

HEARRO

The Customer Magazine
by Harro Höfliger

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Nature meets high-tech

The intelligent aerosol inhaler
by Syqe Medical administers medical
cannabis in exact doses



Another milestone

Neopac presented the first labeled Fleximed® Easymix Tube to the trade professionals at the Interpack 2017 **Page 22**

Colorful, strong, tricky

Pre-dosed portion packs made of water-soluble film for washing machines or dishwashers are the trend. **Page 20**



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4 “We quench our customers’ thirst for innovation”

A glimpse behind the scenes of Harro Höfliger Packaging Systems in Mumbai, India.

6 Just a blink of the eye

Rommelag CMO is a specialist for the aseptic filling of eye drops.

9 It’s the dose that counts

Cannabis has been vindicated as a medicinal plant. The key is the precise release of the active substance.



12 Filling capsules globally

With the Modu-C, Harro Höfliger offers customized solutions worldwide.

14 Definitely a perfect team

Customer Service and Production work hand in hand when customers are in need of qualified support.

18 That goes under your skin

Orfeo Niedermann, Ypsomed AG, on trends in the development of innovative auto-injection systems.

20 Colorful, strong, tricky

Pre-dosed portion packs made of water-soluble film for washing machines or dishwashers are the trend.

22 Potent mixture

Neopac is developing a glass-free primary packaging for parenterally used drugs.

24 Round affair

The Excellence United partners Glatt and Harro Höfliger pool their expertise.

5 News from Harro Höfliger

25 Trade show calendar



Dear Readers,
dear Business Associates,
for decades Production and Service at Harro Höfliger were in the hands of one department: Employees who built a machine and handled the installation at the customer’s location subsequently were also responsible for the service. With the complexity and uniqueness of our specialty machines, this was a very good solution and at the same time a sign of our stability. To this day, our customers appreciate the fact that a familiar technician always shows up for the maintenance of their machine.

However, constant changes require new concepts and a modern approach: For many years we have been expanding our service offer – a task that requires highly qualified employees. At the same time the number of machines installed worldwide is steadily growing, which means that maintenance efforts are increasing overall. We reacted to these new challenges and eight years ago, established the Customer Service division, another strong team for our customers.

Our motto also applies to service: ALL YOU NEED. We invest a great deal of time, money and expertise in order to optimally prepare our employees for every service call. The direct communication between the Production and Customer Service Departments continues, of course. This is the only way we can meet our customers’ high expectations for qualified service.

Over the next few years, we will strengthen our Customer Service both nationally and internationally, and continue to enhance it in terms of quality and efficiency. Together with our business partners we will continue this direction with conviction.

Your

Heinrich Havenstein
Managing Director Production at Harro Höfliger

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“We quench our customers’ thirst for innovation”

Since 2011, Mumbai has been the headquarters of Harro Hoefliger Packaging Systems Pvt. Ltd. Managing Director Sandeep Dharangaonkar tells the success story.

Mr. Dharangaonkar, how did you come to Harro Höfliger?

Before starting with Harro Höfliger, I worked at Indian branch offices of various Swabian machine manufacturers. In the late 2000s, Harro Höfliger was looking for someone to develop business in India, and a part of the job offer was to complete several months of machine training at the headquarters in Allmersbach im Tal. A great opportunity that I took advantage of.

How were the early days of Harro Höfliger in India?

In 2010, before the branch office was

officially established, I moved into an office at the Indian-German Chamber of Commerce in Mumbai. One year later, we opened the branch office under the name of Harro Hoefliger Packaging Systems Pvt. Ltd. and soon after, in 2012, we were able to acquire the first two projects, one inhalation project and one in the field of transdermal administration forms.

Then, after sales service became a topic too?

Yes, when selling the first machine, we were looking for someone to take responsibility for the onsite service. With Rohith Mohanakumar, we gained a real

expert in the field. At present, we have our own team of four service employees. If necessary, they can quickly be onsite at the customer’s location. Service as we define it, however, must not be reduced to corrective maintenance and the delivery of spare parts. We also offer user and machine operator training. Our machines are not ready-made, but are precisely customized to the respective product requirements. Our customers therefore want targeted support that we are happy to provide.

Four employees in the Service Department – this sounds like a lack of space at the Chamber of Commerce.

(Dharangaonkar laughs) There space quickly became too tight. Fortunately, we were able to move into a joint office in 2013 with our Excellence United partner Fette Compacting, who already had a strong presence on the Indian market. Due to our joint trade-show appearances, Excellence United is now also well-known in India.

The branch office grew quickly. What was the key to this success?

I think there are many factors. The most important thing is the ability to quench the customers’ thirst for innovation.

When a customer wants to launch a new product, we can provide early stage support during technology development. Innovative strength under the “German Engineering” label is in great demand and highly valued. Naturally, being able to offer the right product range for our customers’ specific demands is indispensable, and the relationship with the customer also plays a role. Our commitment and our strength, however, is to help the customer with the development of the appropriate process for their product.

What does the future hold for the branch office in India?

We want to gradually expand our customer network. The Indian economy has been growing steadily for years and the strength of the Indian pharmaceutical and medical sector is commonly known. Of course we want to grow too. We are therefore planning to expand our team in the service as well as in the sales area within the next three years. We supply well-known customers in India and also have orders and projects in Bangladesh. Demand in our core niches inhalation and transdermal administration forms is on the rise. But there is also a growing demand for standardized machine concepts such as capsule filling systems. We need to build on that. ■



Expansion of sales network

In May 2017, Harro Höfliger expanded its worldwide sales network with a presence in Singapore, thereby gaining an additional location in the important Asian region. Harro Höfliger supports large parts of Southeast Asia from this centrally located country and, to start their business activities, moved into a branch office of the Excellence United partner Uhlmann. The office, which started with Simone Stoiber as first employee more than half a year ago, quickly gained momentum: Since August Zein Albahar as second colleague is on board.



