced. The analysis also forms the basis for the spare parts package with recommendations for stocking of spare parts at the customer's site.

Manfred Wegner, Technical Specialist

Machine modifications

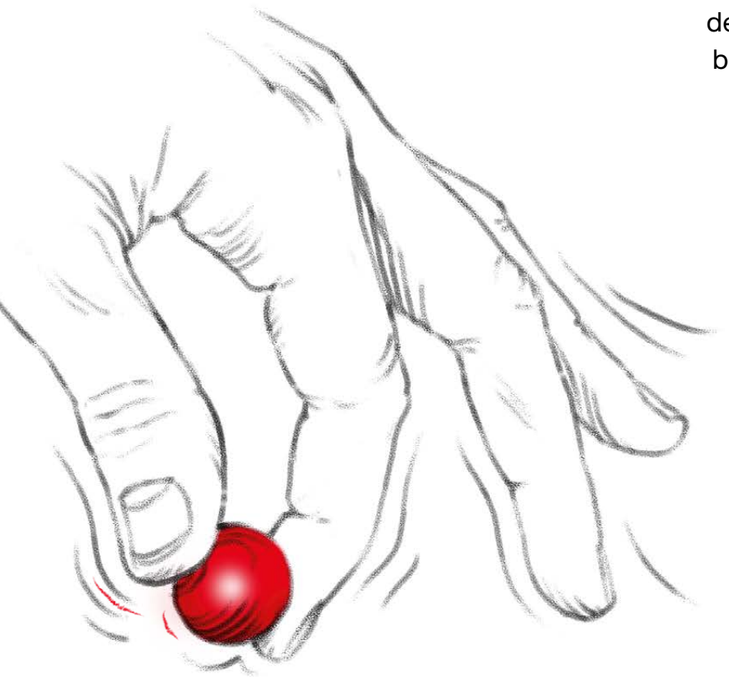
In order to maintain machine performance over the entire machine life cycle and to adapt it to changing requirements, modifications may become necessary over time. New market demands, such as serialization, require the retrofitting of camera systems or coding methods. Customer-driven conversions range from simple part modifications for process improvement, format adjustments in case of product changeovers, to the conversion of complete stations. In the years to come, we will expand our design team so that these tasks can be handled directly in the Customer Service department. During the course of the machine life cycle, components are often discontinued. If this occurs, it is our responsibility to identify the spare parts which are to be either replaced 1:1, or ensure the continued operation of the machine by supplying a conversion kit.

Steffen Nitsch, Team Leader Engineering

STRATEGY

We set ideas in motion

Harro Höfliger has expanded its service portfolio with Device Services, which complete the new Process Services division. From now on, in their own product development efforts, customers will also benefit from our extensive know-how in machine manufacturing.



Janine Kyofsky, Illustration: Bernd Schifferdecker

Harro Höfliger attaches great importance to supporting customers throughout the entire life cycle of products and machines. As with all other company divisions, the service offerings are regularly put to the test. What do customers need and which services can we provide to better support them? CEO Thomas Weller explains: “In order to be able to respond even more directly to our customers’ wishes, we have created the Process Services division headed by Stefan Mayer. Under this umbrella we bring together all services which we can provide to assist customers in the development of a product from concept to market readiness.” What was missing for a long time was a service component that specifically supports customers in the development or optimization of existing devices and medical products. Starting last summer, the so-called Device Services, which are also managed by Stefan Mayer, now perfectly complement our service offerings.

