HARRO

The Customer Magazine
by Harro Höfliger

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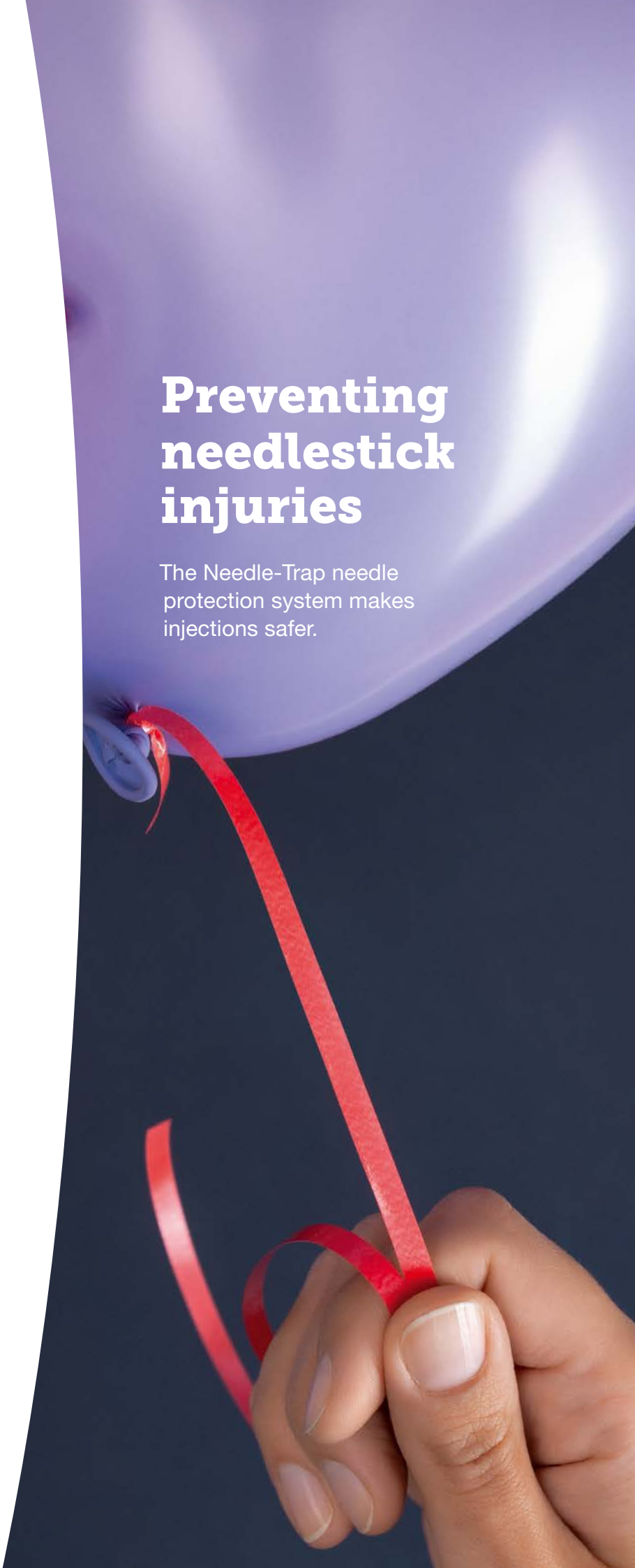
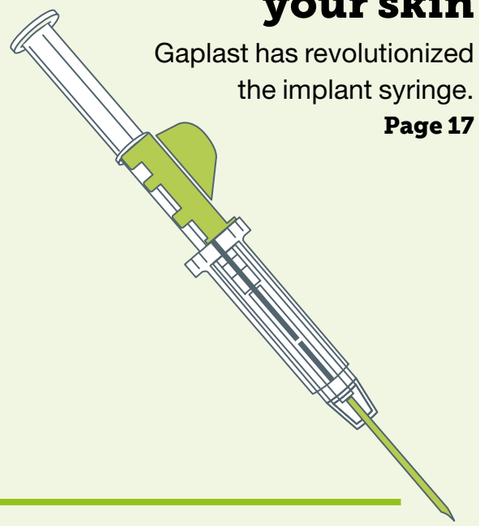
Preventing needlestick injuries

The Needle-Trap needle protection system makes injections safer.



Harro Höfliger

Innovation that goes under your skin



Gaplast has revolutionized the implant syringe.

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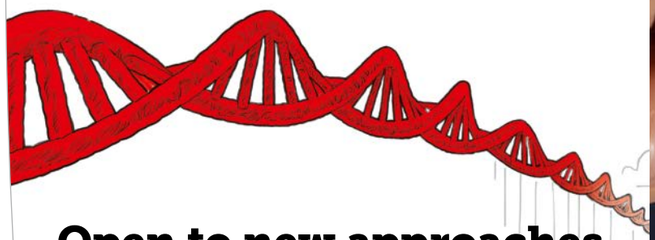

Open to new approaches

Biopharmaceuticals as well as gene- and cell-based active ingredients could open new chances for the pharmaceutical market. Harro Höfliger has solutions for their filling.

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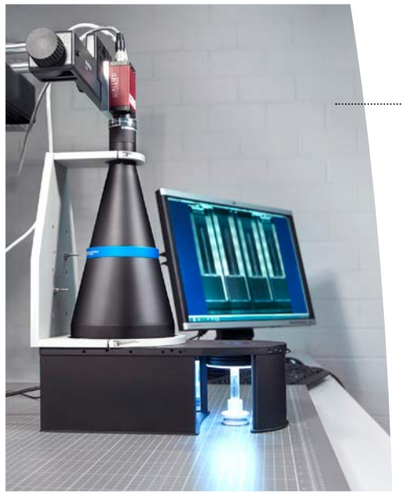

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Dear Readers,
dear Business Associates,

Biopharmaceuticals are gaining ground worldwide, opening up new opportunities in medical science and their market share is growing steadily. Advanced Therapy Medicinal Products (ATMPs) offer hope for the treatment of diseases such as cancer, Parkinson’s, diabetes or Alzheimer’s, for which there have been insufficient or no therapies until now.

However, these gene and cell therapeutics as well as biotechnologically processed tissue products also pose new challenges for pharmaceutical and machine manufacturers. Sterile production throughout and aseptic filling into bags, syringes or vials are crucial. Harro Höfliger’s experts have already developed trend-setting solutions for numerous projects. Yet fewer standards than ever can be established. This is why we work closely with our customers to implement individual, holistic solutions. In order to pick up the pace in this area, we are working relentlessly to develop preassembled modules for flexibly configurable machine platforms. We devote all of our expertise to the development of the necessary aseptic production processes, as you can read in the article on page 10.

