HARRO

The Customer Magazine by Harro Höfliger

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Longer where it matters most

EsoCap advances local therapy in the esophagus

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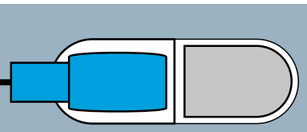

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White Rabbit Studios

EDITORIAL



Dear readers,
Dear business friends,

Some ideas spark excitement from the very beginning. Yet their true test comes afterward, because between a promising concept and a successful product lies a long series of development steps, critical decisions, and carefully managed transitions.

Together with our customers, we explore every day how innovative products can be translated into reliable manufacturing processes. In doing so, we navigate a wide range of requirements and constraints. Often, the challenge is to reconcile novel approaches with the demands of future commercial production.

Every project begins with a conversation. Developing the right solution requires a clear understanding of the challenges at hand and the goals our customers want to achieve. At the same time, scalability is part of the equation from the outset. Processes that prove their value in the laboratory or on a small scale must ultimately perform just as convincingly under industrial production conditions.

This edition of HARRO Magazine offers insights into the many facets of that journey. It highlights the diverse challenges our customers face and the highly individual solutions that emerge from them. Above all, it demonstrates the importance of close collaboration in turning promising ideas into practical, successful applications.

The following pages showcase some of the outcomes of these shared journeys. I hope you enjoy the insights and inspiration this issue has to offer.

Your



Thomas Weller
CEO at Harro Höfliger

EXPANDED EXECUTIVE STRUCTURE

Through two new appointments, Harro Höfliger is setting the course for the future and strengthening the strategic alignment of its technology and sales activities.

Timo Graf, who previously headed the Engineering and Technical Services division, assumed the role of Chief Technology Officer (CTO) on April 1, 2026. He succeeds Peter Claußnitzer, who played a key role in shaping Harro Höfliger's technological development for over 35 years and served as CTO from 2005 onwards. As part of the succession plan, Claußnitzer stepped back from operational responsibilities in mid-2026.

As CTO, Timo Graf is responsible for the company's technological direction with a focus on future-oriented machine concepts, as well as the consistent further development of existing technologies. This leadership transition combines continuity with new impetus for the future portfolio.

Also effective April 1, 2026, Marco Laackmann took on the newly created role of Chief Sales Officer (CSO), assuming overall responsibility for sales across the company. Previously, he led technology sales for the Pharmaceutical Technologies business unit and continues to oversee Pharma Services, which supports the process development of pharmaceutical products.

On July 1, 2026, both Timo Graf and Marco Laackmann were also appointed to the Management Board of Harro Höfliger. "We are continuously evolving our leadership structure," says Markus Höfliger, Chairman of the Supervisory Board of Harro Höfliger. "With the CSO role, we are strengthening the alignment of sales, markets, and customers across all market segments. At the same time, the transition in technology leadership ensures continuity in a business area that is central to process solutions and machine engineering."



New Managing Directors at Harro Höfliger: CTO Timo Graf (left) and CSO Marco Laackmann.

Process development at laboratory scale



With the Happy Cell Factory Lab (HCF Lab), Harro Höfliger has expanded its portfolio for cell and gene therapy manufacturing. The compact system supports automated process development at laboratory scale under production-relevant conditions. It allows targeted manual intervention during process development and is suitable for key process steps such as activation, transduction, and cell expansion. As an entry point to the scalable Happy Cell Factory platform, the HCF Lab lays the foundation for the later transition to automated clinical and commercial manufacturing processes. Developed in collaboration with the Fraunhofer Institute for Production Technology IPT, the HCF Lab is already being used by the Fraunhofer Institute for Cell Therapy and Immunology IZI as part of an ongoing project. Initial results give those involved confidence that the potential of the HCF Lab for laboratory-scale process development can be confirmed.

HARRO WORLDWIDE



Sasha Kang
General Manager
Harro Höfliger Korea

With a representative office in Seoul, Harro Höfliger is further expanding its sales activities in the Asian market and strengthening on-site customer support. Since the beginning of 2026, the office has been led by Sasha Kang, who brings extensive project experience, including work with Excellence United's partner companies. His strong network in the region facilitates direct communication with customers and partners.

Since July 1, 2026, Harro Höfliger has been present in the French market through the newly founded Harro Höfliger France SAS. The company, headquartered in Colmar, consolidates local sales and service activities, thereby strengthening its proximity to customers in France. Gilles Ganter, who previously served as Director of Sales France for Harro Höfliger, is in charge. The goal is to provide even more direct customer support in the future, respond more quickly to requests, and further expand on-site service offerings.



Gilles Ganter
Directeur Général
Harro Höfliger France SAS



Mario Mester
Managing Director
Harro Höfliger (Switzerland) AG

Leadership change at Harro Höfliger (Switzerland) AG: On October 1, 2026, Roberto Zürcher – who established Harro Höfliger's Swiss operations and shaped them for 21 years – handed over responsibility to Mario Mester. An experienced industry and market expert, Mario Mester now takes charge of the sales and service location in Reinach near Basel. The succession has been jointly prepared since January 2026 to ensure a smooth transition. Roberto Zürcher is retiring from his operational responsibilities and will continue to support the company as a member of the Board of Directors.

New management functions

Since October 1, 2026, Niranjan Mirje has served as both CEO and CSO of Harro India. In these roles, he is responsible for the continued development of the Bangalore site and acts as the primary point of contact for customers. Rohith Mohanakumar has been appointed COO and CTO, leading the Operations, Engineering, and Customer Service functions.