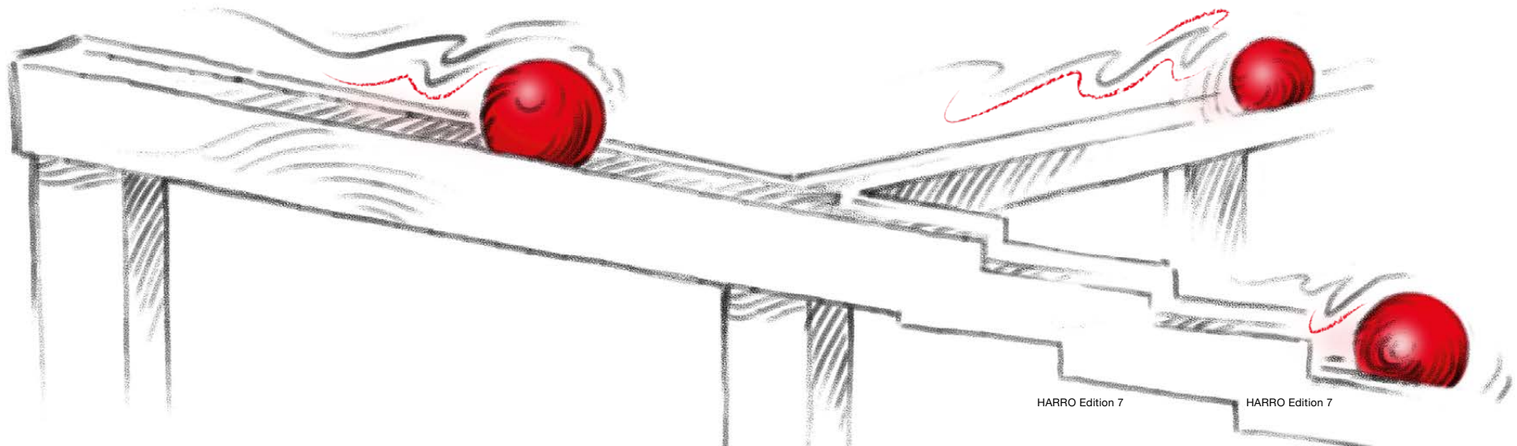
Everything has to fit

With the creation of the new service division, Harro Höfliger also responded to the increasing number of customers who are seeking support for their own product development. “Of course, first and foremost we are machine engineers,” explains Stefan Mayer. “But careful consideration of what is filled and processed on our machines is essential for their design. An optimally designed device is just as important for the successful overall process as perfect product development processes, which we have been ensuring for many years with our Pharma Services.” Thomas Weller adds: “Our customers rightly rely on us to develop processes that can be implemented one-to-one from the laboratory machine to intermediate sizes to high-speed machines. It is only logical that we contribute to the commercially optimal production of a device with this new service component. This expertise allows us to offer a complete solution package.”

Customers benefit from the fact that the four departments within Process Services are closely interlinked. The Device Services experts work hand in hand with their counterparts at Pharma Services, who provide support in process selection, development and optimization at an early stage of product development. The specialists in the Engineering & Innovation Services division, in turn, assist with innovation projects, design test and trial setups, conduct feasibility studies and build prototypes. The focus is always on product safety and the development of proven, robust machines and processes which can be qualified or validated by our Validation Services employees.

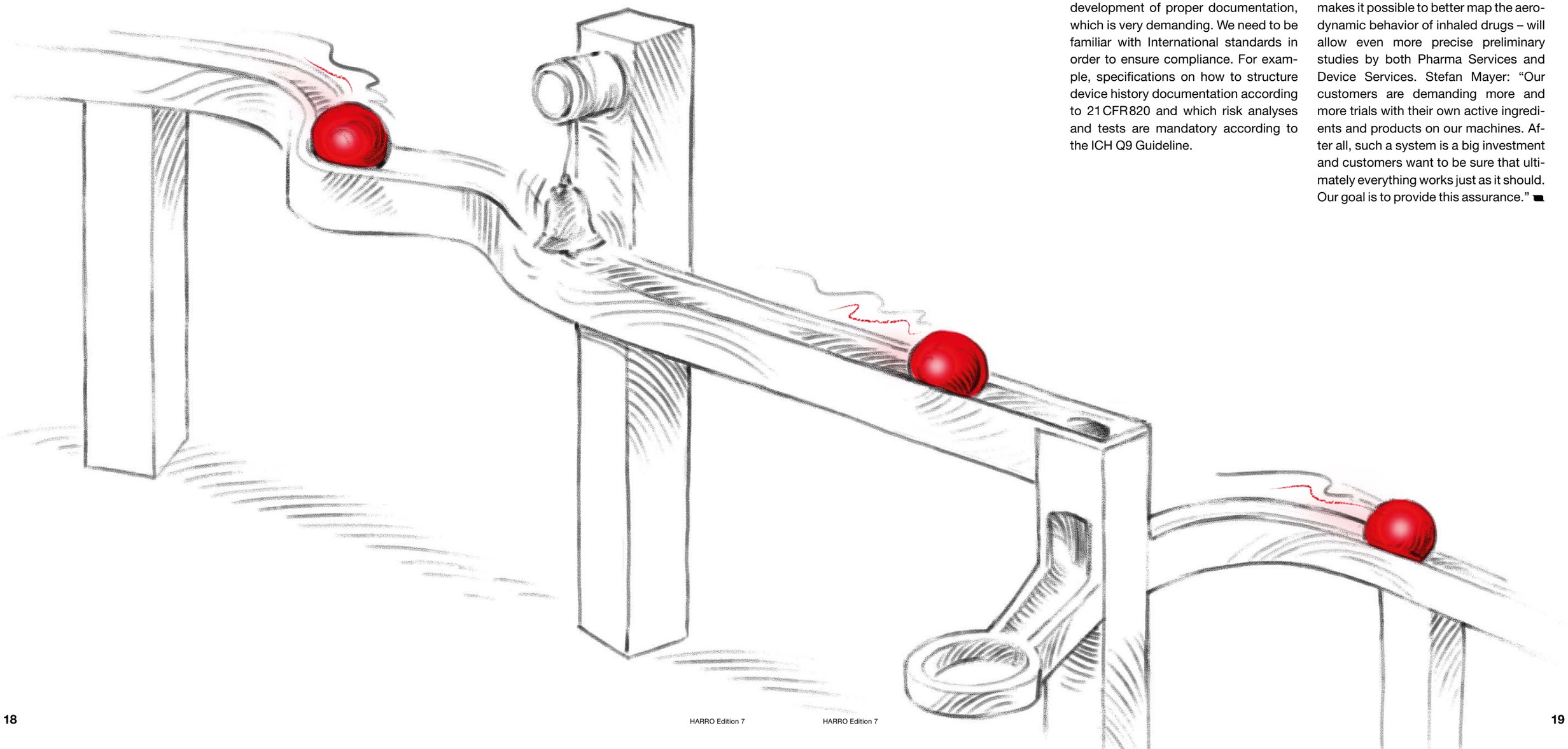
“An optimally designed device is just as important for the successful overall process as perfect product development processes.“