New cleanrooms are being built

Customers from the pharmaceutical industry attach increasing importance to tests with an optimum of practical relevance and machine acceptance tests (FATs) with the original product. In order to be able to address such individual requirements more effectively in the future, Harro Höfliger is going to invest in its cleanrooms. “With an expansion from four to ten cleanrooms, we are offering our customers additional capacity. State-of-the-art air-conditioning technology guarantees individual control of each room. This is the only way to comply with the specified conditional requirements for the processing of highly sensitive products,” says Stefan Mayer, Manager Process Services Division at Harro Höfliger. Since the reconstruction will be carried out in several stages, some cleanrooms will always be available during the modernization. The first new rooms will be ready for use in December 2017. The completion of the building project is planned for the fall of 2018.

The Harro Hoefliger Packaging Systems Pvt. Ltd. team



India

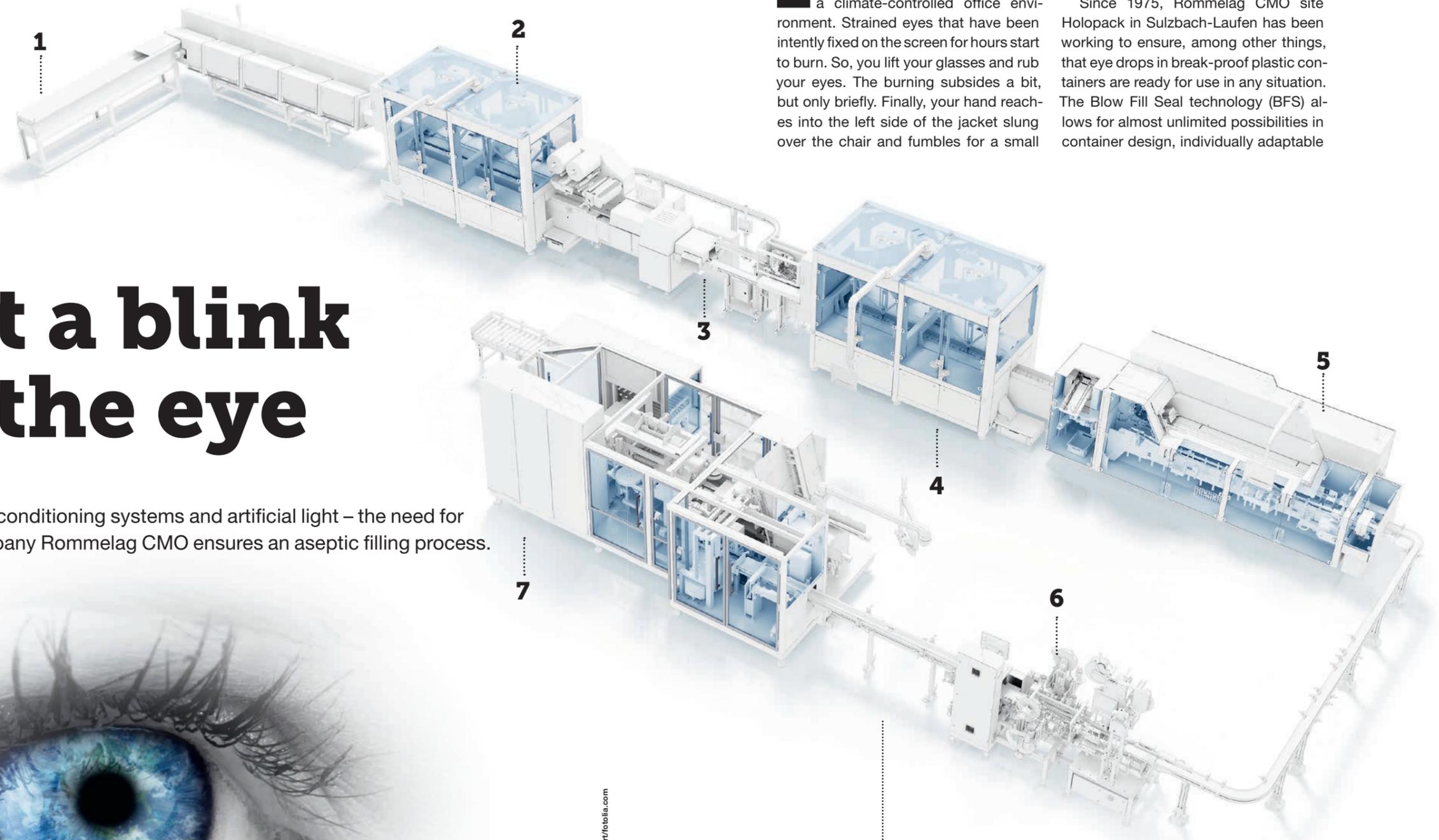
is the largest democracy in the world and is considered the economic superpower of the 21st century. The gross domestic product grows between six and seven percent per year and along with it the strong pharmaceutical and medical industry.

Pictures: Andreas Dallferth, Greens87/Stockphoto.com, Benguhar/Stockphoto.com



Just a blink of the eye

Work at computer screens, air conditioning systems and artificial light – the need for eye drops is on the rise. The company Rommelag CMO ensures an aseptic filling process.



It is a sunny summer day, and the past weeks have not brought much rain – the air is even drier in a climate-controlled office environment. Strained eyes that have been intently fixed on the screen for hours start to burn. So, you lift your glasses and rub your eyes. The burning subsides a bit, but only briefly. Finally, your hand reaches into the left side of the jacket slung over the chair and fumbles for a small

plastic container. You twist off the cap, bend your head back slightly and put one drop into each eye – finally, there is relief!