Biopharmaceuticals are the future. The exciting challenges go hand in hand with our philosophy “The product determines the process” and spur our creativity and innovative spirit.

“ALL YOU NEED” – our promise now and in the future.

Your

Thomas Weller,
CEO at Harro Höfliger

Service with smart glasses

Harro Höfliger relies on high-tech glasses with video transmission to expand their service portfolio. These smart glasses make it possible to observe the wearer's entire range of activities from any terminal device in real time.

An important area of application is support in troubleshooting, for example during machine downtimes: The person at the machine wears smart glasses, sharing the field of view with a connected service contact at Harro Höfliger. This contact can, for example, provide information on important inspection points or project documents into the field of view.

In addition, smart glasses can also be used during the project planning phase or for final acceptance tests. In this case, a Harro Höfliger specialist wears the glasses while the customer observes all activities from a distance. This enables fast and detailed real-time insights without long travel times.

Service specialists can, for example, project documents into the field of view.

Digital platform: HARRO WORLD

On Harro Höfliger's new digital platform HARRO WORLD, we showcase the wide range of our capabilities and solutions. Just like a virtual shop window, HARRO WORLD will provide exclusive insights into innovative technologies. Regular expert lectures and streaming formats will offer great opportunities for in-depth networking. The presentation platform plans to open its digital gates for customers and interested parties in spring 2022.

Greetings from Kilimanjaro

Alexander Haritonov, Sales Director of Harro Höfliger at Moscow, sets himself ambitious goals even for his holiday: When conquering Mount Kilimanjaro, he carried the flag of Harro Höfliger with him. After climbing Elbrus in his native Russia in 2019, Uhuru Peak, at 5,895 meters above sea level, was the second five-thousander that he has now conquered. Alexander Haritonov has been involved in establishing the branch office in Russia right from the start and took over the local sales activites for Harro Höfliger in 2011.

Tom Philippi, Janine Kyofsky

When developing camera solutions, the image processing department cooperates closely with Control Engineering, Mechanical Design and HMI.

"All the camera expertise is pooled in-house"

Since 2012, Harro Höfliger has an in-house image processing department. Hartwig Sauer, Department Leader Vision Systems, tells us what the 23 employees are working on and how customers benefit from their developments.

Mr. Sauer, what do Vision Systems employees do all day?
In a nutshell, we develop camera systems for our machines. 17 application engineers develop individual camera setups for inspection and control tasks. Three employees take care of the user interface, one is responsible for the hardware and one for the machine documentation. And I, as the department leader, coordinate everything.

"Around 70 percent of our machines are equipped with cameras for quality control."

Hartwig Sauer, Department Leader Vision Systems at Harro Höfliger

Can you name a few typical fields of application for camera systems?
There are numerous fields of application. Around 70 percent of our machines are equipped with cameras for quality control. In web-processing machines, cameras often check the correct cutting and packaging of patches. During syringe assembly, for example, we can use surface inspection to detect whether there are defects such as tears or break-offs on certain parts. Another typical application is print image control. The camera checks, for instance, whether the expiration date on the product is legible. Poor print quality results in product rejection.

Why did you bring the development of camera systems in-house a few years ago, and how do customers benefit?
All of this expertise is now pooled in-house. This means we can react much faster to customer requests. When developing camera solutions, we cooperate closely with other areas such as Control Engineering, Mechanical Design and HMI. Even feasibility studies can be carried out quickly thanks to our in-house laboratory. Here, we examine product samples with our extensive camera technology, lighting and test equipment. This is the basis for our tailor-made and individual solutions.

One billion safe injections

For more than ten years, the Needle-Trap needle protection system has made injections safer. And for just as long, Schreiner MediPharm, a business unit of the Schreiner Group, has been working closely with Harro Höfliger: Over 1.2 billion pieces of the internationally used product have been produced on the joint machines.

Each individual Needle-Trap label carries an accurately applied needle catcher.

Gernot Walter, Schreiner MediPharm

More than three times around the world – this is the distance that the labels produced by Schreiner Group each year would cover if strung together. The company with headquarters in Oberschleissheim near Munich, Bavaria, was founded in 1951 and provides solutions for a wide range of applications. The portfolio comprises innovative functional labels including self-adhesive functional parts, RFID labels, printed electronics and security solutions for product and document protection, as well as customized services and value-added services.

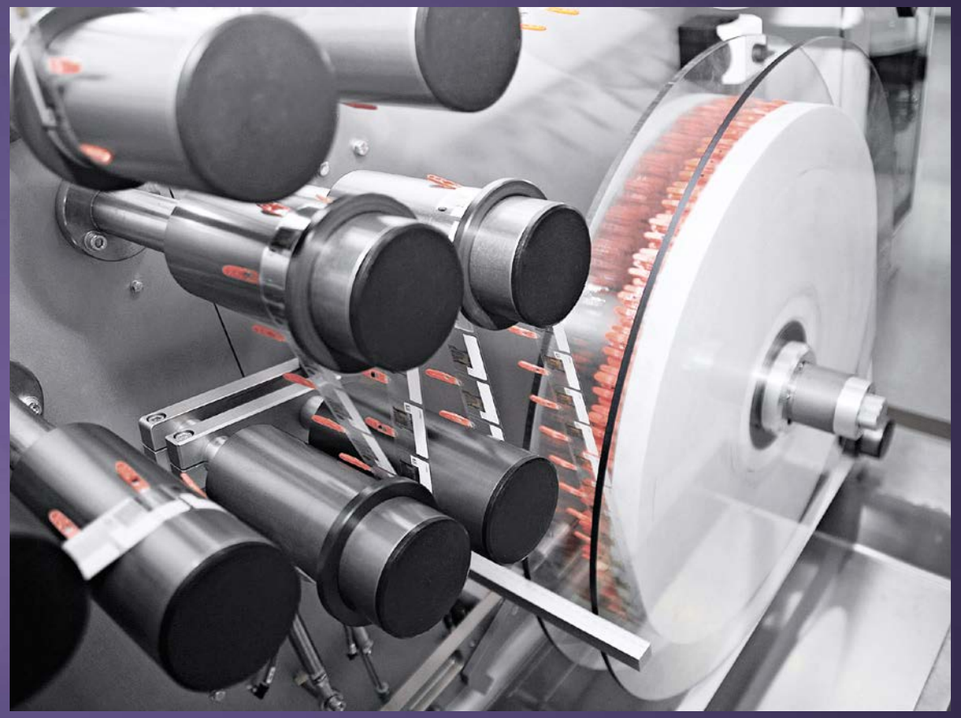
The Schreiner MediPharm business unit specializes entirely in the requirements of the pharmaceutical and medical device industry. “There is a large demand for special labels in the healthcare sector, for example to optimally administer and track products,” explains Stefan Wiedemann, Senior Director Strategic Marketing and Business Development at Schreiner MediPharm. “With our high-quality labels, we are contributing to safe medical treatments.”

