Pharma Flash

Issue 2


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EDITORIAL

Dear Customers,

As the new Executive President at Stäubli Robotics, I am eager to ensure that we not only maintain our existing partnerships with our customers, but also build on them. This applies particularly to our relationships within the pharmaceutical industry.

Stäubli Robotics saw an opening in this sector many years ago, at a time when the pharmaceutical industry was still a niche market for robot manufacturers. The situation looks very different today, with the former niche market having developed into one of the most attractive markets for the future of robotics.

Working in collaboration with industry players over the years, Stäubli has amassed substantial know-how. This benefits our customers in the planning of every new project, including systems and assembly lines for the production of APIs and biotherapeutics; industry-scale filling and packaging of liquid, powder and solid medicines; and production of packaging materials and automated processes in laboratories and pharmacies. Our wealth of experience and range of customized robots make Stäubli an automation specialist you can rely on.

In the future, we aim to take our close cooperation with you to a new level. As I write, we are investing in structural capabilities to strengthen our market focus. To this end, we have recruited Rudolf M. Weiss, an experienced specialist from the pharmaceutical industry, as Global Head of Pharma. Rudolf will lead the way in building up a worldwide organization and forming country-specific teams for the international pharmaceutical market that will design advanced solutions together with you as the manufacturer.

We have in mind comprehensive, digitally networked production and intralogistics concepts. As a solution provider, we want to work with you to realize Industry 4.0-compliant lines that offer the highest degree of production safety, flexibility and process reliability, thereby guaranteeing unprecedented security for your investment. We combine production technology expertise with the right robots, mobile robots and autonomous transport systems to put your ideas for smart pharmaceutical production into practice today. We encourage you to put us to the test!

Best wishes,
Christophe Coulongeat
Executive President Robotics


STÄUBLI

EDITORIAL

Smart solutions for the pharmaceutical industry

Demand for personalized medicines, new treatment options and innovative approaches in prevention and diagnostics are among the key challenges facing the pharmaceutical industry. These seismic shifts offer opportunities not only for traditional pharmaceutical providers, but also for technology companies from outside the sector.

The future success of market players, both established and new, can only be assured if their production structures meet the demands of a rapidly changing industry. Over and above fulfilment of the industry's stringent approvals and certification requirements, factors such as process reliability and flexibility play decisive roles.

With impressive levels of flexibility, robot-based automation solutions are the first choice for small batch production runs in personalized medicine. They offer the additional advantage of reducing human contact to a minimum, and thereby avoiding the risk of contamination. Stäubli has been a partner to the pharmaceutical industry for decades, responsible for pioneering developments such as our acclaimed Stericlean models, which facilitate automation in aseptic environments.

More recently, we have worked in close partnership with OEMs and integrators to expand our robotics portfolio for pharmaceutical applications. We continue to collaborate intensively on further developments which will enable us to offer digitally networked and other automation solutions for just about any conceivable future production scenario.

In joint development work with our customers, we have already achieved a great deal, as you will see in the fascinating case studies presented in this publication. Stäubli's declared goal is to expand cooperation with pharmaceutical manufacturers all over the world in order to make the production of medicines safer, more cost efficient and more sustainable than ever before. If you are currently facing a production challenge, please do not hesitate to contact us. We look forward to hearing from you.

Best wishes,
Rudolf M. Weiss
Global Head of Pharma Robotics

ASEPTIC FILLING

Easy programming – sterile filling

A Swiss plant constructor has set the industry benchmark with its filling line for hyaluronic gel. At the heart of the system is a Stäubli Stericlean robot that fills syringes with the anti-aging substance under sterile conditions. The six-axis robot's uniVAL plc interface allows for convenient and direct programming via the Siemens PLC.

The TX2-90 Stericlean handling a sensitive load.

Stericlean robot filling hyaluronic gel

Hyaluronic (HA) gel is a veritable fountain of youth for the skin. The gel is in high demand, and Zellwag Pharmtech AG, a subsidiary of the Rychiger AG Group (Switzerland), has developed a fully automated filling and sealing system specifically for the product. The Z-810 R-2 machine works under cleanroom conditions to fill syringes with HA gel and then seal them. Both processes take place under vacuum conditions – an essential requirement, since injecting air under the skin is extremely dangerous and must be avoided.