Since 1975, Rommelag CMO site Holopack in Sulzbach-Laufen has been working to ensure, among other things, that eye drops in break-proof plastic containers are ready for use in any situation. The Blow Fill Seal technology (BFS) allows for almost unlimited possibilities in container design, individually adaptable

- 1 Bulk feeding and separation of BFS strips.
- 2 Insertion of BFS strips into the transport chain via picker cells. A camera system verifies the correct position and completeness.
- 3 Flowpacking of BFS. Products without flowpack enter a bypass and are redirected to the infeed station (4) of the cartoning machine.
- 4 BFS feed into product transport of cartoning machine via robot. A camera verifies the position of the products.
- 5 Continuous insertion of products and leaflet into carton.
- 6 Weighing, marking and serializing of cartons via track and trace system. Application of a tamper evident and vignette label.
- 7 Loading of shipper cases. A camera system verifies the serialization code of the respective layer prior to closing the shipper cases. These are automatically aggregated.

Pictures: 123dartist/Stockphoto.com, Stoll von Gáti, vectorfusionart/fotolia.com



to almost any form of usage and administration. The fully automatic manufacture, filling and closing of the units is performed in one operational process. The BFS technology offers the highest level of process and product reliability during aseptic filling.

A tight schedule

Due to rising demand, the partially automated packaging machine facility has reached its capacity limits. For their expansion project around the new Pharma 2020 building in Sulzbach-Laufen, Rommelag CMO partnered with Harro Höfliger, a supplier that offers turn-key lines from product infeed to ready-to-ship carton packaging from a single source. The packaging line was designed to fully meet Rommelag's product requirements.

When selecting a potential partner, excellent references in the GMP environment along with the highest possible machine flexibility was a part of the criteria set forth by Marc Hofmann, Production Manager at Holopack. "With this machine, we want to produce both existing formats and products for new customers at the same time," he explains. Fast project implementation was also one of the crucial criteria.

"A special challenge was to coordinate and meet the tight schedule, since there were only ten months between placing the order with Harro Höfliger and putting the machine into operation," explains Marc Hofmann. It felt just like a blink of the eye. "We were all the while focusing on interdivisional teamwork

and continuous communication and information exchange. The high expertise of our contact persons and the very dedicated project management team guaranteed the success of our project."

One of the highlights for Marc Hofmann was the new approach in machine qualification. The qualification process took place at the Harro Höfliger site and considerably shortened the assembly and start-up period at Rommelag CMO. Upon completion of the project, the individuals responsible at Holopack are extremely satisfied. "The support provided by the Customer Service team is perfect. If a spare part is missing, or if a technician is needed, help is usually onsite in about one hour, and production can be resumed as quickly as possible." Another joint project is currently underway. ■

About Rommelag CMO

Rommelag CMO, Holopack site with headquarters in Sulzbach-Laufen (Baden-Württemberg) was founded in 1976 and is part of the Rommelag enterprise group, the inventor of the BFS technology. Holopack is a specialist in the aseptic filling of liquids and semi-solid substances on their bottlepack machines. Their machines are mainly used in the pharmaceutical, chemical and foodstuff industries.



"After completion of the project we are very satisfied. The support provided by the Customer Service team is perfect."

Marc Hofmann,
Production Manager at Rommelag CMO



Pictures: 123dartist/Stockphoto.com, Helmar Lünig, Rommelag CMO

It's the dose that counts

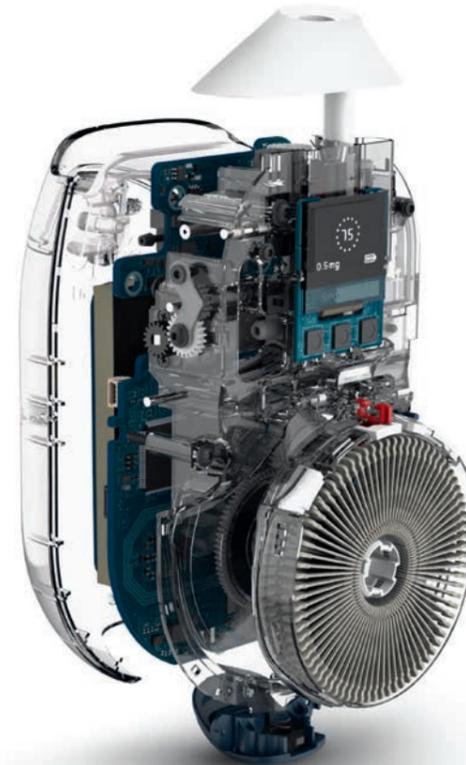
An ancient medicinal plant is making a comeback. Although its recreational use is controversial, the medical use of cannabis can help many severely ill patients. The key to symptom alleviation without serious side effects is precise dosage.



Cannabis sativa. Hemp.



The pocket-sized inhaler is childproof and easy to use. The circularly arranged chips in the pre-loaded exchangeable cartridge contain a precisely measured quantity of pharmaceutical grade cannabis flowers.



High-tech for patients: The release of active substances can be controlled up to a precision of 100 micrograms.

The metal mesh of the "Vapor Chips" enables quick heating of the passing air flow and thus gentle vaporization of the active ingredients.



The founder of Syqe, Perry Davidson, banks on the administration of cannabis in a medically controllable dosage. The first inhaler series and its version for hospital use are from the 3D printer.

The evidence for the therapeutic benefits of cannabis is astonishing. Its active substances, particularly the cannabinoids THC and CBD, ease chronic pain and side effects of chemotherapy, and reduce spasticity and inflammation. Despite this, for decades the plant was never used as medication or only when all other drugs had failed, as it was classified in most countries around the globe as a narcotic drug and was illegal.

Eventually the thinking began to change. Increasing numbers of physicians value the therapeutic potential of the flowers of the plant, the leaves of which resemble a hand with the fingers outstretched. As of spring 2017, cannabis can be prescribed by physicians in Germany and obtained from pharmacies in dried form or as a ready-to-use preparation. A separate authority within the German Federal Institute for Drugs and Medical Devices (BfArM), the Cannabis Agency, monitors the import, quality, dispensation, and in the future the cultivation of cannabis as well. Other countries, such as Canada and 28 states in the United States of America, approved cannabis for medical use and in some cases even for recreational use much earlier.