Simple idea, easy application

Patient safety and the protection of medical personnel was also the driving factor behind one of Schreiner MediPharm’s greatest product successes, the Needle-Trap needle protection system. It addresses a pressing problem in healthcare: In European hospitals and medical practices alone, more than one million needlestick injuries occur every year. Schreiner MediPharm’s Needle-Trap secures the needle after injection, thus minimizing the risk of injury and helping to prevent infections.

“Our teams agreed that precision must come first, as the exact positioning of the needle catcher on the label is an important aspect.”

Stefan Wiedemann, Senior Director Strategic Marketing and Business Development at Schreiner MediPharm



The finished Needle-Trap labels are exactly wound onto reels.

Stefan Wiedemann explains the idea: “A pre-filled syringe always requires a label containing all relevant information. This is where our Needle-Trap comes into play. We combine the label with an integrated needle catcher that serves to secure the needle after injection. Thus, to mark the pre-filled syringe, pharmaceutical manufacturers receive from us a label and a protective mechanism in one, a unique principle.”

Its application is as simple as the idea: Prior to injection, users simply have to bend the needle catcher towards the side and remove the cap. The subsequent injection process is as usual and syringe handling remains unchanged. In order to activate the safety mechanism, the trap has to be pressed against a stable surface with one hand. An acoustic signal indicates when the needle is fixed in the trap and thus secured.

New challenges

Schreiner MediPharm has worked closely with Harro Höfliger since the beginning of product development. Hartmut Thier, Director Web Technologies at Harro Höfliger, describes the early stage of the collaboration. “Needle-Trap posed completely new challenges to web processing. While we had a lot of experience in label processing, the combination with the plastic part – the trap – was new. An initial test set-up quickly showed that our idea for the manufacturing process worked.” Stefan Wiedemann summarizes the challenges: “Our teams agreed that precision must come first, as the exact positioning of the needle catcher on the label is an important aspect.”

A wide range of inspection systems

Based on these requirements, Harro Höfliger designed several production lines over the following years. These ensure that high-precision robots place a needle catcher on each label. At the same time, various inspection systems check whether all traps are perfectly positioned. “This inspection data goes into a digital batch report which enables end-to-end traceability. Thus, it is ensured that only flawless products leave the production lines in order to meet the high quality standards,” explains Hartmut Thier.

Quantity meets quality

To date, Schreiner MediPharm has produced more than 1.2 billion Needle-Traps on the joint machines. According to Stefan Wiedemann, this success is explained by the fact that the product meets the requirements of medical personnel and pharmaceutical industry alike. “Its compact design makes Needle-Trap an efficient and at the same time cost-effective solution. Demand remains high, since our needle protection system can be used for all common pre-filled syringes. And with machines from Harro Höfliger, we do not have to choose between high output and impeccable quality of each single product.”

“Needle-Trap posed completely new challenges to web processing. While we had a lot of experience in label processing, the combination with the plastic part – the trap – was new.”

Hartmut Thier, Director Web Technologies at Harro Höfliger

Step by step toward higher safety

First, bend the trap towards the side by approximately 90 degrees.

Remove the cap.

Perform the injection (as usual).

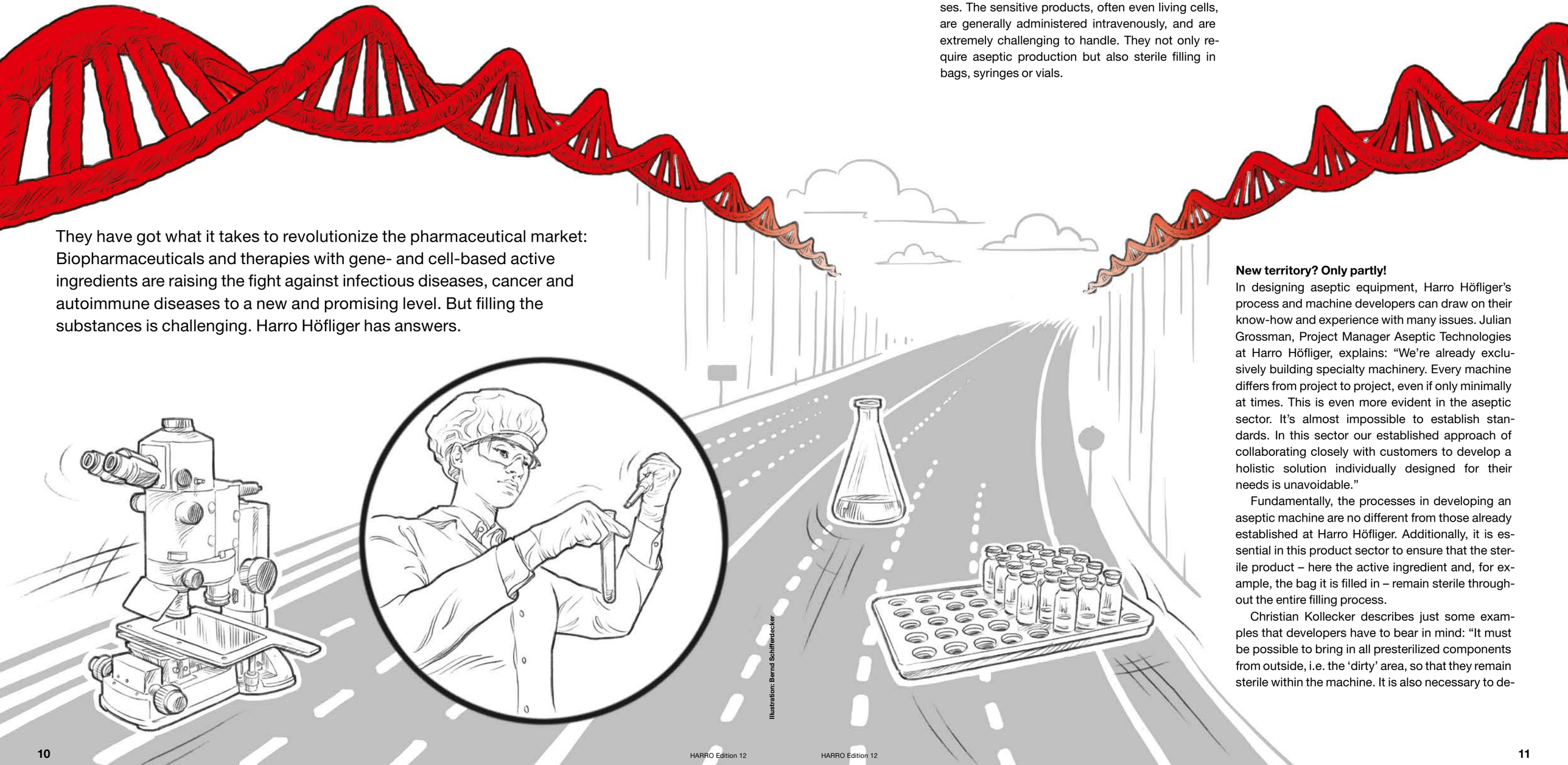
Gernot Walter, Schreiner MediPharm, Janine Kyofsky