In designing the Z-810 R-2 for a Russian cosmetics manufacturer, the Zellwag engineering team's priority was to ensure bubble-free mixing, pressing and filling. Without any air ingress, the gel is safely transported to the filling line and fed under vacuum with an extruder press. Another characteristic of the multi-format system is its high degree of flexibility. Nested and sterile containers with different formats such as syringes, vials and cartridges made of glass or plastic can be processed on the same filling line.

Sterile filling performed by a robot

Thanks to the Stäubli TX2-90 Stericlean six-axis robot, it was possible to design a space-saving layout for handling syringes, vials and cartridges. A Tyvec-sealed tub containing one hundred prepared and sterile syringes arrives at the robot's working area. A linear system peels back the Tyvec foil, and a second linear system lifts the nest of syringes out of the tub.

The robot grips the nest, rotates it 90 degrees, and presents it to the filling station.

Convenient programming of the robot using the uniVAL plc.

The syringes are then filled two at a time, with the gel being extruded from a nozzle. After 50 cycles, all of the syringes are filled. The ultra-dynamic Stericlean robot replaces them in the tub, which is transported by means of a conveyor system to further processing stations.

Filling rates of up to 2 200 syringes per hour are achieved, with the only limits being set by the viscosity of the gel rather than the capabilities of the robot. Indeed, for watery media, up to 6,000 filling operations per hour are possible.

Custom-built for sterile conditions

The entire process takes place in a sterile environment – conditions in which using conventional robots would be unthinkable. Stäubli's unique Stericlean robots are at home in such environments, however. The series was specially developed for critical applications in aseptic production areas of GMP Class A and has proven itself thousands of times over.

The kinematics of the Stericlean six-axis robots are fully encapsulated and sealed tight, with the cabling on the inside. There are no dead spaces, only smooth surfaces on which there is no possibility for the formation of impurities. The unique specifications of these outstanding pharmaceutical robots make them resistant to the harshest of regular sterilization and decontamination procedures, for example with hydrogen peroxide (H_2O_2).

Integration into higher-level control system saves programming effort

Another special and advantageous feature of the entire TX2 series is the uniVAL plc interface. It enables the robot to be configured through the PLC of any well-known manufacturer – in this case a Siemens PLC. This eliminates the need for complex subsystems and interfaces that can be difficult for programmers to adapt to, from configuration to qualification. Operators can continue to work in their familiar environment without having to learn a new robot programming language.

With the Stäubli Stericlean robot, Zellwag has been able to implement a perfect solution for filling hyaluronic gel under sterile conditions, in a compact space, with a high degree of flexibility and minimal programming effort. The robot's hygienic, pharma-compliant design and uniVAL plc interface provided all of the essential prerequisites.