With its own production capabilities and machine solutions tailored to the needs of international growth markets, the site continues to strengthen its position as a key partner within Harro Höfliger's global network.



Niranjan Mirje
Managing Director CEO
Harro Hoefliger Packaging Systems Pvt Ltd.

Atelier Lünig

DELIVERING TREATMENT WHERE IT MATTERS MOST

By helping active ingredients stay where they are needed, EsoCap and Harro Höfliger are enabling new possibilities for the local treatment of esophageal diseases.

Measuring just around 25 centimeters in length, the esophagus is a particularly challenging site for local drug delivery. Any swallowed dosage form passes through within seconds on its way to the stomach. For diseases of the upper gastrointestinal tract, this presents a major hurdle: substances that pass through so quickly have little opportunity to exert a local therapeutic effect. As a result, effective treatment options remain limited for hundreds of millions of patients worldwide.

LOCAL THERAPY FINALLY BECOMES POSSIBLE

This is the challenge EsoCap, a Swiss biotech company based in Basel, set out to address. EsoCap has developed a novel drug delivery platform designed to keep medication precisely where it is needed. The active ingredient is incorporated into a thin polymer film that is rolled up inside a capsule. The capsule is taken using a specially designed drinking aid. During swallowing, the film unrolls through a slit in the capsule, adheres to the esophageal mucosa, and releases the active ingredient directly at the target site.

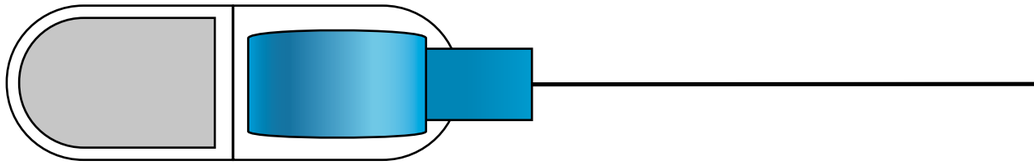
"A study conducted by the University of Greifswald in healthy volunteers demonstrated that the film remains attached to the esophageal mucosa for at least 15 minutes before gradually dissolving. This enables targeted local treatment instead of relying on systemic therapies or frequent dosing," says Dr. Peter Stangier, Director Strategic Planning at EsoCap. He summarizes the vision behind the technology clearly: "Our goal is to sustainably improve the lives of people with serious esophageal diseases through therapies that act directly at the site of disease."



"Harro Höfliger's technological expertise impressed us greatly."

Peter Stangier
Director Strategic Planning
EsoCap

KEY COMPONENTS AT A GLANCE



The placebo sinker acts as a weight element to facilitate swallowing

The thin rolled-up film contains the active ingredient

The retainer connects the drug-loaded film to the device

A HIGHLY ADVANCED SYSTEM

The effectiveness of the EsoCap principle has already been demonstrated in the Phase II clinical study ACESO for the treatment of eosinophilic esophagitis (EoE), a chronic inflammatory disease of the esophagus. According to Peter Stangier, the long-term goal is to incorporate a variety of therapeutic compounds into the film-based delivery system to treat various esophageal diseases.

While simple to use, the system relies on a carefully engineered combination of components. In addition to the drinking aid, capsule, drug-loaded film, and placebo "sinker" that serves as a weight element, a key component is the so-called retainer. This thin thread connects the film to the drinking aid, enabling the film to unroll through a slit in the capsule. After approximately 10 to 15 seconds, the retainer dissolves in the mouth.

For reliable drug delivery, the capsule requires an opening that allows the retainer to pass through without obstruction. At the same time, the retainer must be securely attached to the film. This is where Harro Höfliger's expertise in process and device engineering comes into play. For EsoCap, the company developed two manual work stations for laboratory activities and the production of clinical samples. One station creates the slit in the capsule, while the second welds the retainer to the drug-loaded film.

Creating the capsule opening requires precise positioning, consistent accuracy, and gentle handling. The capsule must not be damaged, and the opening must be located exactly where the retainer will later exit. For attaching the thread, Harro Höfliger uses ultrasonic welding. This process creates a reliable bond without requiring additional materials, a significant advantage in a sensitive pharmaceutical application.



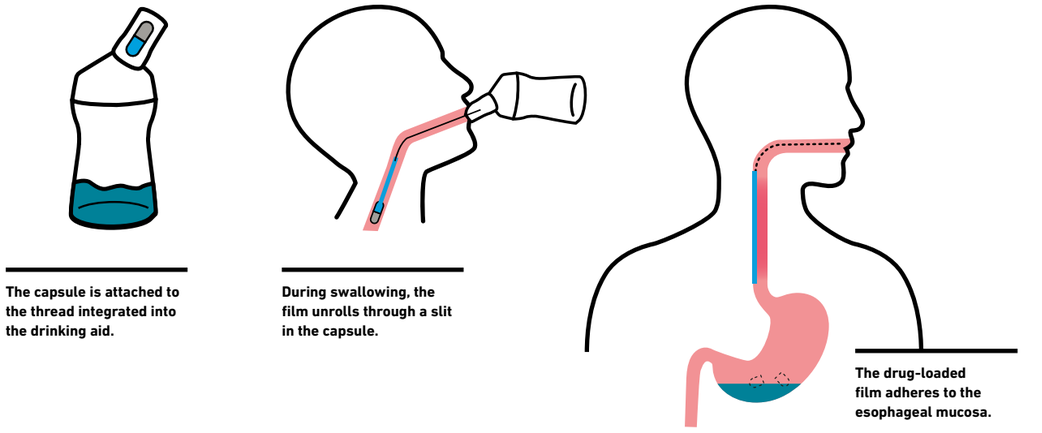
"We consider scalability from the very beginning."