Secure the needle by placing the trap against a hard, stable surface, using one hand. Then press down the trap.

Bend the trap until the needle audibly clicks into the plastic part.

Dispose of the syringe with the secured needle in the nearest sharps container.

Open to new approaches



They have got what it takes to revolutionize the pharmaceutical market: Biopharmaceuticals and therapies with gene- and cell-based active ingredients are raising the fight against infectious diseases, cancer and autoimmune diseases to a new and promising level. But filling the substances is challenging. Harro Höfliger has answers.

Illustration: Bernd Schifferdecker

Since the successful use of mRNA vaccines against COVID-19, awareness of biotechnological medications has spread beyond the circle of experts. The pharmaceutical industry has been increasingly using highly effective and patient specific therapeutic approaches for years in the fight against diseases. Since 2012, EMA (European Medicines Agency) and the US FDA (Food and Drug Administration) have approved several gene therapeutics that can be used to adjust genetic defects in order to cure diseases. In the next three years the FDA expects around 800 new licenses. The sensitive products, often even living cells, are generally administered intravenously, and are extremely challenging to handle. They not only require aseptic production but also sterile filling in bags, syringes or vials.

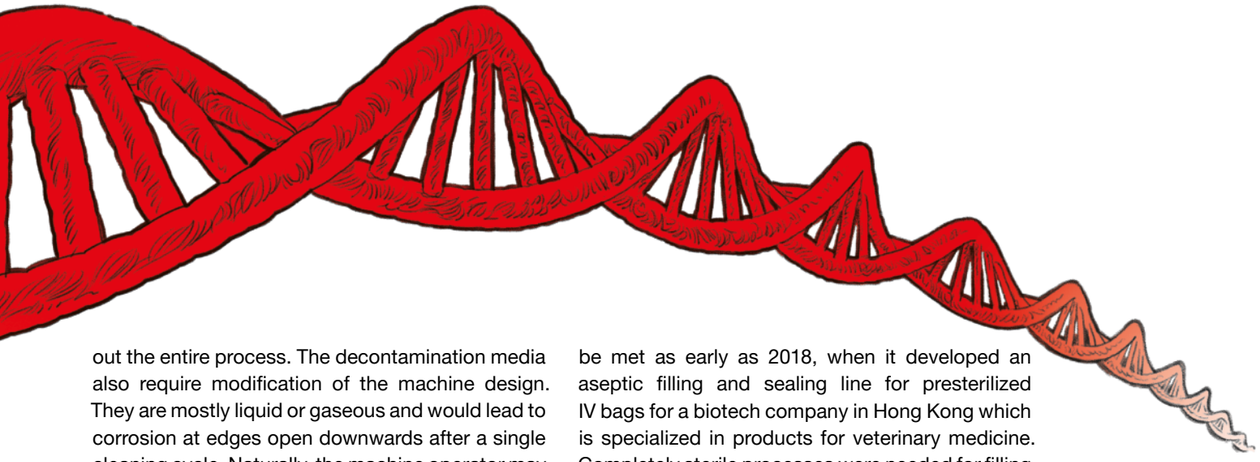
Harro Höfliger has been dealing for years with the challenges of the bridge between flexible primary packaging and the demanding production requirements for aseptic bag filling. Christian Kollecker, Sales Director Aseptic Technologies at Harro Höfliger, explains: “Our motto ‘the product determines the process’ is right on the nail here. We draw on our full know-how for developing aseptic production processes. Together with our partners we develop completely new machine platforms to offer our customers unique and individually configurable solutions.”

New territory? Only partly!

In designing aseptic equipment, Harro Höfliger’s process and machine developers can draw on their know-how and experience with many issues. Julian Grossman, Project Manager Aseptic Technologies at Harro Höfliger, explains: “We’re already exclusively building specialty machinery. Every machine differs from project to project, even if only minimally at times. This is even more evident in the aseptic sector. It’s almost impossible to establish standards. In this sector our established approach of collaborating closely with customers to develop a holistic solution individually designed for their needs is unavoidable.”

Fundamentally, the processes in developing an aseptic machine are no different from those already established at Harro Höfliger. Additionally, it is essential in this product sector to ensure that the sterile product – here the active ingredient and, for example, the bag it is filled in – remain sterile throughout the entire filling process.

Christian Kollecker describes just some examples that developers have to bear in mind: “It must be possible to bring in all presterilized components from outside, i.e. the ‘dirty’ area, so that they remain sterile within the machine. It is also necessary to de-



out the entire process. The decontamination media also require modification of the machine design. They are mostly liquid or gaseous and would lead to corrosion at edges open downwards after a single cleaning cycle. Naturally, the machine operator may only reach into the machine through special glove systems."

A resounding success through know-how

Harro Höfliger proved that these requirements can be met as early as 2018, when it developed an aseptic filling and sealing line for presterilized IV bags for a biotech company in Hong Kong which is specialized in products for veterinary medicine. Completely sterile processes were needed for filling the highly sensitive bioactive ingredients. Besides an active open RABS technology (Restricted Access Barrier System), this machine also used the 'one-time docking' principle for the first time. In this the IV bags are filled using an aseptic triple filling head. The connection to the filling nozzle is kept in place throughout all gas purging, evacuation and filling processes until the transfer from the machine. This minimizes the risk of particle entry and keeps the residual oxygen content of the bag low.