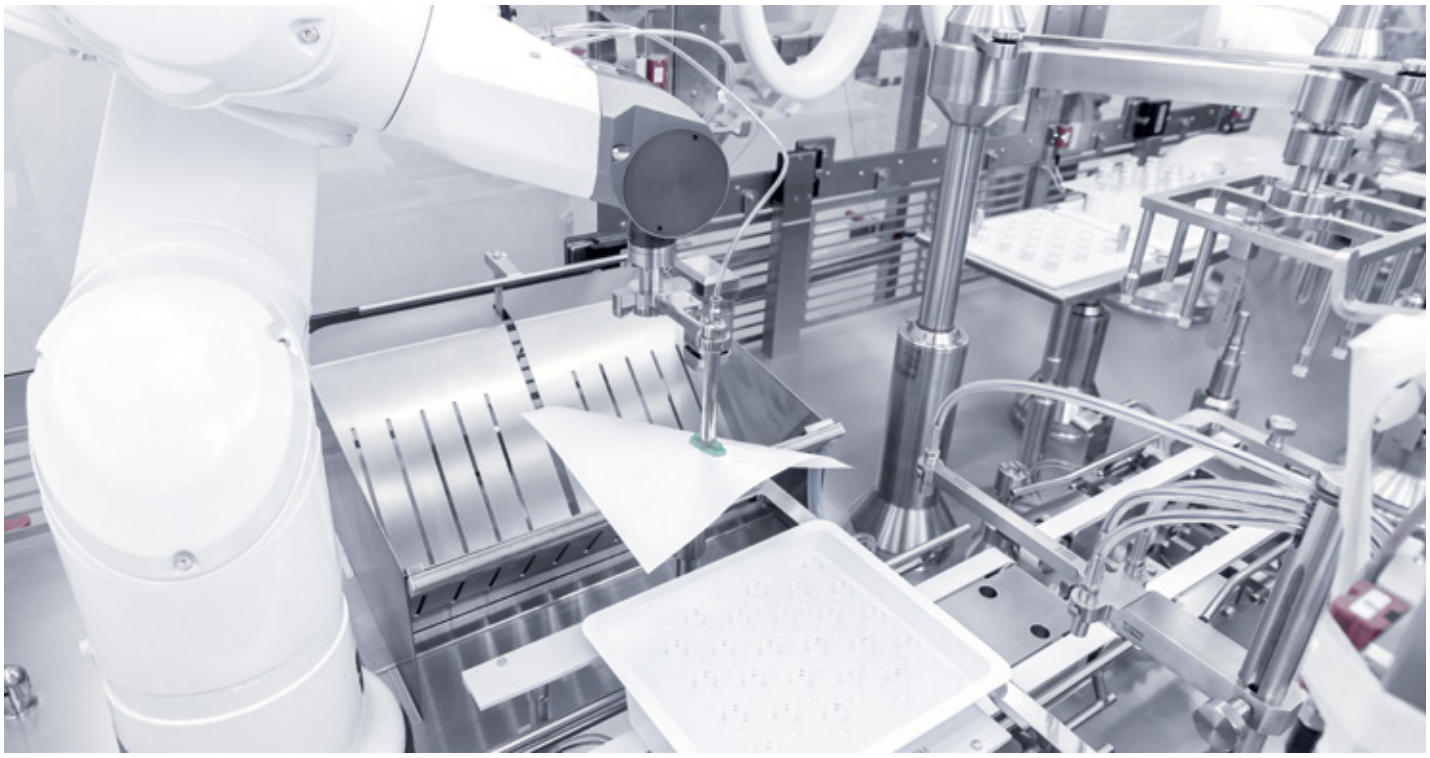
Video Zellwag

System advantages at a glance:

- Robot design allows a simplified plant layout
- Central programming for enhanced functionality and efficiency
- Rapid process adaptation and format extensions, even after installation
- Reduction in subsystems and interfaces for streamlined programming and qualification

ASEPTIC FILLING

Smart pharmaceutical packaging



Three Stericlean robots create the conditions for flexible and hygienic handling.

OPTIMA combines several robotics solutions into one system

An extraordinarily flexible machine able to efficiently package different medical products into different containers: This is how OPTIMA has envisaged the future of pharmaceutical packaging and has now set out to turn its concept into reality. Three compact Stericlean robots from Stäubli manage the core tasks.

The system developed by OPTIMA Pharma GmbH, headquartered in Schwäbisch Hall, based on its MultiUse concept is uniquely versatile and able to handle different batch sizes and pharmaceutical products with ease. Medicinal products can be volatile or viscous, potentially oxidation-sensitive or aggressive. They may also contain active or highly active ingredients.

The system is equally flexible when it comes to the types of containers. Production begins with three container types in the pipeline – syringes, vials and cartridges – in a total of 10 formats, all of which should be able to be transported with almost no format changes to the grippers or transport systems. The high value of the medicinal products also means other demands must be met. “Yield” functions, such as re-filling and re-dosing, are therefore equally important.

The solution is robotics

How can these high requirements be met? OPTIMA’s answer: through robotics, or more precisely, through several different

The MultiUse system from OPTIMA allows the packaging of syringes, vials and cartridges.

The smooth surface of the Stericlean robots are easy to clean and meet the hygiene requirements of the pharmaceutical industry.

robotics solutions innovatively combined. It was, in fact, the use of Stäubli Stericlean robots that made this combination possible, since they meet all of the criteria for working in aseptic conditions.