Martin Lober
Teamleader Device Services
Harro Höfliger

FROM LAB DEVELOPMENT TO COMMERCIAL SCALE

The two stations were developed within Harro Höfliger's Device Services division. There, Martin Lober and his team work at the intersection of product concepts, device optimization, and future manufacturing processes. They advise customers throughout device development while also supporting the production of small-scale batches.

A SOPHISTICATED DRUG DELIVERY SYSTEM



The capsule is attached to the thread integrated into the drinking aid.

During swallowing, the film unrolls through a slit in the capsule.

The drug-loaded film adheres to the esophageal mucosa.



The connection thread, which rapidly dissolves when exposed to saliva, is cut to length and welded to the film.

Even at this stage, process scalability and future industrial production are considered from the outset. "Our goal is not simply to solve the task at hand. At Harro Höfliger, we always think several steps ahead," says Martin Lober. "Many customers approach us with an innovative concept or a device in the early stages of development. The challenge is understanding exactly what a product needs to perform reliably and how the process must be designed to support future automated manufacturing."

TEAMWORK WITH A SHARED VISION

"With a novel dosage form such as ours, every detail contributes to the performance of the overall system," says Stangier. "What impressed us most about Harro Höfliger was its technological expertise in translating our innovative EsoCap drug delivery technology into a precise, reliable, and scalable pharmaceutical product."

His observation highlights what makes collaborations like this successful: medical innovation requires a deep understanding of both product and process from the earliest stages of development. EsoCap has developed a way to keep active ingredients in the esophagus long enough to achieve a sustained local effect. Harro Höfliger helps ensure that the device's key functional elements perform reliably and as intended.

The result is a novel therapeutic option based on the EsoCap platform technology, which enables active ingredients to be released precisely, locally, and directly at the site of disease. Its potential extends beyond EoE and may enable new treatment approaches for other esophageal disorders, including gastroesophageal reflux disease (GERD), Barrett's esophagus, and esophageal cancer.

Manual slit punching station.



INTERVIEW



5 QUESTIONS FOR PATRICK GONCALVES

Modern catheter products make an important contribution to greater independence and quality of life for many people. In the field of continence care, Harro Höfliger develops manufacturing solutions for a broad range of catheters and related products. Patrick Goncalves, an expert in web converting within the Web Converting Technologies business unit, discusses current trends and technological challenges.



Mr. Goncalves, what exactly is continence care, and what role do these products play for users?

Continence care includes products that help people empty their bladder safely and reliably. Intermittent catheters play a particularly important role and are commonly used by people with neurological conditions or following a stroke. By helping to reduce residual urine, intermittent catheters can help lower the risk of urinary tract infections. In my view, the key benefit is that these products enable many people to live more independently. Because they are often used several times a day, comfort, discretion and ease of use are essential.



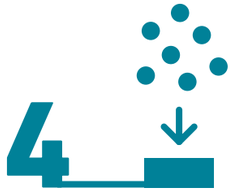
How is the continence care market evolving today?

We are currently seeing several developments at the same time. On the one hand, demand is increasing as the population ages. On the other hand, the products themselves are continuously evolving. In discussions with customers, we consistently see strong interest in solutions that are easier to use and fit more seamlessly into everyday life. As a result, manufacturers are increasingly looking for production solutions that can support these innovations.



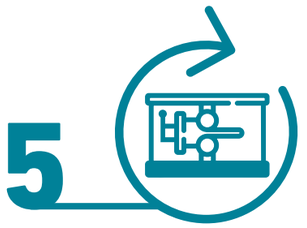
What innovations are shaping modern catheters?

Ease of use is a key driver of innovation. Many products today are much more compact than they were just a few years ago and can be carried discreetly. Other developments improve bladder drainage or make one-handed operation possible. A great deal of development work goes into these features. Ultimately, the goal is always to make catheterization as simple and convenient as possible for the user.



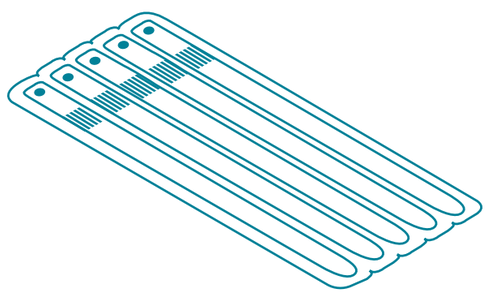
What sets Harro Höfliger apart in the field of continence care?

We have been active in a wide range of continence care projects for many years and have built extensive expertise across the relevant processes. A key foundation is our experience in web converting technologies, particularly when it comes to handling films and other sensitive materials. This know-how plays an important role in many continence care applications, including coating and winding processes as well as sleeving. In this process, the catheter is enclosed in a thin protective sleeve, helping to keep it protected during use.



Why is the turnkey approach so important to your customers?

A turnkey approach allows us to support customers as comprehensively as possible across the value chain. They benefit from the breadth of our technologies and the close collaboration between different disciplines. Web converting technologies often provide the foundation, complemented by expertise in assembly and packaging technologies. This approach allows us to cover large parts of the value chain and support customers at an early stage as they develop new products, evaluate materials, or refine manufacturing processes.