An integrated, laser-based Wilco HSA (Head Space Analysis) module provides an in-line measurement of the oxygen content. A high-precision measurement of mass flow using the Coriolis effect is performed during liquid filling by a sensor which ensures that each infusion bag has been filled to exactly the right amount. All fill media are supplied in a sterile manner by aseptic rotary distribution. The opening is tightly sealed by radio frequency welding to minimize the heat transfer to the active ingredient. An integrated CIP/SIP system (Cleaning in Place/ Sterilization in Place) ensures perfect cleaning after each batch.

Christian Kollecker summarizes: "In this project we implemented a lot of things which stricter regulations would soon make standard practice for several of our customers. And this showed us what the important things were for aseptic machines: Short throughput times and high process reliability by integrating process analytical technology wherever possible and necessary."

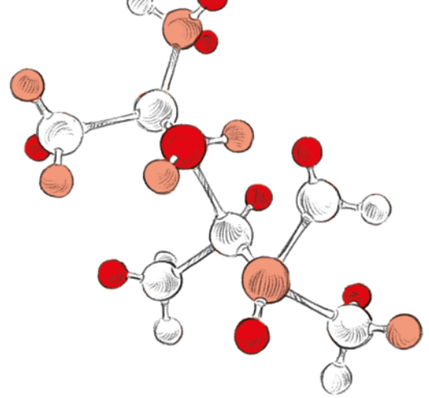
"Our motto 'the product determines the process' is right on the nail here. We devote all of our expertise to the development of aseptic production processes."

Christian Kollecker, Director Aseptic Technologies at Harro Höfliger

Safely filled

The specialists at Harro Höfliger focus on filling presterilized bags. Kollecker explains: "Naturally, we can also fill syringes and vials, but the large, long-chain molecules of biotech products often form highly viscous solutions that have to be diluted to larger volumes. Infusion bags have clear advantages here."

The experts especially have a wealth of experience with filling presterilized bags. As Grossmann knows, the devil here is again in the details: "Dealing with the new substances is new territory for us as well. Whether it is living cells or so-called lyophilized powders that emerge like cotton candy, we have to develop the right filling method for each substance." To deliver good solutions to customers quickly, Harro Höfliger relies on flexibility through modularity.

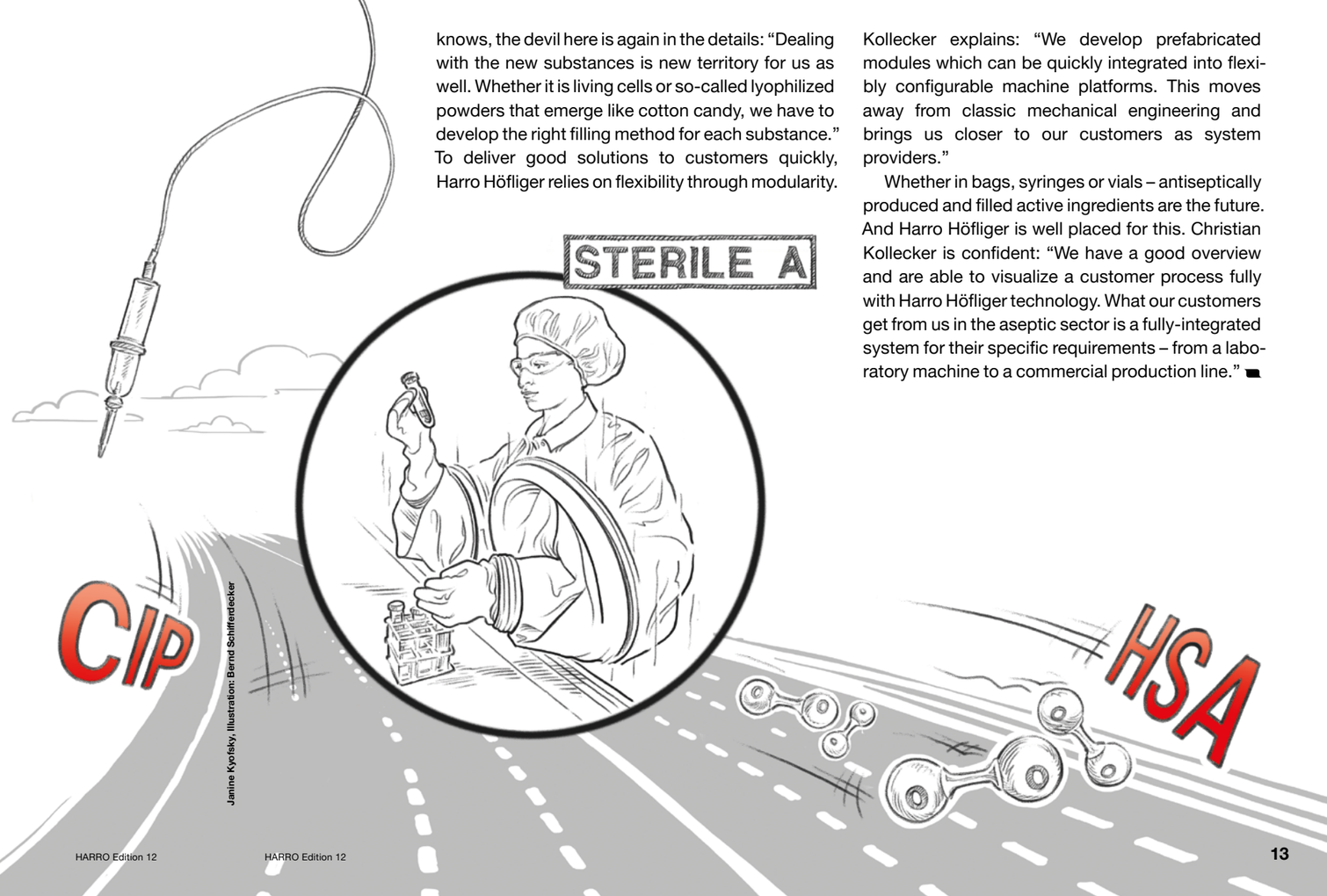


"We, too, are entering unchartered territory when it comes to dealing with these new substances. Be it living cells or lyophilized powders – we have to develop the right filling method for each substance."

Julian Grossmann, Project Manager Aseptic Technologies at Harro Höfliger

Kollecker explains: "We develop prefabricated modules which can be quickly integrated into flexibly configurable machine platforms. This moves away from classic mechanical engineering and brings us closer to our customers as system providers."

Whether in bags, syringes or vials – antiseptically produced and filled active ingredients are the future. And Harro Höfliger is well placed for this. Christian Kollecker is confident: "We have a good overview and are able to visualize a customer process fully with Harro Höfliger technology. What our customers get from us in the aseptic sector is a fully-integrated system for their specific requirements – from a laboratory machine to a commercial production line."