Stefan Mayer, Leader Process and Device Services



"This complementary expertise of our Device Services specialists allows us to offer our customers a complete solution package."

Thomas Weller, CEO



Janine Kyofsky, Illustration: Bernd Schifferdecker

An eye on details

Customers can benefit greatly from the support rendered by Device Services. For example, the FDA (US Food and Drug Administration) regulations regarding device optimization have become more strict. In the future it will no longer be so easy to change individual production steps after an approval, even if they do not fundamentally interfere with the function of the device. Every subsequent change inevitably means a great deal of effort, in the most serious case even a new approval, resulting in lost time and high costs. It therefore pays to design an inhaler or injector right from the start so that it is suitable for all production stages up to series production on a high-end machine without later adjustments.

The often complex joining processes of devices, that often consist of small components, can be reliably tested in trial applications at Harro Höfliger. And in the case of pre-developed devices, our specialists have a keen eye for detail. For example, an infeed angle that perfects a good device. "In addition to our knowledge in mold making and material science, our many years of experience come into play," explains Mayer. "We have worked with countless devices from customers and have also developed our own with the XTray®. This gives us a sense of what a product should look like and where there is still room for improvement."

Our Device Services specialists also take care of the extensive, quite complex development of proper documentation, which is very demanding. We need to be familiar with International standards in order to ensure compliance. For example, specifications on how to structure device history documentation according to 21 CFR 820 and which risk analyses and tests are mandatory according to the ICH Q9 Guideline.