The MultiUse system combines several different types of robotics and technologies. Three high-precision Stericlean 6-axis robots from Stäubli's TX60 and TX60L ranges are used. The first of the three 6-axis robots removes sealed Tyvek covers from the tubs. The second removes the containers from the nest using a vacuum gripper and places them into the transport system. From here they are transitioned into a zone for highly potent active ingredients.

The third Stericlean 6-axis robot is responsible for ensuring that there are no empty spaces left in the tubs, which can occur when rejected products are filtered out. It removes the containers from an oval conveyor and fills them to maximum capacity. This way every tub is guaranteed to be filled with the full quantity of 100%-checked syringes at the end of production.

In-house programming forms the basis of the control architecture

All robotic functions were programmed in-house by OPTIMA, which has brought about sophisticated solutions. For example, the third Stäubli Stericlean robot automatically ensures there are no empty spaces in the tubs that may have occurred due to the removal of rejected products.

Thanks to the central programming of all associated robot systems forming the basis of the control architecture, a high level of transparency is provided, and all interface-related questions are rendered superfluous. Any automated solution comprised of subsystems would be overstretched in its capacity here.

Another benefit of central programming: MultiUse machines will need to be adjusted to new demands more frequently throughout their lifecycle. If the user has a central point of contact for programming, these adjustments can be made more easily and certifications for amended processes are also easier to manage.

Maximized usage times, highest product yield

Functions such as loading and emptying mechanisms, "re-dosing on request", re-capping and re-stoppering allow users to process every last drop of their product and package it safely.

The main characteristic of this system is, however, its extraordinary flexibility, which is made possible thanks to the application of state-of-the-art and highly adaptable automation hardware – including the three Stericlean robots. Another benefit: OPTIMA does not have a linear system layout, meaning users are able to take advantage of new opportunities for optimal space utilization. This is what makes the MultiUse concept, when used alongside Stäubli 6-axis robots, a machine that will change the future of pharmaceutical packaging.

ASEPTIC FILLING

Big strides for small batches

Stericlean robots for aseptic filling and sealing

An operator manually transfers containers into a tub opening module. Operator safety and product sterility are ensured.

When it comes to automated filling and closing of ready-to-use syringes and cartridges, machines for smaller batches are in growing demand. An innovative multi-format robotic filling and closing machine with a Stäubli TX2 Stericlean robot working under aseptic conditions offers the necessary flexibility.

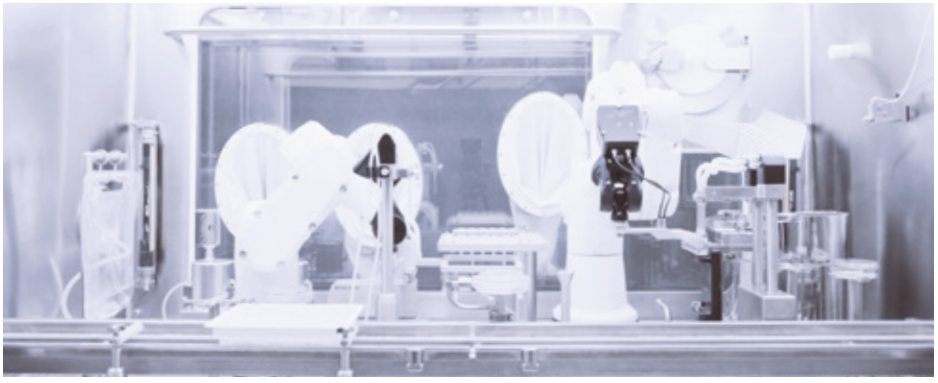
As smaller batches are a clear trend in pharmaceutical production, new machine generations have to be flexible. At the same time, high standards of quality and efficiency must be fulfilled, and adherence to aseptic processing requirements is more complex than ever. Under these conditions, robot-based AAP (Advanced Aseptic Processing) systems are the perfect solution. The GENiSYS® R aseptic small batch filling and closing machine from Automated Systems of Tacoma (AST) is a prime example.

This flexible modular system automates aseptic filling and closing of ready-to-use vials, syringes and cartridges in strict accordance with cGMP requirements, and it can be integrated with isolator-barrier or RABS (Restricted Access Barrier System) technologies.