Among the pioneers is Israel, where Professor Raphael Mechoulam and the scientists working with him were the first to identify the most important substances in cannabis and also discovered the human system of cannabinoid receptors. Today, well over 25,000 Israelis legally receive medical cannabis, and the research is supported by the health ministry. This is manifested in the commitment of Perry Davidson, founder and CEO of the start-up Syqe Medical from Tel Aviv, who is dedicated to increasing acceptance of cannabis as a medical treatment both in the general public and among patients. He aimed at delivering to patients the lowest possible, reproducibly precise and medically controllable dosage, without adverse psychoactive effects wherever possible.

Smart metered-dose inhaler

Syqe Medical therefore developed an intelligent aerosol inhaler that is capable of electronically controlling the dispensation of the active substance in 100-microgram increments and immediately transmitting all relevant data to the attending physician via a smartphone app. First series of the devices are manufactured at Syqe using a 3D printer. They contain a replaceable magazine with 75 single doses, each with 10 to 15 milligrams of cannabis in rigorously controlled quality. During the inhalation procedure, the dried herb is heated, but does not burn; the volatile substances evaporate. In contrast to when it is taken orally, the pain-relieving, relaxing effect sets in just a few minutes after inhalation.

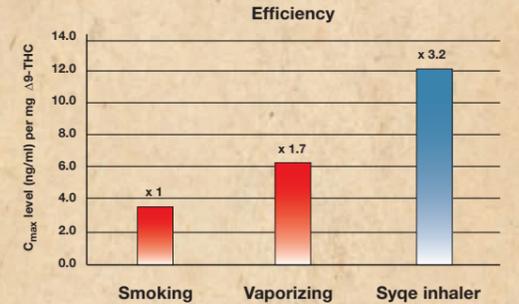
For the microdosing of cannabis in the cartridges for the inhaler, Perry Davidson decided that the technology from Harro Höfliger was the best option. "The administration of untreated plant material via a metered-dose inhaler is a very special challenge, and there is very little empirical evidence to work with," he says. "During our research we quickly discovered Harro Höfliger. Their diverse range of dosing systems and relevant experience with unusual inhalation projects convinced us that they were the right choice. We've been collaborating successfully since early 2016."

Davidson was also impressed by the imaginative ideas incorporated in the initial series of dosing tests by the specialists at Harro Höfliger. Because the test cannabis was still on its way from the supplier, they simply used powdered industrial hemp, which is easily and legally available. ■

About Syqe

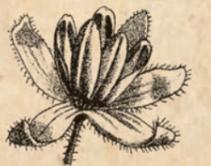
Syqe Medical in Tel Aviv is developing medical administration forms for cannabis and other botanicals and employs a multi-disciplinary team of electronic and mechanical engineers, industrial designers, chemists, biologists, physicians and pharmacologists. The enterprise was founded by Perry Davidson in 2011.

Pictures: Eyal Izhar, Syqe Medical



Effective inhalation

The most efficient administration route for medicinal cannabis is inhalation. Studies have shown that the quantity of THC released with the Syqe inhaler is three times higher than during smoking.



Cannabis and its effects

The cannabis plant (*Cannabis indica* or *sativa*), a form of hemp, is rich in ingredients, including more than 100 cannabinoids. The most important of these are delta-9-tetrahydrocannabinol (THC, dronabinol) and cannabidiol (CBD), the content of which may be as high as 20 percent, depending on the variety. Hemp grown for fiber and commercial uses have only traces of these substances. THC acts on the nervous system via the body's own receptors, changing the perception and sensitivity to pain. The non-psychoactive CBD can, among other things, stimulate appetite and inhibit tumor growth.

Only the female plants supply the raw material for the drug known as cannabis. Dried flowers are also known as marijuana, while the oily resin is also called hashish, or hash. In the plant, the cannabinoids THC and CBD are present as acids, which are converted into the pharmacologically active forms only when heated. Cannabis extracts as well as synthetically produced THC and CBD are also available as ready-to-use pharmaceutical preparations (drops, oral spray, capsules).

Filling capsules globally

From trials to the production of small series and test samples up to high-speed production of 200,000 capsules per hour – with the Modu-C, Harro Höfliger offers customized solutions for every phase of the product. Individually developed functions are not uncommon. We asked Modu-C users on different continents how they utilize their Modu-C.

"As a leading CDMO of inhalation powders, we purchased the Modu-C LS in 2010 to increase our capsule filling capabilities. Having the machine onsite has definitely contributed to us winning additional business in this area. The Modu-C LS has enabled us to fill low fill weight capsules containing difficult to handle powders with very good filling RSDs."

Martin Wing-King, Director of Business Development and Project Management, Pharmaterials, United Kingdom



"For many years, Boehringer Ingelheim has been relying on the technology of Harro Höfliger. Our four Modu-C HS for the dosing of pellets into capsules fulfill our high demands for reliability and output."

Recep Ercanoglu, Technology Coach Encapsulation, Boehringer Ingelheim, Germany



"Operator safety in production is a high priority at Novartis. The Modu-C LS Containment combines safe handling of active ingredient containing powder with excellent ergonomic design."

Hans-Peter Mennet, Head Internal Supply, PHAD Orals, Novartis Technical R&D, Switzerland



"The Modu-C LS scores points with its extraordinary flexibility – to us it is the first choice as a flexible capsule filling machine during technical development."

Dr. Norbert Rasenack, Head Process-Development & Equipment Engineering, Novel Oral Products, Novartis Technical R&D, Switzerland



"We greatly appreciate the excellent partnership with Harro Höfliger and the highly sophisticated machine technology. Initially we started production with a Modu-C LS. Now we could easily transfer the processes to three faster Modu-C MS machines. Excellent upscaling!"

Dr. Aleksandr Malin, CEO, Nativa, Russia



"I would like to thank everyone for all their hard work and dedication, not only for the previous months but especially for the two weeks that I have been onsite at Harro Höfliger. The commitment and dedication you have shown to this project is remarkable. Not only have we assembled a team to solve issues and make progress, we had fun doing it."