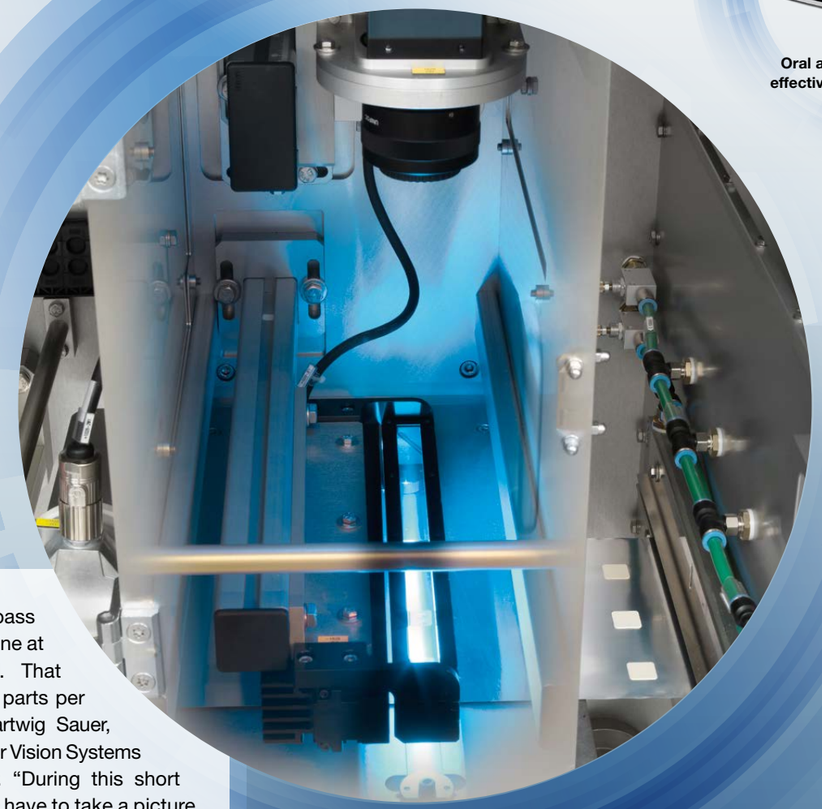
Ideal conditions

Harro Höfliger invested heavily in the new Process Services division. This began with additional manpower and training, such as for the new documentation department. But it also entailed an investment in equipment and new cleanrooms. In addition to the four newly installed cleanrooms equipped with humidity and temperature control, six more will go into operation in the fourth quarter of 2018. In two of them even highly potent substances up to level OEB 5 (permissible exposure limit of less than 1 µg/m³ breathing air) can be tested. A special airlock technology makes sure that no substances spread to the outside.

New laboratory equipment such as a New Generation Impactor – a device that makes it possible to better map the aerodynamic behavior of inhaled drugs – will allow even more precise preliminary studies by both Pharma Services and Device Services. Stefan Mayer: "Our customers are demanding more and more trials with their own active ingredients and products on our machines. After all, such a system is a big investment and customers want to be sure that ultimately everything works just as it should. Our goal is to provide this assurance."

Cameras are on!

On the PMK web processing machines, camera systems ensure that oral active ingredient films leave the conveyor belt flawlessly.



Oral and buccal films are effective aides against pain.

Oral (ODF) and buccal films (MBF) can be effective aids in the fight against severe pain. Once placed on or under the tongue, the thin ODF strips dissolve quickly and the active ingredient is released. MBF adhere to the oral mucosa and release the active ingredient. First, a polymer matrix containing active ingredients is produced in a special coating process. The PMK production and packaging machines then convert the polymer matrix into strips and package the films into individual pouches. Camera systems carefully monitor every step.

During web conversion, the films are cut length- and crosswise. Typical ODFs are rectangular between two and ten square centimeters in size. MBFs usually have rounded corners for better comfort inside the mouth. A flexo printer, for example, then imprints the active ingredient content and the product name. This is where the first of three image processing modules is used. It checks whether the imprint is correct and easy to read for the patient. “The challenge is that 1,050 parts per minute pass through the machine at maximum speed. That means almost 18 parts per second,” says Hartwig Sauer, Department Leader Vision Systems at Harro Höfliger. “During this short period of time, we have to take a picture of each product, evaluate it and send the result to the machine control system.” If the camera detects a faulty imprint, the products are marked virtually and ejected at the end of the machine.

Not a millimeter too small

For the flawless products, the next step is to pack them in 50 x 50 millimeter pouches, primarily made of child-resistant packaging material. To this end, the films are transferred to the lower packaging material web. A camera checks whether the product has the correct geometry – i.e. the exact length, width and contour – and is positioned in the center. If the product were positioned in the sealing area, the pouch would not seal and close properly. In addition, the films are checked for possible contamination by particles, product or packaging material residues. Only then will the upper packaging foil be applied and the pouch sealed.

Prior to sealing, the packaging material web is also printed with a batch number, expiration date and a 2D data matrix code. A third camera station checks for correct printing. “Since these films are often used in pain therapy, it is especially important that all information is accurate and legible. No mistakes can be made here,” explains Sauer.