The GENiSYS R is optimized for small batch filling, with a focus on dosing precision and high yield. Thanks to the Stäubli Stericlean six-axis robot, a 100% in-process control (IPC) is possible. This makes it ideal for clinical and commercial applications in drug manufacturing, compounding, cell and gene therapy (CGT) development, personalized medicine and other areas.

Perfect solution: Stäubli Stericlean robots

A core component of the modular filling and closing system is, depending on the user's requirements, a Stäubli Stericlean TX2-40 or the somewhat larger TX2-60. These six-axis robots are entrusted with a variety of delicate and repetitive yet critical tasks within each step of the aseptic process: bag and tub opening, filling, stoppering, sealing/closing, and reject handling. If some tasks along the production line need to be executed manually, the GENiSYS R can easily accommodate that need while



The GENiSYS R fill/close module during vial processing.

A robotic arm prepares to place a finished vial back into the nest.

Stäubli robots hard at work filling and stoppering a nest of ready-to-use vials.

ensuring operator safety and product sterility.

The combination of modular design and advanced robotics allow the GENiSYS R to be configured to meet different process requirements and containers without the cost or extra time associated with customization. Operators can program recipes specific to container formats and drug products, as well as precise robot movements and pump settings, using the intuitive human-machine interface (HMI), ASTView®. This can include fine-tuning needle fill depth and speed to prevent bubbling, or exact positioning in a given space to mitigate air disturbance, for example – with minimal downtime during changes.

Impressive flexibility

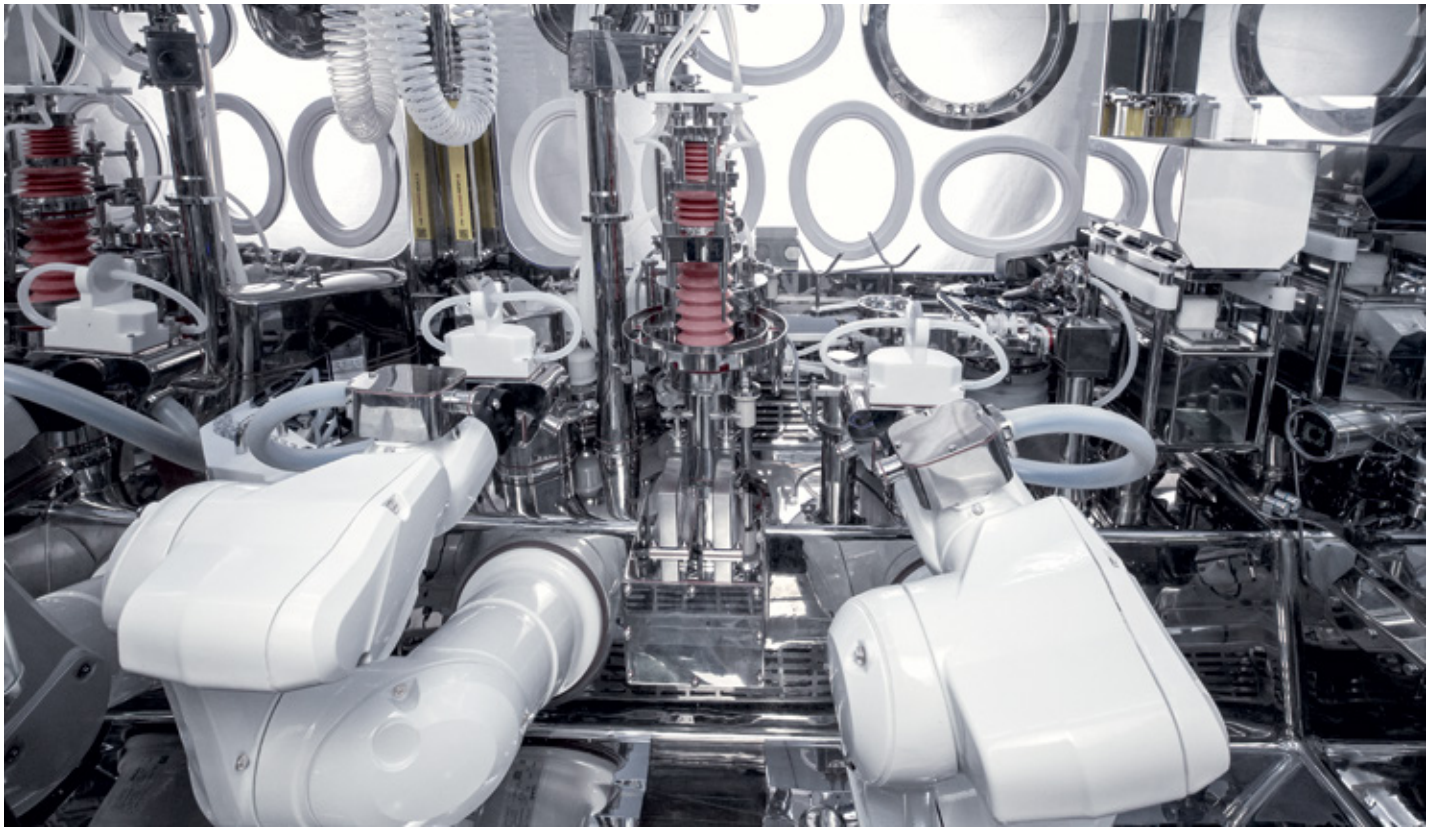
The system's modular design also provides flexibility with regard to the degree of automation desired: Bag and tub opening can be manual, semi-automated, or fully automated, while filling and vial sealing are always fully automated.