Janine Kyofsky, Illustration: Bernd Schifferdecker

Adobe Stock / jayzynism

The focus is on the eyes

In the Eye Care Technologies divison – a separate product field of Harro Höfliger – everything revolves around solutions for the production and packaging of ophthalmic products.

Contact lenses inspire the imagination in many ways. In the blockbuster “Mission Impossible”, they make it possible to photograph secret documents in the blink of an eye. During the Olympic Games, the British sprinter Linford Christie made clever use of it as an advertising space for his sponsor’s logo. Even the eye color can be intensified or temporarily changed, if desired. For most contact lens wearers, however, the ultra-thin vision aids that provide all-around clear vision are primarily an alternative to corrective glasses.

The majority of people with poor sight opt for soft contact lenses, which are available in a wide variety of designs: daily, weekly, 14-day or monthly lenses. Precise manufacturing processes and comprehensive quality controls guarantee that contact lenses not only reliably correct visual defects but are also gentle on highly sensitive eyes. Jochen Stein, Director Eye Care Technologies at Harro Höfliger, knows about the demanding processes: “For more than 20 years, this company has been dealing with eye care products and offers, among other things, fully automated solutions covering the entire value chain for contact lenses all the way to their distribution. In addition to lens manufacturing, whether bifocal or multifocal, for short-sightedness or for long-sightedness, for the correction of astigmatism or even as an implantable intraocular lens, we cover all of the following packaging steps. That is, primary packaging into blisters for product protection, secondary packaging into cartons and tertiary packaging into shipping cases – naturally including all in-process controls and labeling.”

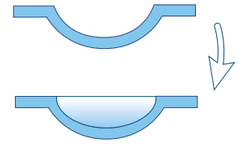
Gentle handling of the sensitive lenses

Nowadays, commercial contact lenses are mainly made by molding silicone hydrogel or hydrogel and then packaged into blisters. At the beginning, there is an injection mold into which a liquid monomer mixture is dosed. Adding energy in the form of temperature or UV light triggers polymerization and results in curing of the lens. However, before further processing, it must become soft again and retain moisture. After the so-called hydration, it is carefully released from the mold in a fully automated process and then individually packaged into blisters with saline solution. Harro Höfliger technology is used to seal the blisters and laser code them with data such as, for example, lens type, eyesight and diameter.

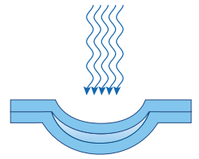
Fully automatic cartoning is one of Harro Höfliger’s key strengths. Jochen Stein: “In addition to packaging machines for large volumes, we also offer intelligent solutions for lot size 1 such as may be required for intraocular lenses (IOLs). These implantable lenses are customized for each patient and, for instance, are inserted into the eye during cataract surgeries.” →

Harro Höfliger’s portfolio:

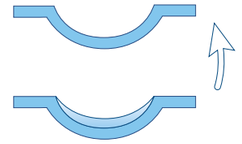
1. Dosing of monomer mixture into injection mold



2. Attaching of a second mold and closing

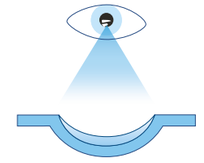


3. Curing of the lens by heat or UV light

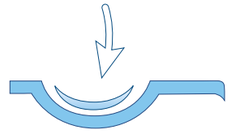


4. Removal of the mold after polymerization is complete

5. Hydration of the cured lens

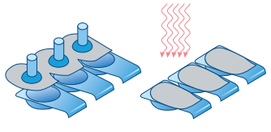


6. Camera inspection for quality control

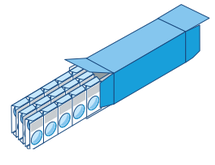


7. Removal of lens for packaging process

8. Dosing of saline solution into the single blisters



9. Sealing of the blisters and printing



10. Packaging of the blisters into cartons

Products for eye care
Maximum precision is also crucial for another medical device from the Eye Care Technologies range: Injection systems specifically designed for the eye. In line with their turnkey approach, Harro Höfliger not only offers reliable joining techniques for the sensitive individual components, but also solutions for the subsequent packaging. The know-how in filling, assembly, packaging and labeling of eye care devices also plays an important role when it comes to eye drops, gels and ointments.

Eye drops are not only filled into classic vials and as hygienic single doses into blow-fill-seal plastic ampoules. Even two-chamber tubes for ophthalmic mixture applications are possible, as offered by Neopac with their Fleximed® Easymix tube. Two components are separated by a seam in a medical tube. The thin barrier opens under pressue. With this method, two liquids as well as one liquid and one powder component can be mixed. Filling and sealing of the plastic laminate tube and the central bar are performed on machines from Harro Höfliger. Depending on the application, the tubes can be equipped with different closures, application and dispensing aids.

Smart future
By the way, high-tech lenses should not be reserved for Hollywood scripts, they could also provide added medical value. Contact lenses with biosensors, for instance, are under development. Possible applications include the measurement of blood sugar levels in the tear fluid and alert in case of deviating values – a smart trend that could make quite a few finger pricks obsolete.

Research is also being conducted on virtual-reality-lenses that digitally extend the real world and feed in information such as heart rate or even navigation data on mini-displays. When that will be? We will see.

“We provide intelligent solutions for lot size 1, for example for introcular lenses that are tailored to the individual patient.“

**Jochen Stein,
Director Eye Care Technologies
at Harro Höfliger**

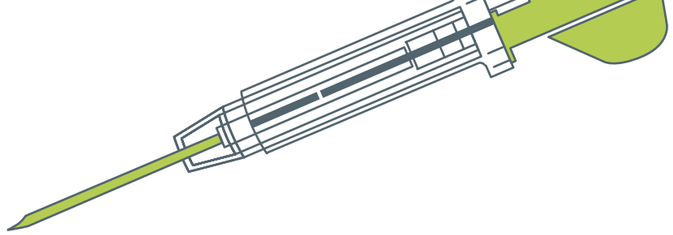
Filling and welding of tubes with eye drops takes place on machines from Harro Höfliger.

Janine Kyofsky

Innovation that goes under your skin

With the development of a new implant syringe, Gaplast has revolutionized the application of subcutaneously administered drugs.