Salvatore Scimemi, Process Technologist, Acorda Therapeutics, USA



"Since May 2014 we have been working with a Modu-C MS with drum dosing and integrated AMV sensor. Throughout the entire project we worked very closely with the experts from Harro Höfliger, and we are very satisfied with the machine."

Pastor Barrios, Chief of Electrical Engineering, Scavone Group, Etics, Paraguay



"Since we installed the Modu-C MS we managed to fill our Food Supplements Products successfully with RSD less than 0.9% despite a fill weight up to 1,100 mg. Thanks to the Trolley concept, we decided to offer other customers our experience and services to fill tricky products in capsules and to develop CMO business."

Dr. Mohamed Shalaby, CEO, Nerhadou, Egypt



"The Modu-C MS doses the inhalation powder very precisely and efficiently. By means of the AMV system, the mass is determined and the quality of our products ensured."

Tiejun Li, President, GM Shadong Jewim, China



Definitely a perfect team

The development of a technically qualified Customer Service program is particularly challenging in the specialty and customized equipment industry. Harro Höfliger takes on the task and leaves nothing to chance.

Heinrich Havenstein and Jackson Heslop have a very dynamic working relationship. They are respectively responsible for the Production and Customer Service divisions at Harro Höfliger and have the challenge of coordinating an extensive variety of customer requests. Any conflicts, however, are quickly resolved because they both focus on the same question: How can we quickly and efficiently help our customer? “When service support is needed, then we work professionally to find the correct solution – and we always find one,” explains Heinrich Havenstein, Managing Director Production at Harro Höfliger.

For the last several decades, the production team was responsible for the installation, start up, and service of the equipment worldwide. “Our customers appreciate that even years later, the same technician who built the machine was always the one who came to service the machine. For them, this was a constant in the agile pharmaceutical world,” says Havenstein. But with an increase in company size, this model reached its limits. Since 2009, the company has continuously expanded the Customer Service area. Today Harro Höfliger employs specially trained service engineers, who are an integral part of the machine projects at an early stage.

As part of the 2020 company strategy, it has now been established as an independent division, which is growing continuously. “Independent, but not separate,” emphasizes Jackson Heslop, Director Customer Service. “Our goal is to expand the needed resources and develop the level of expertise necessary to be able to self-sufficiently fulfill more and more of the Customer Service projects. At the same time we can always count on the knowledge and support from our colleagues in Production, since they have often been working on the machine project for over a year.”

Jackson Heslop and Heinrich Havenstein rely on a close cooperation and a lively exchange of information and ideas while managing these projects. “Even if we are formally organized into two divisions, we work closely together and are

Illustration: Bernd Schifferdecker

always moving in the same direction,” points out Havenstein.

Quality has to be right

The company invests a lot of time and money in the development of the necessary resources. Our representative will always make sure that every question will be answered,” explains Heslop. Extensive training measures also provide the service team with optimum technical knowledge to be able to communicate and respond quickly.

“Internationally, we need personnel close to our customers’ location. This requires that we first bring their knowledge up to par with the high quality level of Harro Höfliger,” emphasizes Havenstein. Therefore, applicants receive training in the Production area in Allmersbach, while taking seminars offered by the Chamber of Industry and Commerce (IHK). The technicians work in the assembly area for at least six months before starting their work abroad.

“Our worldwide customers need a dedicated contact person who cares about and responds to their concerns.”



Jackson Heslop,
Director Customer Service

This practical training program on the Harro Höfliger equipment is mandatory for all applicants. “Even experienced service technicians receive this in-depth training on our machines and get to know our corporate culture,” Jackson Heslop explains this thoroughness.

A look to the future

With additional team members, Heslop would like to continue to achieve more flexibility in the day-to-day business, but also offer new services. “We would like to play an even more active role in supporting our customers.” During regular service visits, the Customer Service team should not only conduct maintenance and repair work, but also act in an advisory capacity upon request – for example, in the management of a consignment inventory or in the streamlining of processes. This is in line with the vision that Thomas Weller, CEO at Harro Höfliger, has for the Customer Service division: “Instead of just supplying

“Understanding our customers’ needs is important to us and – as has always been our philosophy – the personal contact.”



Heinrich Havenstein,
Managing Director Production

machines, we would like to become a solution provider. This includes taking an all-encompassing look at our customers’ production and presenting them with suitable solutions at an early stage.”

Customer satisfaction as a benchmark

At Harro Höfliger, the portion of turnover generated by services increases every year in relation to total turnover. But that is not the focus for Weller, Havenstein and Heslop. “We want to support our customers and ensure that their systems run reliably. For us customer satisfaction is the most important factor,” says Weller. And in order to ensure customer satisfaction, Jackson Heslop has a strategy roadmap which is currently being implemented. One of the focus areas is providing prompt assistance, which starts with order processing: “Every minute counts when ordering spare parts. This is one area where we are implementing solutions to make our processes even faster and more streamlined.”

If a service support is required, the experts at Harro Höfliger have already taken precautionary measures and launched the Service Portal together with the partner companies of Excellence United. This service can be used to remotely diagnose and correct many errors and to carry out maintenance work without the need for a technician on site.

It is however better, according to Jackson Heslop, to not let it come to failures: “Many customer service challenges are predictable. We want to continually look into the future in order to be prepared for the moment.” Customers already have access to a 3D spare parts catalog via the Service Portal. Each part is listed in a spare parts list, which is created individually for each machine. The list rates the expected wear, the probability of unexpected failure, and the resulting effects. “This is how we can clearly advise our customers which parts to stock for tactical reasons so that they can be replaced quickly. This also

“Instead of just supplying machines, we would like to become a solution provider. This includes taking an all-encompassing look at our customers’ production.”



Thomas Weller,
CEO

assists in planning our service team to be available to support with preventive maintenance activities,” says Heslop.