In all steps of the process, the Stäubli robots perform with high dynamics yet at the same time with utmost smoothness. The robots carefully manipulate the nest and vials with even movements, which is essential to reduce particle generation. Furthermore, this ensures the integrity of all critical process steps. Unplanned manual interventions, which risk compromising the aseptic environment, can be excluded.

The use of Stäubli robots engineered for aseptic environments plays a significant role in the GENiSYS R's high flexibility, enabling the precise filling and closing of ready-to-use nested, pre-sterilized vials, syringes and cartridges. Without the unique Stericlean robots, the fast changes between recipes and formats demanded in small batch processing would simply be impossible.

Customer advantages:

- Modular design allows for maximum flexibility
- High performance when processing small batches
- Stericlean robots ensure that aseptic conditions are maintained
- Fast change of recipes and formats



A total of three Stäubli TX2-60 Stericlean robots operate in Romaco Macofar's MicroRobot 50 microdosing machine.

PRODUCTION OF SOLIDS

Robots under isolation – with utmost precision and flexibility

Stericlean robots dose cytotoxic products

Filling and dosing of cytotoxic medical products under isolation: This is the very demanding task of the MicroRobot 50, designed and manufactured by Romaco Macofar. Three Stäubli Stericlean robots handle critical process steps.

The robot-assisted filling system is specially designed for processing highly potent and cytostatic medications used to treat cancer and autoimmune diseases, for example. With this capability, MicroRobot 50 fits perfectly into the Romaco Macofar product range. The company, based in Bologna, Italy, is a member of the Romaco Group, a leading international supplier of processing and packaging equipment for pharmaceutical applications. Within the group, Romaco Macofar is focused on primary packaging

> "A company that manufactures highly potent and cytotoxic drugs, e.g. for oncology, needed a machine to fill these drugs into injection vials aseptically under isolator protection – with a speed of 50 vials per minute and capacities from 20 mg to 2 g per vial."

Dr. Carlo Cattenati
Head of Product Management, Romaco S.r.l

for powders and liquids for pharmaceutical products under sterile conditions.

The initiative to develop the MicroRobot 50 came from a customer. "A company that manufactures highly potent and cytotoxic drugs, e.g. for oncology, needed a machine to fill these drugs into injection vials aseptically under isolator protection – with a speed of 50 vials per minute and capacities from 20 mg to 2 g per vial. This was the starting point of our work," said Dr. Carlo Cattenati, Head of Product Management at Romaco S.r.l. Isolation, in this case, was important for two reasons. Sterility is crucial in order to avoid the intrusion of contaminants. And the operators' safety must be assured because highly potent drugs like cytostatic APIs are handled. So manual handling had to be excluded and a new concept with three robots was selected.