Tailor-made nanoparticles

With its FR-JET® technology, leon-nanodrugs (LEON) enables scalable nanoparticle manufacturing, from early-stage formulation development to GMP production.

Nanoparticles, particularly lipid nanoparticles (LNPs), have become a key technology in modern pharmaceuticals. These tiny structures serve as carrier systems that stabilize sensitive active ingredients, such as nucleic acids like mRNA, protect them from degradation, and deliver them directly into cells. Many innovative therapeutic approaches are only possible because of these capabilities.

"Our goal is a seamless path from R&D to GMP manufacturing."

Dr. Wolfgang Hofmann
CEO
LEON



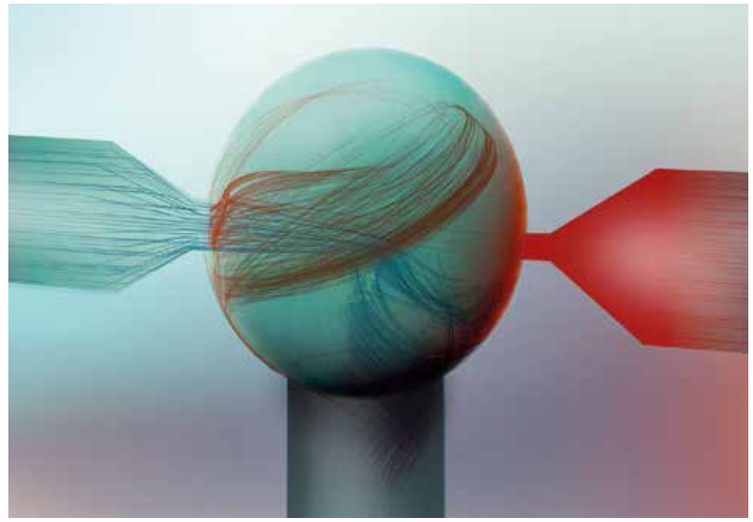
At the same time, manufacturing nanoparticles is highly complex, as they are formed during formulation under precisely defined conditions that determine their properties. Even the slightest deviations can affect characteristics such as particle size, homogeneity, and encapsulation efficiency, and therefore the quality and efficacy of the final product.

The transition from the laboratory to manufacturing is particularly challenging. For many applications, it represents the critical bottleneck, as processes that work at small scale often cannot be scaled up easily. Reproducibility and seamless process transfer are therefore essential prerequisites for the industrial production of nanoparticle-based therapies.

SCALABILITY BY DESIGN

This is exactly where LEON comes in. Based in Planegg near Munich, the company develops technologies that enable the reproducible manufacture of nanoparticles across all stages, from development through GMP production. To achieve this, LEON follows a consistent, end-to-end technology approach. At the core of its portfolio is the patented FR-JET® technology, a specialized mixing geometry that brings active ingredient and carrier solutions together under defined conditions, forming the basis for controlled nanoparticle formation.

FR-JET® technology brings active ingredient and carrier solutions together under defined conditions, enabling controlled nanoparticle formation.



Magnific



NANOme® is the industry's first pumpless, fully disposable cassette-based equipment for nanoparticle manufacturing.

This principle remains identical across all systems, from early-stage formulation development with NANOscreen®, through process development with NANOlab®, to the GMP systems NANOme® and NANOus® for clinical and commercial applications.

FLEXIBILITY MEETS GMP MANUFACTURING

NANOme® is specifically designed for applications where maximum production output is not the primary focus, but rather flexibility, speed, and efficient use of resources. Typical applications include Advanced Therapies such as mRNA-based or personalized therapeutics. In this field, the focus is often on small, frequently changing batches. NANOme® is ideally suited to these requirements.

SCALABLE TECHNOLOGY PORTFOLIO



Starting point for development: screening and evaluation of new nanoparticle formulations.

NANO screen



Foundation for process development and reproducible scale-up to larger production volumes.

NANO lab



Flexible GMP platform for small batches and clinical applications in the field of Advanced Therapies.

NANO me



GMP solution for the large-scale manufacturing of nanoparticle-based therapeutics.

NANO us

Atelier Lünig, LEON



SEAMLESSLY TO GMP

"With FR-JET®, we eliminate the greatest risk in mRNA-LNP scale-up: unpredictability. One mixer and one design space support the entire journey from the first R&D batch to GMP production," says Wolfgang Hofmann, CEO of LEON.

"This means less re-optimization, fewer CMC disruptions, and most importantly, no lost time on the path to clinical milestones. With NANOme®, we also close a critical gap in GMP manufacturing for personalized mRNA and genome-editing therapies by combining small batches, a compact footprint, fast turnaround times, and closed aseptic processes."

"Together, we make nanotechnology more accessible worldwide."

Marco Laackmann
CSO
Harro Höfliger



PARTNERSHIP FOR GLOBAL REACH

To make technological solutions such as NANOme® available to a broader international market, LEON and Harro Höfliger entered into a strategic partnership in February 2026. LEON contributes its expertise in nanoencapsulation and process development, while Harro Höfliger complements the collaboration with extensive GMP experience and an international sales and service network. As a global authorized partner, the company connects customers to LEON's FR-JET® technology and scalable system portfolio.

"Global demand for nanoparticle-based therapies continues to grow. Through our partnership with LEON, we are able to support customers even more effectively in implementing innovative product concepts while providing direct access to a forward-looking technology," says Marco Laackmann, Chief Sales Officer at Harro Höfliger.

Customers benefit from shorter development timelines and reduced complexity on the path to commercialization, ultimately accelerating the availability of new therapies.