Researching the future

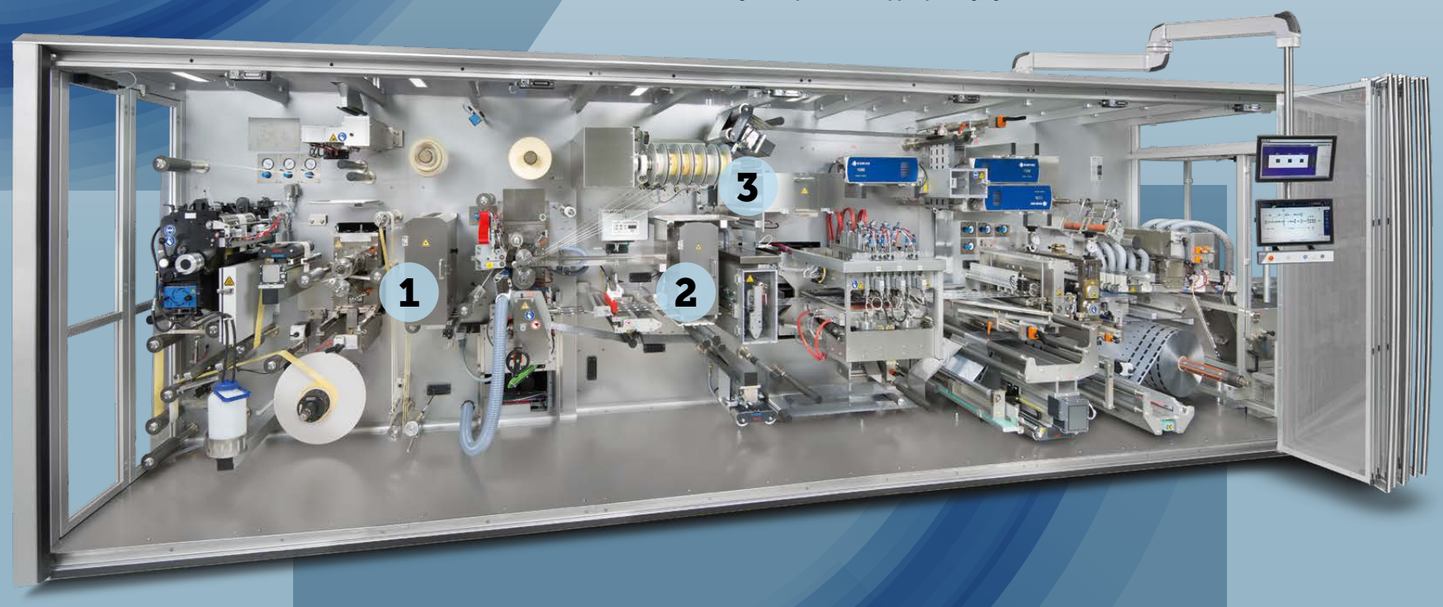
Accuracy and process monitoring are also important for other forms of packaging. “More than 50 percent of our machines require camera controls,” says Sauer. “We used to work with external companies, but then our customers always had two different contacts.” This is now in the past. For the last six years, Harro Höfliger has had its own image processing department. In the camera laboratory, 17 application engineers examine which camera light color and wavelength can be used to best map specific features for subsequent examination of the required test criteria with complex image processing software. They are also conducting research into future technologies such as thermal imaging and deep learning. “In the future this will enable our machines to detect errors better and faster to further improve exact production of medication.”

“More than half of our machines require camera controls.“

Hartwig Sauer, Department Leader Vision Systems at Harro Höfliger

Camera stations monitor every step of the model PMK production and packaging machines:

1. **Checking the imprint of active ingredient content and product name**
2. **Checking the position before packaging into four-side sealed pouches**
3. **Checking the imprint of the upper packaging material web**



Helmar Lünig, Janine Kyofsky, shutterstock.com/Lyudmyla Ishchenko

“This product is a real stroke of luck”

Sometimes a good idea just ends up in a drawer. A pity, because every now and then there are real treasures among them. Just like the Delta Pouch, which Fritz Major, Head of Sales at Harro Höfliger, introduces in an interview.

What is this exciting “find” you have here?
Some years ago, the so-called Delta Pouch was developed by one of our customers for the innovative packaging of powder for beverages or sauces and instant soups. We were commissioned with the design of the prototype machine. Unfortunately, the product did not make it to the top of their internal innovation list and literally disappeared into a drawer.

And now it reappeared?
Exactly. It is a pity when a good idea is not pursued at this stage. The entire basic development is complete, and marketing measures can begin promptly. Meanwhile, the product and design patents as well as the utility models have been released. We hold the patents for machine technology. This is a real stroke of luck for someone who recognizes the potential of the product and wants to make use of it.

What potential is there?
Compared to square or stick packaging, the pouch offers a better film volume ratio, meaning more product with less material consumption. This is because the individual packages are filled “bottom-up”, and held at an angle, which means that a higher fill level can be achieved. Due to the small cross-section at the opening aid, the contents are also easier to dose or dispense.