Today, implants containing active ingredients (also known as “rods“) are firmly established in the field of long-term medication. Due to the retarding release of the active ingredient, they replace the daily intake of tablets or the administration of injections. That way, they provide protection and safety for patients – either human or animal. However, administering them with the help of commercially available implant placers often involves a number of hurdles. Frequently, the implant is not pushed into the injection channel, but into the surrounding tissue; not rarely, administrations have to be repeated several times because the needle’s retraction causes the medication to shift or be pulled out a bit again. With their new type of implant syringe, Gaplast, a packaging manufacturer from Upper Bavaria, Germany, aims to minimize these unpleasant side effects during administration.



It all began with an idea

"The idea goes back to the mid-1990s," recalls Ingmar Kneer, team leader in the medical technology sector at Gaplast. "At that time, we received the first inquiry from a large German generic manufacturer for the development of an implant syringe. Innovation and ingenuity are firmly anchored in our DNA, and quite quickly we came up with a new type of mechanism. It pulls the cannula out of the patient's tissue after the implant has been applied into the injection channel. This ensures reliable administration."

Today, this device is available with a depot for one or three months. Ingmar Kneer: "It is used, for example, in the treatment of oncological diseases, but also for the long-term medication of hormones in human and veterinary medicine. Additional long-term or depot applications have already been initiated."

"Every step fulfills the highest standards without compromising functionality or visual appearance."

Ingmar Kneer, team leader in the medical technology sector at Gaplast

Gaplast's device is available with a depot for one or three months.

Gaplast GmbH

Full functionality

Only approved "pharma proof" or "medical grade" materials are used in the manufacture of implant syringes. The main material – a modified styrene-acrylic copolymer – guarantees full functionality as well as stability of shape and color. "We can provide evidence that our implant syringe shows significantly less color deviations and deformations caused by sterilization than comparable medical devices," says Ingmar Kneer.

Tight network

In order to grant the highest level of quality, Gaplast not only relies on particular materials, but also on a close exchange with a specialized partner network. "The intensive exchange with all partners is a matter of course for us," explains Ingmar Kneer. "We heavily involve them in process step development, thus making sure that all components are precisely matched for production."

Careful handling

Harro Höfliger is part of this network – the company designs high-precision machines for the pre-assembly of devices and the insertion of implants. They make sure that the implant is assembled and packaged to operate properly and in top quality – although very tight tolerances (e.g. in the stylet area) are used here. Not only the syringe body has to be kept intact, it must also be guaranteed that the syringe itself remains optically flawless. During the assembly process, this requirement is met by supplying individually packaged implant syringes in trays and carefully inserting them into the feeding units using precise pick-and-place technology. Numerous in-process controls (IPCs) ensure consistently high functionality. Camera systems on the machines provide seamless monitoring of the filling and feeding process. Ingmar Kneer sums up: "Every process step fulfills the highest standards without compromising functionality or visual appearance of the device."

The implant syringe is used, for example, in the treatment of oncological diseases.

About Gaplast GmbH

For more than 30 years, the packaging manufacturer with headquarters in Altenau (near Oberammergau, Germany) has been an owner-managed family business and is a healthy industrial company today. Originating from a management buy-out by the senior boss Roland Kneer, at two locations in Upper Bavaria, the company develops and produces intelligent and sustainable bottles, closures and applications made of plastic for well-known companies all over the world. Gaplast considers itself a solution finder and provides customers with all components from a single source for tailor-made product solutions. Meanwhile the company employs about 300 people and trains apprentices in nine professions. In 2020, the annual turnover amounted to 44 million euros. Gaplast is DIN ISO 9001 and 15378 certified, ISO 13485 is in preparation.

Inhale easy …

Since 2004, the Respimat® has been ensuring easy inhalation for patients with diseases such as asthma and COPD. In 2019, Boehringer Ingelheim launched the new generation of this inhaler: Now that multiple filling is possible with up to six active agent cartridges, this Respimat® re-usable is disposed of less frequently. In an interview, Markus Kirchner (Head of Engineering Assembly, Boehringer Ingelheim microParts GmbH) and Stefan Gais (Senior Sales Director, Harro Höfliger) report about the collaboration related to the environmentally friendly device.

Mr. Kirchner, what is the link between you and the Respimat®?
When I joined Boehringer Ingelheim microParts in 2007, the Respimat® with its high complexity, combined with the propellant-free drive and the active long lasting soft mist, fascinated me right from the start. In addition, the high demands placed on production and verification processes, make an engineer's tasks challenging and interesting. From 2007 to the present, I have been able to work in the three manufacturing technology areas in various positions, actively contributing to and shaping the increase in capacity and the refinement of the manufacturing and testing processes.

Since 2019, there is a re-usable version. Can you give us more details?
The active agent cartridge can be replaced up to six times per device – patients need only two instead of twelve inhalers per year. Besides an improved environmental footprint, another advantage is simplified usage, which we optimized based on patient feedback. For example, the housing is now longer, facilitating turning and thus loading of the Respimat®. The numeric dose indicator has large numbers and is color coded, making it easy to see the leftover doses before locking. The highlight, however, is the automatic detachment of the transparent case bottom part the moment the cartridge is locked and has to be replaced. Despite these optimizations, only the dose indicator and the case assembly are new. This enabled us to keep changes in production relatively small.

Markus Kirchner explains how the environment and the patients benefit from the new Respimat®.

For the production of the re-usable Respimat® you rely, among other things, on machines from Harro Höfliger. Why?
We have already used technology from Harro Höfliger for the production of the established Respimat®. Because of the good partnership in the past, it was an obvious choice to cooperate with Harro Höfliger again regarding the production of the Respimat® re-usable. Our collective experience has resulted in many synergies. For example, we jointly developed special exchange sets to enable flexible production.

"Our collective experience has resulted in many synergies."

Markus Kirchner, Head of Engineering Assembly at Boehringer Ingelheim microParts GmbH

Helmar Lünig

Mr. Gais, what features make the assembly technology in the machines for Boehringer Ingelheim microParts stand out?
A special challenge was to adapt the machine's assembly technology for the established Respimat® version in such a way that the re-usable inhaler version can be produced with it too. It helped that the core components of the Respimat® and the cartridge itself are identical in both versions. As a result, changes in the assembly technology were only necessary at a late stage in the process – when the inner subassemblies are inserted into the new housing. In close cooperation, we have succeeded in making the necessary adjustments by developing new exchange sets. Depending on the order situation, Boehringer Ingelheim microParts can now flexibly switch from one Respimat® version to the other.