Listening instead of analyzing

Mundane customer satisfaction surveys do not come into question for Heinrich Havenstein or for Jackson Heslop. “We are always looking for a personal discussion. Checklists and questionnaires are not at all our thing. Understanding our customers’ needs is important to us and – as has always been our philosophy – the personal contact,” explains Havenstein. Thomas Weller agrees: „We are solid partners for our customers throughout the entire lifecycle of a machine. We listen to them and take them seriously. This is how we not only manage to remain market leaders, but also remain personable. This is important to us.” ■

Illustration: Bernd Schiffendecker, Pictures: Andreas Dalferth, Janine Kyofsky, Tom Philipp



With the 3D spare parts catalog on the Excellence United Service Portal, searching for replacement parts for highly complex machines is quite simple.

The Service Portal offers additional service functions, which Jackson Heslop (left) explains on a tablet.

That goes under your skin

Auto-injectors are a simple and safe way of self-medication, and have long since surpassed the classic syringe.

Since 2005, Orfeo Niedermann, Business Development Director at Ypsomed AG, has been working with partners from the pharmaceutical and biotechnology industry on the development of innovative injection systems for self-medication. In an interview with HARRO, he talks about the trends in this field.

Mr. Niedermann, could you please describe the usage and operation of an auto-injector?

Auto-injectors are injection devices with a built-in inner syringe. By triggering a pre-loaded spring, the contents of the syringe are administered within a few seconds. Our YpsoMate® auto-injector can be operated in two simple steps. The patient removes the protective cap and presses the injector onto the skin. A click signals the beginning of the almost painless injection process via a short, thin needle into the subcutaneous fat layer. The second click indicates the end of the injection. Before, during and after

medicating, the auto-injector's needle is shielded in order to protect the user and third parties from unintentional injuries.

Which medication can be administered?

Typically, auto-injectors are used to administer modern, biotechnologically produced drugs – for example against in-

flammatory diseases such as rheumatoid arthritis, multiple sclerosis or asthma. The most common self-injecting drug is insulin for diabetes. Here, mostly pen injectors with an adjustable dose are used. The active ingredient is stored in a cartridge instead of a syringe, and can be used several times until the cartridge is emptied completely.

“To equate needle-free with pain-free is a fallacy.”

Orfeo Niedermann,
Business Development Director,
Ypsomed AG



Pictures: Ypsomed AG, Helmar Lünig



This is how the YpsoMate® is made

The twelve individual parts of the YpsoMate® are pre-assembled into two components at Ypsomed in Switzerland. During final assembly, the front and rear injector units are connected with the syringe, which contains the active ingredient. This step normally takes place at the customer's location. Beginning this year, Ypsomed offers a final assembly service in Burgdorf. Harro Höfliger offers suitable machine solutions for both assembly stages.

Could the needle be replaced sooner or later?

Needle-free application systems were already developed 20 years ago. When patients are asked if they prefer drug administration with or without a needle, they will decide against the needle. At least until they have tried the needleless injection for the first time. “Needle-free” means that the liquid jet of the drug, that is administered with high-pressure, penetrates the skin and hits more nerve endings than a thin sharp needle. To equate needle-free with pain-free is therefore a fallacy. For this reason, I do not see needle-based injection systems in jeopardy – on the contrary, the demand is growing steadily. Further development trends appear to be directed towards smart injection devices.

What does smart injection device mean in concrete terms?

Smart injectors are digitally networked. For example, they are capable of detecting whether they are correctly used by

the patient. They can record treatment-relevant data, such as administered dose and injection time, and make the information accessible to a physician through a connected smartphone. The Ypsomed SmartPilot is an example of a smart injection device. This reusable add-on for the YpsoMate® transforms the autoinjector into a device connected to the Internet, which offers numerous possibilities for further optimization of the therapy. ■

Detailed interview



A detailed interview with four additional questions about production and market situation can be found online at:

www.harro-magazine.com

About Ypsomed

Ypsomed AG with headquarters in Burgdorf (Switzerland) is the leading, independent developer and manufacturer of user-friendly injection systems for self-medication. With innovative Swiss-made products such as pens, auto-injectors and large-volume patch injectors, Ypsomed meets all the demands that pharmaceutical enterprises make for self-injection.

Colorful, strong, tricky

The market share of water-soluble portion packs in bright colors for washing machines and dishwashers is rising continuously. On the road to production readiness, manufacturers must consider quite a few details.

At Harro Höfliger, production processes are first tested on small-scale laboratory machines in order to insure they work smoothly on a large scale.



Pre-dosed packs (pouches) made of water-soluble film, advertised as tabs, caps or pods, are the trend. Without unpacking, consumers can put them in the dishwasher or washing machine, where the polyvinyl alcohol film (PVOH) dissolves and releases the powder, gel or liquids. That way, consumers always use the exact quantity and mixture of detergents intended by the manufacturer, thus avoiding frequent overdosing. That is not only good for the laundry, but also protects the environment.

On the way to a detergent or dishwasher product, Harro Höfliger provides customer support from the laboratory stage to high-speed production. “The companies approach us with a design where shape, number of chambers and fill media have already been determined,” explains Jürgen Luka, Engineering & Innovation Services (EIS) Department. “For example, they want a pouch with three chambers containing 15 grams of powder, five grams of gel and five grams of liquid. Our task is to develop a machine process that is capable of bringing the film into the right shape, to precisely dose the desired fill media, seal it tight and subsequently punch it out.”