And from a purely visual perspective?
The packaging is unique. Folded into a square, this results in stacks that are convenient to pack. Due to the integrated tear-off edges, the triangular pouches can also be sold individually. This is important for developing countries where single-item sale is common. In the small shops the hanging “Delta-Pouch-garland” is a nice way to display a product.

“The entire basic development for the Delta Pouch is complete.“

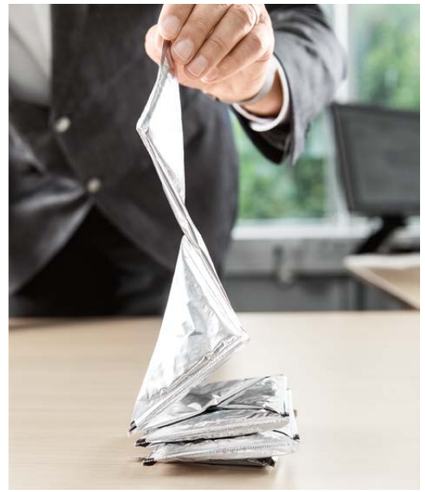
Fritz Major, Head of Sales at Harro Höfliger

Which contents could you imagine for the Delta Pouch?
At present, the format is dimensioned for a fill quantity of about seven grams. Theoretically, any powdered product can be filled, for example, from the fields of nutrition, curative nutrition or perhaps protein for athletes.

Is there any room for variation in filling quantity and package size?
To a certain extent, we are flexible in both cases without major need for modifications. However, the fill media has to be powder.

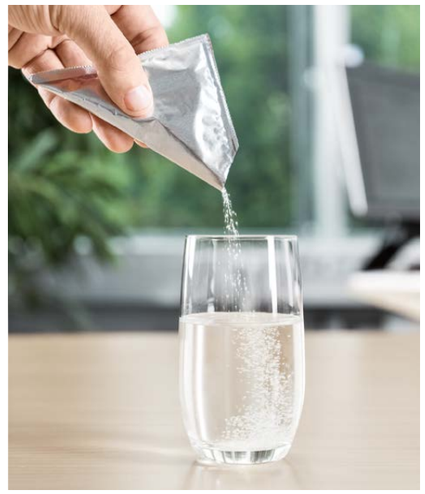
If I have a good utilization idea, can I contact you?
We would love to hear from you. As with all our machine concepts, we can easily transfer the concept of the prototype into a high-performance machine for series production.

Janine Kyofsky



Whether individually or as a convenient square: The packaged Delta Pouches are a real eye-catcher.

Tear-off edges enable individual portioning of the delta-shaped pouches.



The small cross section makes portioning easy.

Three months protection

The contraceptive Sayana® Press by Pfizer Inc. was specifically developed to meet the needs of women living in some of the world's poorest countries.

The need for contraception in the developing world remains high. There are more than 200 million women in developing countries who want to delay or prevent pregnancy, but are not using contraception. And, according to the World Health organization (WHO), promotion of family planning – and ensuring access to contraceptive methods – is essential to securing the well-being and autonomy of women.*

Pfizer's contraceptive Sayana® Press was specifically developed to meet the needs of women in developing countries where they may face challenges in obtaining contraception, such as travelling to health facilities, social barriers, and a general lack of information about available contraceptive methods. The active ingredient, depo medroxyprogesterone acetate, commonly referred to as DMPA, comes in the prefilled, single-use, auto-disable Uniject™ delivery system developed by BD (Becton, Dickinson and Company). The delivery system eliminates the need for the user to prepare a needle and syringe, and allows it to be administered outside a clinical setting, with the potential for self-injection if locally approved. Each subcutaneous injection prevents ovulation and provides contraception for three months.** Because of its unique contraceptive delivery technology, Sayana® Press is compact, discreet, and easily transportable. This combination of syringe, needle and medication is manufactured in part with technology from Harro Höfliger, in cooperation with its Excellence United partner Bausch+Ströbel and Skan.

The prefilled, single-use delivery system eliminates the need for the user to prepare a needle and syringe.