At the core of the process: three robots

The first robot picks up the sterile vials and transfers them, two at a time, to the powder dosing point. The second robot grips the powder-filled vials and transfers them to the stoppering area. A vacuum-assisted applicator picks up the stoppers and deposits them on top of the vials held by the robot, surveyed by a vision system. The third robot is located at a double station that closes the closures with a controlled crimp force. A rotating blade, powered from a controlled servo motor, takes over the folding of the crimps.

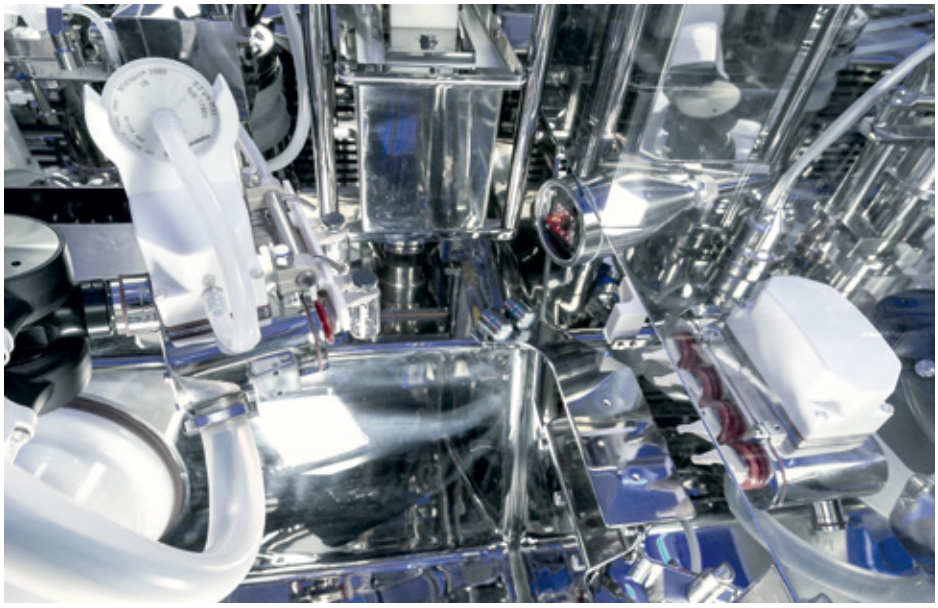
With the filling and capping process finished, the vials are transported to the packing station. Vials with missing rubber caps or rings are identified and sent directly back to the filling station. Thus no valuable product is lost, and the yield is 100 %.

The logical choice: TX2-60 Stericlean

The robots have to be very precise, and they must operate with high reproducibility, because at 50 vials per minute, they achieve 72 000 cycles every single day. And of course, they have to be able to work in a sterile and isolated environment, which includes the ability to withstand frequent and demanding washdown processes.

Given these requirements, the Stäubli's TX2 series robots in Stericlean design were the natural choice for Romaco's engineers. They are fast, precise and completely washable, not only with water but also VHP decontamination. Further, the Romaco engineers appreciated the robot's high load capacity despite its very compact envelope. They see yet another advantage in the high safety standards of the robot´s CS9 controller.

The Stericlean robots have a unique hygienic design and can be cleaned with VHP.



The robots have to be precise and reliable as they reach 72 000 cycles in a single day.

The three Stäubli TX2-60 robots are integrated into the control system, supplied by Schneider Electric, as slave nodes. Sercos 3 is used as a communication channel. The robots have been programmed in VAL 3. Their software infrastructure is shared in all basic functionalities and differs only in the handling task.