The road to the sample product

The development of the process starts with the theoretical creation of the design. To that end, Harro Höfliger calculates the required volumes, computes the machine dimensions and edits the customer’s design. Then our employees create the format parts, in most cases first with a 3D print, subsequently as a casting mold made from milled aluminum. This is followed by an analysis of the dosing processes and the product optimization. “Bulk density, flow rate and flowability are crucial for the fill media,” explains Luka. “If the powder causes too much

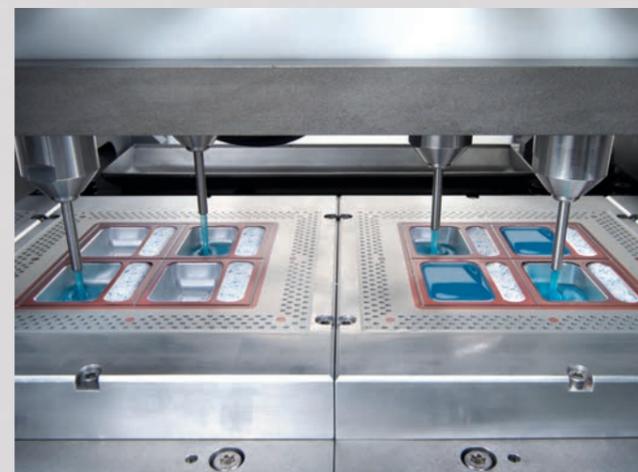
dust and the gel flows too slowly or stops, we will search for a solution together with the customer.”

Initial sample products for the customer are manufactured on Harro Höfliger’s laboratory machine. For this purpose, the engineering team first selects the appropriate PVOH-film which is thermoformed to shape and filled with the respective media. After that the filled chambers are covered with a lid film and are heat sealed. Depending on the shape, the pouch is then punched out (special formats or round format) or cut out (square shape).

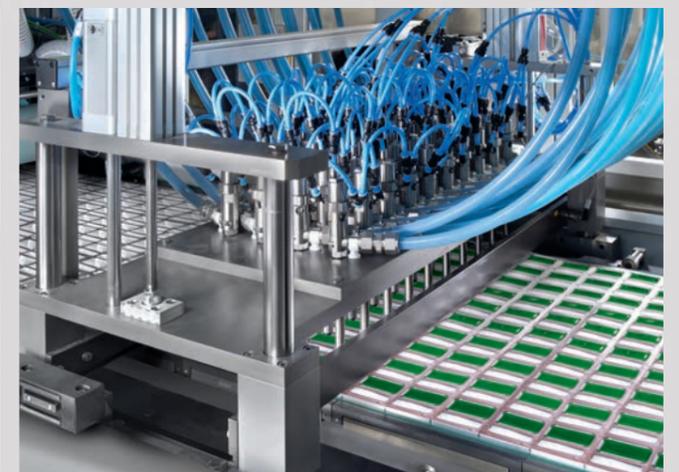
Rigorous testing

Harro Höfliger tests whether the pouches comply with the relevant regulations, and documents everything for the customer. “According to EU regulations, a detergent pouch, filled with gel or liquid, must remain tight for at least 30 seconds before dissolving,” says Jürgen Luka. “This is tested in a container with water.” The long dissolution period serves to protect children should they put a pouch in their mouth. In addition, a bitter-tasting compound is added to the film that triggers a disgust reflex in humans and results in spitting out the pouch. A load test makes sure that the pouches can withstand a weight of at least 100 kg, as mandated. These requirements are taken into consideration during the process development. If necessary, the products are optimized accordingly.

The process which is developed on Harro Höfliger’s laboratory machines can be scaled up in identical quality to the company’s large production lines. On the high-speed machines of Harro Höfliger, up to 1,800 multiple chamber pouches per hour can be produced. ■



High-performance filling with the PFMK.



Small-scale filling with the PFMT.

Pictures: Helmar Lünig, Professor25/Stockphoto.de

Potent mixture

The Swiss packaging specialist Neopac is developing a glass-free primary packaging concept for parenterally used drugs. Harro Höfliger has been providing assistance with the process development since the test phase.

The Fleximed® tube is a transparent, flexible medical tube made of synthetic laminate offering significant advantages in comparison to conventional small glass bottles or ampoules. In addition to break resistance, ease of use and safety are among the most important features.

With Easymix, a product from the Fleximed® product family, Neopac goes even one step further. This two-chamber tube enables simple and safe preparation of mixtures for injections or infusions. The two chambers are separated from one another by a flexible barrier: A seam opens under pressure to the rear chamber, which enables mixing. With this method, two liquids as well as one liquid and one powder component can be mixed. At present, Neopac is in various clinical trial phases with several potential customers.

For the aseptic filling and sealing of the tubes, Neopac relies on the know-how of Harro Höfliger. "In our search for a potential partner, we were looking for technology leaders in the industry," says Ralf Künzi. Since 2011, Harro Höfliger has been a partner in the process devel-



opment of the Fleximed® product family. In the early phase of the collaboration, the company supplied a semi-automatic laboratory machine, which can fill the tubes with liquids as well as powders and is equipped with an integrated sealing tool.

Clever labeling

Labeling the Easymix tube created an especially major challenge. Regarding the basic requirements for label solutions, Ralf Künzi says: "You have to fit a lot of information on the label, which is required for regulatory purposes. Furthermore, the information must be permanently attached to the tube." Simply adhering the label was not an option due to the complex tube geometry. Here, the label experts from Schreiner MediPharm came into play.

"Accordingly, we had to find a labeling solution which does not limit the functionality of the Easymix tube. It is also imperative that the user has an unobstructed view of the content," Maximilian Jaeger explains the criteria. "This is why we developed a new label with a front and back part that surrounds the

More stability

Liquid active ingredients which are used in the field of parenteral medicine often do not remain stable for long. This is why they are stored in powder form and mixed with a solvent prior to application. The tube's multi-layer structure offers the necessary high barrier protection against water vapor and oxygen. At this year's Interpack in Düsseldorf, the first labeled Fleximed® Easymix Tube was presented to the trade professionals – another milestone on the road to market launch.



"Harro Höfliger is the clear leader in specialty machine engineering for parenteral packaging."



Ralf Künzi, Business Development Manager Medical, Neopac

"We often seek new ways which break with established approaches."