Women should decide for themselves when to become pregnant. The broad availability of contraceptives helps them to do this.

istockphoto.com/JordiRamisa, PATH/Gabe Bienczycki

Joint efforts

Pfizer collaborates with the Bill & Melinda Gates Foundation (BMGF) and the Children's Investment Fund Foundation (CIFF) to help broaden access to Sayana® Press for women living in some of the world's poorest countries. As per the terms of the collaboration, organizations seeking to reach the poorest women in a defined set of priority countries can obtain the medication for USD 0.85 per dose if they have successfully passed through a process to qualify. They can then decide to make it available to women at a very low cost or even free of charge.

The effort is supported by a consortium of public- and private-sector donors and aid organizations including BD, the United Kingdom's Department for International Development (DFID), UNFPA, the United Nations Population Fund, and the United States Agency for International Development (USAID). These organizations play an important role in ensuring that women in the world's poorest countries have access to a full range of contraceptive options.

Since 2014, more than 16 million units have been shipped to 23 countries across sub-Saharan Africa and Southeast Asia, potentially reaching more than four million women.

This commitment of all organizations helps support the goals of the United Nations 2030 Agenda for Sustainable Development to drive positive and essential change around the world, and Family Planning 2020 (FP2020), a global partnership to ensure that by 2020 an additional 120 million women have access to and use a method of modern contraception. ■

*** World Health Organization Family Planning/Contraception Fact Sheet. http://www.who.int/news-room/fact-sheets/detail/family-planning-contraception Last accessed August 2, 2018.**
**** Sayana® Press professional and patient information, including the risk of bone mineral density loss and other warnings and precautions for use, can be found at https://www.medicines.org.uk/emc/product/3148.**

About Pfizer Inc.

Pfizer Inc., with headquarters in New York City, was founded in 1849. It is one of the world's largest research-based pharmaceutical and biomedical companies, dedicated to discovering, developing and manufacturing pharmaceutical and health care products. The global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products.

See you!

Ametropia has probably been found in humans since our earliest existence. The history of correcting eyesight using vision aids such as glasses or contact lenses, however, is very short.

The Roman orator Cicero was still more than two millennia away from ultra-light varifocals or daily lenses. To his annoyance, he had to have slaves read documents to him because of declining eyesight. It is true that in ancient times people recognized the magnifying effect of glass spheres, and even Archimedes studied the bundling of light through concave mirrors. But it was not until the 11th century that the Arab mathematician Alhazen became the mastermind of optics, with his work on the functioning of the eye and the refraction of light by means of converging lenses.

Italian monks used this knowledge in the 13th century and cut concave, i.e. bulbous “reading stones”. They were held in front of the eye or used as magnifying glasses. Among clerics and the wealthy, these reading aids quickly became popular with far-sighted and presbyopic people. The starting material was often the silicate mineral beryl – hence the German word “Brille”. Soon, the first somewhat adventurous designs such as forehead band glasses were available to fasten two lenses firmly in front of the eyes which kept the hands free. A milestone in terms of razor-sharp vision was achieved in the 15th century. From that point forward, correction of short-sightedness was achieved through the use of scattering lenses ground to a convex shape.

Thinner, lighter, more precise

The glasses, which became increasingly affordable, provided an infinitely better quality of life, and with their help, more and more people were able to pursue professions that demanded a sharp eye. This formed the basis for the development of sophisticated machines and technological progress.

Nevertheless, visionary creative minds were not satisfied with the steady refinement of corrective lenses and frames. They sought to modify the refractive properties of the eye directly at the cornea. In 1508, Leonardo da Vinci pondered immersing the eye in a water-filled glass jar – a rather awkward approach. It was not until 1880 that a solution became apparent. His level of suffering may have driven the physician August Müller to research “corneal lenses”. With minus 14 diopters he was extremely short-sighted. His two-centimeter glass lenses showed excellent results in a self-experiment, however the sensitive eyeball tolerated them only under local anesthesia.

The predecessor of our modern plastic contact lenses originated in the 1950s. The hard lenses made of plexiglass only covered the cornea, floated on a tear film and were rarely considered bothersome after the initial phase. In the following decade, the production of soft contact lenses made of other polymers began. They conform to the shape of the cornea, thereby ensuring that they are comfortable to wear and stay in place. This has become the most popular type of lens. These days, improved materials ensure high oxygen permeability for our most important sensory organ and, with proper hygiene, even allow for several days of uninterrupted wear.

Whether the choice is made in favor of extended wear rigid gas permeable (RGP) or disposable lenses – i.e. daily, weekly or monthly lenses – depends besides medical aspects only on the requirements of the wearers: Correction of aberrations of the eye or a purely cosmetic medium, for example to intensify the color of the iris?