A key element of the system is its preassembled single-use cassette, which integrates all product-contact components, including bags, tubing, and valves. The cassette is replaced after each batch, eliminating the need for cleaning processes altogether. This significantly reduces the time between batches while also minimizing the risk of cross-contamination.

NANOme® also takes a distinctive approach to fluid transfer. Instead of conventional pumps, fluid movement is driven by compressed air. As a result, no mechanical product-contact components are required. This design not only simplifies operation but also helps minimize material loss, a critical advantage when working with high-value active pharmaceutical ingredients. As a result, NANOme® is one of the most efficient formulation systems on the market for these therapies.



ASEPTIC PROCESSING STARTS WITH ENGINEERING



How GMP-compliant design, barrier technology, and interdisciplinary expertise contribute to the safe manufacture of sterile pharmaceuticals.

The requirements for aseptic manufacturing continue to grow, driven by one clear objective: patient safety. The key regulatory framework for sterile pharmaceutical production is provided by EU GMP Annex 1, which focuses on systematically preventing contamination throughout the entire manufacturing process. Cleanability, materials and surface finishes, sealing concepts, airflow management, and barrier technology are among the most critical considerations.

Harro Höfliger has translated these requirements into a clearly defined technical engineering standard for aseptic equipment, based on a detailed design concept for GMP-compliant machine design. "With this white paper, we provide our customers with a reliable basis for joint planning and alignment as early as the proposal phase," explains Jörg Rosenland, Department Leader Mechatronic Solutions within Pharmaceutical Technologies. Together with his team, he develops customized solutions that bring together process reliability, contamination control, and regulatory compliance.

Hygienic Design and GMP-compliant design are two cornerstones of modern aseptic equipment concepts. The first creates the conditions for hygienic operation and effective cleaning, while GMP-compliant design ensures that the equipment meets the requirements for manufacturing, quality assurance, documentation, and qualification in regulated pharmaceutical environments.

CLEANLINESS BY DESIGN

Cleaning and disinfection are fundamental elements of any contamination-control strategy. Neither product residues from a previous batch nor particles or microorganisms may compromise product quality. For this reason, equipment is designed from the outset to enable safe and thorough cleaning. All manually cleaned surfaces are fully accessible. Crevices, undercuts, and sharp edges are avoided to prevent cleaning cloths from snagging or releasing fibers. "In aseptic production, cleaning must always be followed by decontamination to eliminate microorganisms," explains Jörg Rosenland. "For machines equipped with RABS, this involves a demanding manual process. In isolator-based systems, decontamination is carried out automatically using vaporized hydrogen peroxide, or VHP."

Product-contact components can be removed without tools and reinstalled under sterile conditions after cleaning and autoclaving. For liquid dosing applications, typically fixed filling systems with Cleaning-in-Place and Sterilization-in-Place capabilities (CIP/SIP) or Single-Use Systems (SUS) are in use.

Together with his team, Jörg Rosenland develops solutions for the safe and compliant implementation of aseptic processes.



Atelier Lünig



Decontamination of bagged tray stacks prior to fully automated debagging inside the isolator.

GREEN FOR FULL MATERIAL RESISTANCE

The regulations themselves do not specify which materials must be used in aseptic equipment. "That is where the experience of both our team and our customers becomes essential," says Jörg Rosenland. "High-grade stainless steel and polyether ether ketone (PEEK) are almost always required for product-contact components. Inside an isolator, stainless steel and only a small number of approved plastics are used. In RABS applications, the use of aluminum components can also be considered in close consultation with customers, provided their cleaning and decontamination agents will not damage the surfaces."

To determine which cleaning and disinfecting agents are suitable for different materials, the Pharma Services team at Harro Höfliger has conducted extensive compatibility testing. The resulting database provides a robust foundation for equipment design. "Customer-specific cleaning agents may be assessed and incorporated into the material-selection process. For media we have not yet tested, we can carry out dedicated compatibility studies," explains Jörg Rosenland. "These findings are valuable not only for aseptic applications but also for many other machine platforms developed by Harro Höfliger."

Material-agent combinations are evaluated using a straightforward traffic-light system: green indicates full compatibility, yellow indicates acceptable non-critical effects, and red signals critical changes.

NO COMPROMISES ON INTEGRITY

Leak tightness plays a particularly important role in isolator-capable equipment. "Because isolators are decontaminated with hydrogen peroxide, a leak test is performed before every decontamination cycle," says Jörg Rosenland. "If the aseptic zone is not completely sealed from adjacent machine areas, even the smallest leak, for example from an unsuitable screw connection, can cause a pressure drop and trigger extensive troubleshooting efforts."

Dynamic seals on moving axes must operate without lubrication while preventing particle generation. To meet these requirements, Harro Höfliger continuously evaluates suitable materials and sealing concepts.

CONTROLLING AIRFLOW WITH PRECISION

Unidirectional airflow (UDAF) plays a vital role in aseptic manufacturing. Filtered air moves uniformly from top to bottom, protecting products and product-contact surfaces from potential contamination. Any structural element within the critical zone can influence airflow patterns and potentially compromise the continuous "first air" protection of the product. Together with the barrier technology team led by Tobias Schwarz, Jörg Rosenland's team visualizes airflow behavior through computer simulations and uses the results to optimize the machine design. Smoke studies on the actual machine later confirm whether the physical conditions match the simulation or require further refinement.



Fully automated filling and sealing of cartridges transferred into the oRABS pre-sterilized.