Maximilian Jaeger, Product- and Process Manager, Schreiner MediPharm

tube like a bag. The experts from Harro Höfliger have also made it possible to apply this tube bag with a machine. As machine manufacturers, they have been able to add a different perspective with regard to processes," continues Jaeger. In general, Ralf Künzi sees great market potential for the Fleximed® tubes: "We are certain that in the next few years we can win several customer projects,

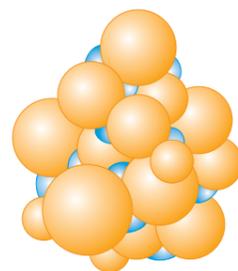
each of which will have different requirements that demand customized developments." For Künzi it is important that he can rely on the partners who have already been involved in the development of the product, "because we have gone through common learning processes and now have shared knowledge. Together with the two project partners, we have an extremely potent mix of innovative strength." ■

About Neopac and Schreiner MediPharm

Neopac with headquarters in Oberdiessbach (Switzerland) was founded in 1906 and has been producing synthetic tubes since 1954. Neopac is part of the Hoffmann Neopac AG, an independent family-owned enterprise based in Thun (Switzerland), specializing in the development and production of tubes for the safeguarding of healthcare products. The annual production output is more than 600 million tubes.

Schreiner MediPharm with headquarters in Oberschleißheim near Munich is a leading developer and manufacturer of innovative, multi-functional special labels and labeling solutions for the pharmaceutical industry and medical technology. Thanks to the enterprise's special know-how, Schreiner MediPharm has made a name for itself as a powerful development partner and reliable quality supplier for leading pharmaceutical companies.

Round affair



For the trend subject of active substance pellets, the Excellence United partners pool their expertise: Glatt offers a variety of technologies for their production, the dosing systems come from Harro Höfliger.

More and more frequently, pharmacists use pellet-based formulations instead of monolithic tablets or powder capsules. There are many good reasons for this solid oral administration form. Among others, this method is characterized by dust-free processing, stability, good dosing and mixing capability, excellent flow properties as well as the possibility to apply layers. Coating allows taste masking, the delayed and controlled release of active substances, or simply comfortable swallowing.

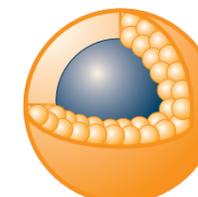
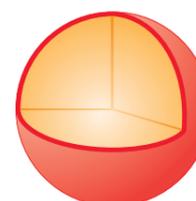
Filled into the XStraw® drinking straw, the drug globules are dispersed and transported when suction is applied while drinking – a method which is especially suited for children and the elderly. The practical single-dose packaging into sachets is also gain-

ing in importance. The four-side sealed pouch machine PPH by Harro Höfliger produces and fills the flat pouches with very small pellet quantities from 10 mg upwards. With the Modu-C series capsule filling machines, dosing of specific quantities of pellets into hard capsules – also in any combination with powder, tablets or micro-tablets – is accomplished using pellet stations on flexible and changeable trolleys.

Depending on the field of application and the requirements for pellet type and size, active substance loading and the quantities to be produced, different manufacturing processes are used for the multifaceted granules. For decades, Glatt has been the market leader in machine engineering for the refining and processing of solids in powder form for the pharmaceutical, fine chemical and food industries. For many years they have been dealing with multi-particulate



For active ingredients with a bitter or unpleasant taste, pellet coating provides taste-masking properties.



drugs such as granules and their specially shaped pellets and micro-pellets. As a pioneer in fluidized bed technology, the Excellence United partner offers machines for all common production processes, both in batch and in continuous operation.

The extrusion of moist powder mass is one of their traditional technologies. The pellets with an average size of 500 to 2,000 micrometers are then rounded in the subsequent spheronizing process. During layering, liquid or powder active substances are applied to the starter pellets in very even layers, usually followed by functional coating.

Direct pelleting from powdery active ingredients or auxiliary materials enables the production of very evenly shaped pellets. The MikroPx® technology, a continuous fluidized bed agglomeration process, produces highly dosed micro-pellets in a size of 100 to 400 micrometers



Precise dosing of pellets into the XStraw® with technology from Harro Höfliger.

with a narrow particle size distribution and active ingredient contents of up to 95 percent. They are particularly easy to swallow and ideally suited for an oral drug delivery device such as the XStraw® drinking straw – a successful example of the cooperation between the Excellence United partners. ■

One single system, four processing options: The GPCG 2 LabSystem offers drying, granulating, coating, and pelletizing.



About Glatt

For more than 60 years, the Glatt Group with headquarters in the town of Binzen has been specializing in the processing and refining of powdered solids for the pharmaceutical, food/feed and fine chemical industries. Their core technology is the fluidized bed process for granulation and drying, pelletizing and coating of solids. In addition to laboratory, pilot and production machines for batch operation or continuous processes, Glatt also offers product and process development, product handling and contract manufacturing.



Pictures: Glatt Group, Heimar Lüning

“The optimum interaction between product, device and machine expertise – that is what Excellence United’s customers benefit from.”



Philippe Tschopp,
Head of Business Development
Pharmaceutical Services,
Glatt

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Frankfurt, Germany
24.10. – 26.10.2017

PDA
Vienna, Austria
07.11. – 08.11.2017

China Pharm
Shanghai, China
07.11. – 10.11.2017

Compamed
Düsseldorf, Germany
13.11. – 16.11.2017

Pharmtech
Moscow, Russia
21.11. – 24.11.2017

P-Mec India
Mumbai, India
28.11. – 30.11.2017

DDL 28
Edinburgh, United Kingdom
06.12. – 08.12.2017

Arab Health
Dubai, UAE
29.01. – 01.02.2018

Pharmapack
Paris, France
07.02. – 08.02.2018

CPhI South East Asia
Jakarta, Indonesia
27.03. – 29.03.2018

Interphex
New York, USA
17.04. – 19.04.2018

RDD 2018
Tucson, USA
22.04. – 26.04.2018

Achema
Frankfurt, Germany
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