The history of the contact lens has not been fully told yet. As a smart product it could offer additional medical value. For example, tear fluid could potentially be used to measure blood sugar. We will see … ■

shutterstock.com/Syda Productions

Invisible glasses

There are various methods for the manufacture of contact lenses such as molding, lathe or cutting processes. The basis for all lenses is plastic (monomer), which cures to polymers using heat or UV light. In a further step, the products are hydrated by adding saline solution – making them soft and flexible. The manufacture of the contact lenses is followed by safe and sterile packaging into blisters which are printed with all the important data.

“Digital Excellence” at ACHEMA

About 145,000 visitors came to the world’s leading trade show for process technology to find out about new products and trends. One of the highlights: “The Cube” by Excellence United.

In June 2018, ACHEMA in Frankfurt focused primarily on digitization topics. With their motto “Discover Digital Excellence”, Harro Höfliger, Bausch+Ströbel, Fette Compacting, Glatt and Uhlmann were on the right track. For the first time, the Excellence United partners presented fully integrated solutions for Pharma Production 4.0 in the joint exhibition area “The Cube”. The centerpiece of the production line for continuous manufacturing of solids was the jointly developed IoT hub, an open platform for software development and system integration of entire production lines. It enables the networking of machines from Excellence United partners as well as machines from other manufacturers.

“The Cube” attracted a large crowd, but beyond that, Harro Höfliger's own future-oriented technologies met with great interest among trade visitors. In addition to production processes at every automation stage, the focus at the approximately 500 m^2 exhibition booth was on augmented reality applications for maintenance and training.

Harro Höfliger presented its own future-oriented technologies from lab to production on approximately 500 square meters.

ACHEMA2018

At the Excellence United exhibition area, visitors were able to obtain valuable information about solutions for Pharma Production 4.0.

Inhalation Insights on tour

The next stops in the Dry Powder Inhalation Technology (DPI) symposia series will be Argentina and Brazil.

Following the successful kick-off session in Kuala Lumpur and three other events in the US, Inhalation Insights will continue in South America in November. At the symposia series, jointly initiated by Harro Höfliger and partner companies, industry experts will talk about the challenges and new developments in DPI technology. Presentations and panel discussions will focus on providing direct information and access to useful expertise in key DPI areas such as carrier material, filling and device technologies, quality assurance and the latest market trends.

“Our series of events and the associated transfer of know-how are very well received by the participants. We are pleased that there is such significant interest in practical insights into the production and development of DPI products,” says Marco Laackmann, Leader Business Unit Inhalation at Harro Höfliger.

The participants use Inhalation Insights to gain first-hand information along the entire process chain, from powder characterization to safe packaging for sensitive products.

INHALATION INSIGHTS

Visit us:

Compamed
Düsseldorf, Germany
12.11.–15.11.2018

RDD Asia
Kerala, India
14.11.–16.11.2018

Pharmtech
Moskow, Russia
20.11.–23.11.2018

Inhalation Insights LATAM
Buenos Aires, Argentina
20.11.2018

Inhalation Insights LATAM
Sao Paulo, Brazil
22.11.2018

ALL4Pack
Paris, France
26.11.–29.11.2018

DDL
Edinburgh, GB
12.12.–14.12.2018

P-Mec India
Delhi, India
12.12.–14.12.2018

Pre-Filled Syringes & Injectable Drug Delivery
London, GB
16.01.–17.01.2019

DDP
Palm Beach Gardens, USA
28.01.–01.02.2019

Arab Health
Dubai, UAE
28.01.–31.01.2019

MD&M West / ATX
Anaheim, USA
05.02.–07.02.2019

Pharmapack
Paris, France
06.02.–07.02.2019

ICE Europe
Munich, Germany
12.03.–14.03.2019

CPhI Bangkok
Bangkok, Thailand
12.03.–14.03.2019

Interphex
New York, USA
02.04.–04.04.2019

ICE USA
Louisville, USA
09.04.–11.04.2019

Pharma Kongress
Düsseldorf, Germany
09.04.–10.04.2019

Powtech
Nuremberg, Germany
09.04.–11.04.2019

Pharmintech
Bologna, Italy
10.04.–12.04.2019

RDD Europe
Estoril, Portugal
07.05.–10.05.2019

KIHE
Almaty, Kazakhstan
15.05.–17.05.2019

ExpoPack
Guadalajara, Mexico
11.06.–13.06.2019

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We look forward to your visit.

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