BARRIER TECHNOLOGY AS A KEY PROCESS

Alongside controlled airflow, barrier technology plays a central role in aseptic manufacturing. Its objectives are clear: protect the product from external contamination, safeguard operators and the environment, and enable efficient, user-friendly operation. The choice of barrier system depends on the product and process requirements. One of the key principles of Annex 1 is minimizing manual interventions in critical areas. As a result, the industry is increasingly moving beyond open barrier systems (oRABS) toward closed systems (cRABS) and isolators. Airflow strategies, pressure concepts, and transfer systems are all designed to support the safe movement of materials into and out of these controlled environments.

TESTING USABILITY IN PRACTICE

A safe and productive aseptic process also depends on effective interaction between operators and equipment. In closed barrier systems and isolators, activities inside the already decontaminated chamber are performed through integrated glove ports. This can make handling tasks significantly more challenging, particularly when working with delicate tools such as tweezers.

"Components that require autoclaving must be positioned so they are easy to reach and can be installed in the correct sequence," says Jörg Rosenland. "Reaching over already installed components is not acceptable, because particles could be transferred directly or indirectly through glove movement and the resulting air turbulence."

Positions, movement paths, and workflows are evaluated in advance using CAD models and virtual environments. Physical 1:1 mock-ups are then created and tested together with customers. Relevant machine and operator areas are built as wooden models, while change parts are produced using 3D printing or manufactured in steel to match their final weight.

Required manual tasks within the isolator or RABS, such as loading products, clearing faults, or decontaminating surfaces, are performed through ergonomically positioned glove ports.



Atelier Lünig

Customer teams assess operation and handling from multiple perspectives, ranging from routine use to qualification activities. Accessibility, assembly and disassembly procedures, and installation sequences are all carefully reviewed. If the concept performs as intended, the design moves forward. If opportunities for improvement are identified, the findings are fed directly back into the engineering process.

ASEPTIC EXPERTISE SINCE 1988

The roots of this expertise go back decades. Harro Höfliger's first aseptic project involved a machine solution for an oncology product. A sensitive, drug-containing depot implant had to be inserted into a prefilled syringe under aseptic conditions.

Initial discussions began in the summer of 1988. Following a short development and testing phase, the first small-scale syringe filling and assembly machine was delivered in 1989. Just two years later, Harro Höfliger supplied its first high-performance system for the automated filling, assembly, labeling, bagging, and packaging of syringes. That successful start marked the beginning of a long-standing partnership.

As regulatory requirements continued to increase, two highly automated isolator-based production lines were delivered in 2022, representing the current state of the art in aseptic manufacturing.

Aseptic filling of complex infusion products. Robots load pre-sterilized IV bags onto the rotary platform.





READY FOR MORE

As combination products and pen injector technologies continue to evolve, manufacturers face increasing pressure to accelerate time-to-market while ensuring reliable, scalable production. The example of Nemera's PenVARIO™ platform shows how design, manufacturing and scale-up can be aligned from an early stage.

The rise of modern GLP-1 therapies is reshaping the market for pen injectors and other injectable drug delivery systems. While pen injectors were once mainly used in insulin therapy and certain hormone treatments, manufacturers are now facing a new level of demand. Production volumes are increasing, time-to-market expectations are tightening, and industrialization is taking on greater strategic importance. In some cases, outputs of several hundred devices per minute are required after only a short lead time. This makes it all the more important to consider the entire path through to commercial manufacturing from the outset.

A PLATFORM FOR DIVERSE REQUIREMENTS

Nemera, one of the world's leading providers of drug delivery device solutions and combination product services, is well positioned to address these requirements with its platform approach. Rather than developing individual devices for specific projects, the company relies on platform

Atelier Lünig, SCHOTT Pharma cartriQ® 3mL Nemera TirzePenVARIO™ Copyright

technologies that can be configured for different drugs, indications and customer requirements. This allows different applications to be realized on a shared technological basis.

"Manufacturability must be considered from the very beginning."

Emeline Campana
Program Manager
Nemera



The disposable, variable and multidose pen injector is compatible with 1.5 mL and 3 mL cartridges and is suitable not only for GLP-1 RAs (glucagon-like peptide-1 receptor agonists) and insulins, but also for applications involving systemic hormones such as follicle-stimulating hormones (FSH) and parathyroid hormones (PTH).

PRODUCTION BEGINS WITH DESIGN

As Program Manager at Nemera, Emeline Campana is responsible for various pen and on-body injector projects. She explains: "A device cannot be developed in isolation from areas such as filling and assembly. These factors need to be considered from the very beginning. In early development phases, however, it is often still unclear what the future manufacturing environment or actual market demand will look like. This makes a Design for Manufacturing approach all the more important, with manufacturability already considered during product development."

Failing to consider these requirements early can result in later design adaptations, additional development effort and project delays. Taking a holistic approach from the beginning therefore helps ensure that device development and subsequent industrialization are aligned throughout the product lifecycle.

SCALABLE PEN PRODUCTION

To establish manufacturability at an early stage, Harro Höfliger's semi-automatic Assembly Lab can be used. The full compatibility between Nemera's PenVARIO™ platform and the Assembly Lab provides a ready-to-use combination for early assembly processes and initial production steps. Combining the flexible device platform with a compatible assembly solution helps reduce integration complexity and development risks while preparing the ground for subsequent scale-up.



The semi-automatic Assembly Lab enables early manufacturability assessments.

COMPONENTS OF PENVARIO™



All device components must be assembled with precision to ensure reliable performance.