Apart from the assembly technology, Harro Höfliger has also designed two new lines for the re-usable Respimat®. What are their tasks?
In the Respimat® re-usable, cartridge and dose indicator are connected with each other. Both machines have the core task to weld these components with each other. It sounds easy, but the technology behind it is sophisticated. First, various camera controls verify the flawless quality of all dose indicators and cartridges. Then a robot gripper system joins the parts together and welds them at 16 ultrasonic stations working in parallel. A test mechanism makes sure that every dose-indicator-cartridge-combination works as intended.

The control cabinets are located on top of these lines. How did that come about?
Ultrasonic welding is time consuming. In order to still achieve maximum output, we use the aforementioned entire 16 welding stations which need a lot of space. At the same time, there were clear specifications regarding the size of the lines: They should not exceed four meters, which is two and a half meters less than initially planned. For this reason, we arranged, for example, the welding stations in opposite directions on our assembly platform MOT, thus saving a lot of space. In addition, we positioned the control cabinets not next to but directly on top of the machines. They are easily accessible for operators via a staircase.

"To achieve maximum output, we use 16 welding stations."

Stefan Gais, Senior Sales Director at Harro Höfliger

Maximum output in a small space: It was not easy to meet the requirements of Boehringer Ingelheim for the lines. Stefan Gais explains how it succeeded.

… and minimize plastic

With fogging, operators do not have to open the machine door. Instead, they wet the production area from the outside with purified water.

Helmar Lünig, Merck

Double protection

Precise capsule filling with highly potent powder and optimum operator protection – this was Merck's requirement when they approached Harro Höfliger. As a result, the experts in Allmersbach developed two special functions and integrated them into the Modu-C LS Containment capsule filling machine.

Medicines containing highly potent substances must be safe, and not just for patients. Already during the production of such medicines, for example for use in cancer therapies, machine operators must be protected as best as possible from any contact with the product. This aspect is of particular importance to the pharmaceutical and chemical company Merck.

Jeffrey Campbell, Director of Engineering MRL, Pharmaceutical Sciences at Merck New Jersey reports about the beginning of the cooperation with Harro Höfliger: "In our search for a capsule filling machine with the highest operator protection, the Modu-C Containment caught our attention." It was specifically developed for the testing of new active ingredients as well as the production of small batches with toxic and highly potent substances.

"Initial dosing tests in Harro Höfliger's cleanrooms showed that the machine is ideally suited for our product," reports Jeffrey Campbell. "Immediately afterwards, we made a reference visit to a

"In our search for a capsule filling machine with the highest operator protection, the Modu-C Containment caught our attention."

Jeffrey Campbell, Director of Engineering MRL, Pharmaceutical Sciences at Merck New Jersey

Swiss company who already works with a similar system from Harro Höfliger. We had the opportunity to study handling, cleaning, and interfaces in operation directly on site and to talk to the operators. After that, it was clear that this was the right concept for us too."

One machine – two new developments

The basic machine design was now found – but Merck had two special requirements: First, a guarantee that no powder dust would remain on any capsule after leaving the machine. Second, Merck wanted to enable their machine operators to clean the machine without the need for a reliance on personnel protective equipment.

In order to remove powder dust from the capsule shell, many companies rely on an external capsule deduster. "However, the important thing for us was to save space in the cleanroom. Harro Höfliger therefore developed a deduster that is directly integrated into the machine," says Jeffrey Campbell. In this deduster station, each filled capsule passes several ring brushes, which remove even the smallest amounts of powder mechanically. Philipp Hoffmann, Mechanical Design Engineer at Harro Höfliger: "After development of the station was completed, we first tested it with very sticky whole egg powder. This showed that our in-house development can keep up with external dedusters."

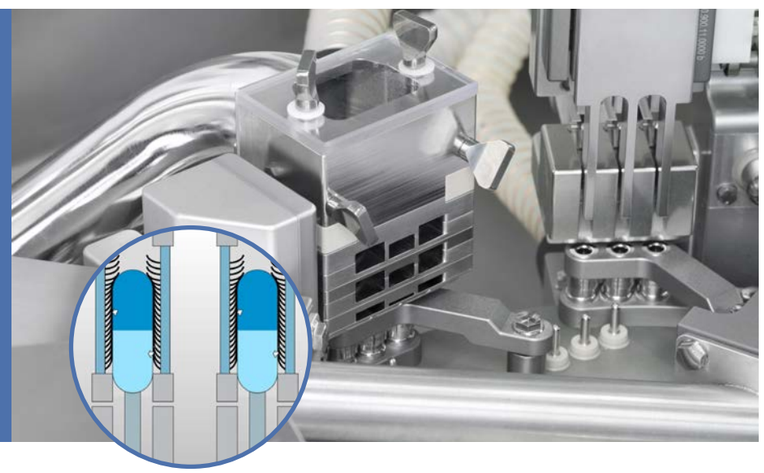
With the newly developed fogging station, the experts fulfilled the request for cleaning without the need for a reliance on personnel protective equipment. Philipp Hoffmann explains what makes this station special: "With fogging,

"After development of the station was completed, we first tested it with whole egg powder. This showed that our in-house development can keep up with external dedusters."

Philipp Hoffmann, Mechanical Design Engineer at Harro Höfliger

Deduster station

The dedusting process takes place inside the Modu-C machine. In the deduster station, each filled capsule passes several ring brushes which remove even the smallest amounts of powder mechanically.



Janine Kyofsky, Helmar Lünig

For Merck, Harro Höfliger equips the Modu-C LS Containment capsule filling machine with two special functions for cleaning and capsule dedusting.

operators do not initially have to open the machine door. Instead, they wet the production area via glove ports with purified water, using a manual hand spray gun. Alternatively, the spray mist can also be generated automatically by nozzles inside the machine. Product dust is bound in the process. The containment can then be opened for the actual cleaning, without blowing up dust."

Factory Acceptance Test from a distance

When the machine, which was designed according to the UL safety standards applicable in the US, was ready for shipment, an acceptance test of a special kind was scheduled. Jeffrey Campbell: "Due to the COVID-19 travel restrictions, there was no way we could be present at the Factory Acceptance Test. Harro Höfliger therefore positioned two cameras on site: One provided the overall view of the machine, the other the view into the interior. Via livestream, we were able to attend the test comfortably from New Jersey – and convince ourselves across the Atlantic of the impeccable operation of our new system."

About Merck

Merck, a leading science and technology company, operates in the fields of healthcare, life science and performance materials. Around 58,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live: From developing precise genome-editing technologies to discovering unique ways to treat diseases, all the way to providing applications for smart devices – Merck is everywhere. In 2020, Merck generated a turnover of 17.5 billion euros in 66 countries.

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Harro Höfliger