"Scalable production starts with a solid process foundation."

Daniel Matias
Customer Technical Support Manager
Nemera



The Assembly Lab allows pharmaceutical companies to evaluate assembly processes early on and implement initial production steps without having to invest directly in high-speed equipment. The insights gained in this phase also provide a basis for the subsequent transition to higher output levels. Early integration can help reduce development risk, accelerate time-to-market and avoid late-stage design modifications.

"The more process knowledge is available from the early phase, the more specifically the transition to larger production volumes can be prepared," says Daniel Matias, Customer Technical Support Manager at Nemera. He works with customers to evaluate pen injector platforms and develop suitable manufacturing concepts. "For pharmaceutical companies, this reduces the effort and, above all, the risk involved in scale-up, for example through significantly simplified validation."

Depending on the required volumes and further requirements, various assembly platforms are available in later steps, enabling production concepts to be scaled from low-speed to high-speed applications while maintaining a consistent process basis.

ONE COORDINATED RESPONSE

The close collaboration between Nemera and Harro Höfliger creates ideal conditions for this seamless transition. If challenges arise, teams from both companies jointly analyze the root cause in every project phase and develop a coordinated solution. Because processes, points of contact and technical interfaces are already well established, the coordination effort required from the customer is significantly reduced, helping to accelerate the entire project.

By bringing device and assembly expertise together from an early stage, Nemera and Harro Höfliger can support customers across the transition from device development toward scalable manufacturing while reducing the risks associated with later integration.

In a market defined by rising volumes and increasing speed, this direct line of communication is a key advantage. The benefits become visible long before high-volume manufacturing begins: before the first pen is even assembled.

The Apic, Nemera

INTO THE CAN. OUT OF THE BOX.

For decades, the filling process for MDIs remained largely unchanged. With Dry-Filling, Harro Höfliger is taking an entirely new approach, creating multiple advantages through the consistent separation of API dosing, crimping, and propellant filling.

A single press of the inhaler is all it takes: a precisely measured dose is released and can be inhaled. This is made possible by an MDI, short for metered-dose inhaler. Inside the inhaler is a can containing a mixture of active ingredient and propellant. The propellant ensures that the active ingredient is released as a fine aerosol cloud, allowing patients to receive a predefined dose of medication with every actuation.

While these inhalers are simple to use, manufacturing them requires a highly controlled production process. This is more important than ever today, as modern propellants with lower global warming potential are transforming the market. Some of these propellants are highly flammable and therefore require adapted safety concepts and production environments.

NEW REQUIREMENTS, NEW APPROACH

"The market is currently facing the major challenge of integrating new propellants into existing manufacturing realities," says Kris Brosig, Inhalation Specialist at Harro Höfliger. "Established filling technologies such as Single-Stage Pressure Filling, Two-Stage Filling, and Dual Filling continue to form the foundation of many commercial MDI products. However, not every formulation and not every manufacturing strategy benefits equally from conventional approaches. Together with Pharmatec Solutions Ltd., we therefore developed Dry-Filling: a new process concept that addresses current market requirements while offering a range of additional benefits."

"Dry-Filling is reshaping the process architecture of MDI manufacturing."

Kris Brosig
Inhalation Specialist
Harro Höfliger



In conventional manufacturing processes, the active ingredient and propellant are combined into a mixture early in production. Dry-Filling follows a fundamentally different concept. Instead of preparing the mixture first and then carrying it through production, the individual components remain separated for as long as possible.

Metered-dose inhalers (MDIs) are among the most common delivery systems for inhaled medications.



The can is at the heart of every MDI. It contains the active ingredient and propellant needed for each actuation.



The process begins with dosing the powdered active ingredient into the open can. During the subsequent crimping step, the valve is attached and permanently sealed under vacuum conditions. Only in the final stage is the propellant introduced through the valve stem into the hermetically sealed unit.

"With this approach, we consistently separate the critical process steps and thereby reduce propellant handling throughout the manufacturing environment," explains Kris Brosig. "Our claim, 'into the can. out of the box.', captures the idea perfectly: we focus on bringing the active ingredient and propellant into the can with maximum precision, while deliberately moving beyond the thinking behind conventional filling processes."

INCREASING SAFETY, ELIMINATING BOTTLENECKS

Because the propellant is introduced only during the final process step, the need for ATEX zones, which are designed to protect against potentially explosive atmospheres, is significantly reduced. When working with flammable propellants, this can greatly simplify both facility planning and explosion protection measures.

The new process offers additional advantages as well. Conventional manufacturing relies on large vessels in which the active ingredient and other components are mixed together. These mixing vessels tie up capacity, require extensive cleaning, and often lead to longer downtime during product or batch changeovers. Dry-Filling eliminates centralized mixing and blending steps altogether. As a result, cleaning efforts are reduced, interruptions become shorter, and overall equipment effectiveness (OEE) can be improved.

FROM LAB TO PRODUCTION

Dry-Filling is already available at Harro Höfliger on a laboratory scale today. Dedicated tabletop systems are available for each of the three core process steps, enabling manufacturers to evaluate the approach with their own products and gain valuable development insights.

"With our laboratory equipment, we not only demonstrate that the process works in principle, but also generate reliable product-specific data," says Kris Brosig. "The results speak for themselves. In dosing trials, for example, we achieved a relative standard deviation of less than 0.7 percent."

The findings generated during laboratory testing provide the foundation for scaling the process to industrial production. A concept for a high-performance production line based on the same process architecture is already available, covering outputs from 100 to 250 cans per minute.

EVERYTHING FROM A SINGLE SOURCE

MDI products are by no means new territory for Harro Höfliger. As Kris Brosig explains: "For many years, we have built extensive expertise in assembly, including valve assembly, as well as downstream packaging processes. With Dry-Filling, we are now adding a crucial upstream step to our portfolio."

In this way, Dry-Filling complements existing capabilities in assembly and packaging and extends Harro Höfliger's involvement further upstream in the MDI manufacturing process.

"We are not only thinking MDI filling 'out of the box'," says Kris Brosig. "At the same time, we support the product through assembly and packaging all the way to 'into the box' and, as the only supplier on the market, cover the entire process from a single source."

DRY-FILLING AT LAB SCALE

1. POWDER DOSING





The Drum Lab uses Harro Höfliger's proven drum dosing technology to achieve precise and reproducible dosing results at lab scale.

2. VACUUM CRIMPING





Unlike many conventional solutions, the Crimping Lab moves the can towards the processing head during the crimping process.

3. PROPELLANT FILLING





The Propellant Lab enables controlled filling of the propellant through the valve stem, allowing for realistic testing of the filling principle.

INTEGRATED LINE



Commercial MDI filling line designed for 100 to 250 cans per minute, based on the principles validated at lab scale.

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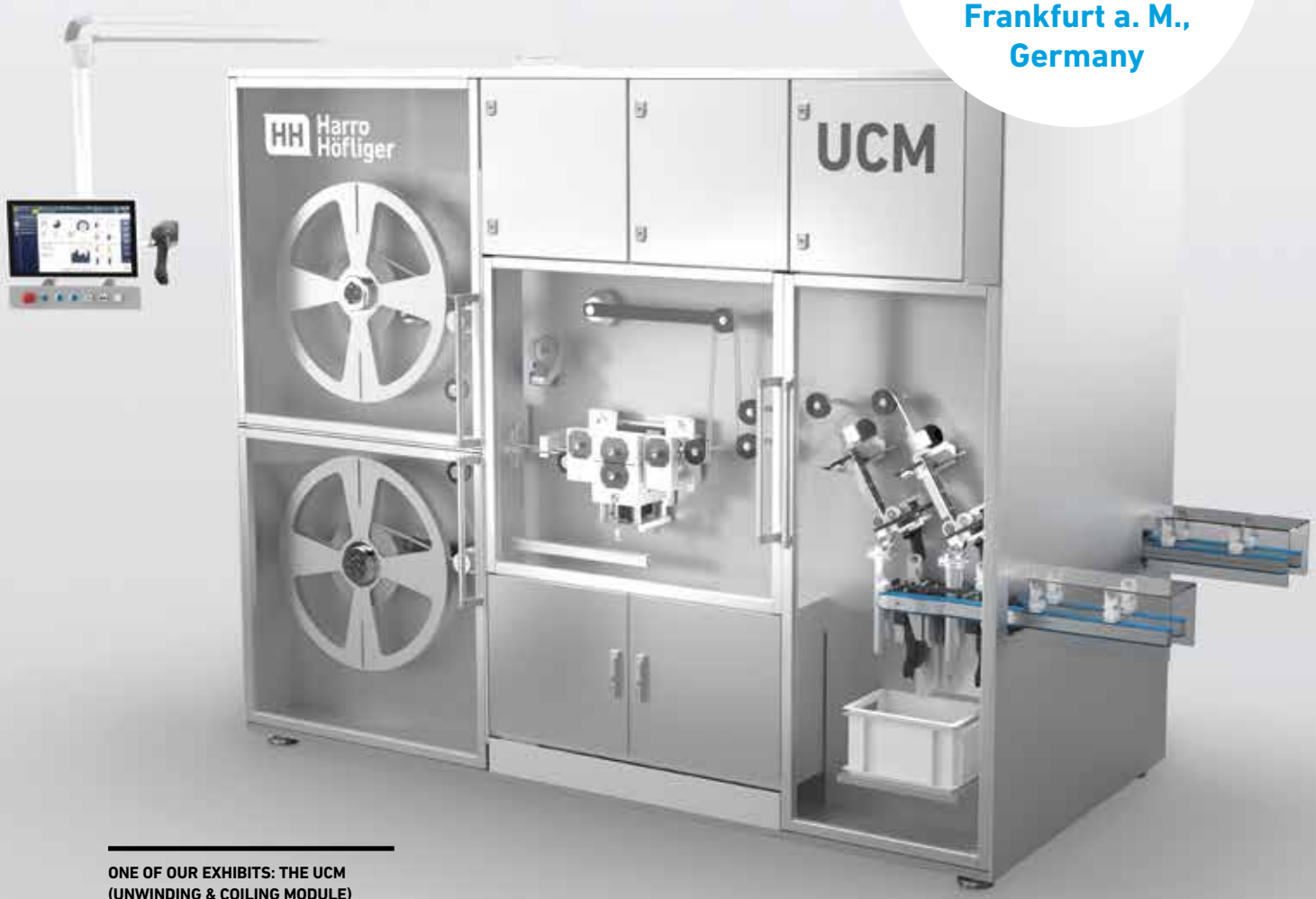
June 14 – 18, 2027

Frankfurt a. M., Germany



ONE OF OUR EXHIBITS: THE UCM (UNWINDING & COILING MODULE)

The machine unwinds and inspects blister strips for dry powder inhalers before winding them into coils for downstream assembly.

IMPRINT

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