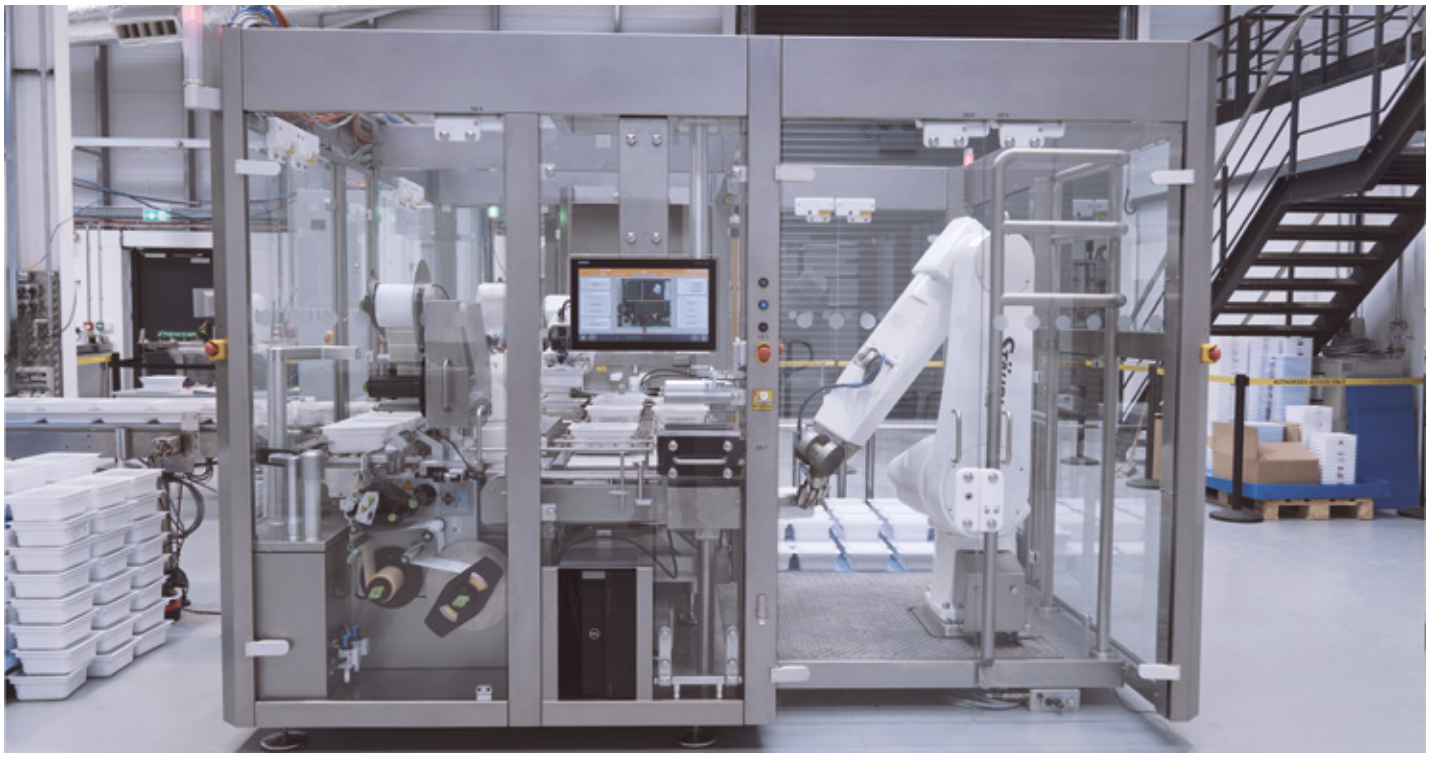
The MicroRobot 50 has been installed inside an ISO 5/Grade A OEB 5 isolator. Cleanliness is easy to achieve, compared with conventional handling technology. Moreover, the machine can be equipped with a “Robotic Cleaning Kit”: Robots with dedicated spray guns clean the system’s interior in accordance with a validated process.

The sterile filling system can dose not only different kinds of powders, for example antibiotics, but also liquids. Another big plus the robots bring to the MicroRobot 50 is minimizing the format parts to a few components, which ensures the desired flexibility. Romaco Macofar’s managers also cite the professional support of Stäubli‘s Italian team throughout the entire engineering process.

Highly flexible and powerful: the MicroRobot 50 microdosing machine from Romaco Macofar.

STERILE SECONDARY FILLING

End-of-line inspection under hygienic conditions



A compact cell: Three robots cooperate when inspecting and palletizing tubs with 100 syringes each. 36 000 syringes per hour are processed with utmost precision and safety.

Robot cell for inspection and packaging of 36 000 syringes per hour

For a global market leader in the pharmaceutical industry, Irish systems integrator Ward Automation in Sligo engineered and manufactured a compact and flexible robot cell for the end-of-line testing, labeling and palletizing of 36 000 syringes per hour. Three Stäubli robots with hygienic design are responsible for container handling.

What is the safest and most economic way to test and palletize 36 000 syringes per hour at 100% accuracy with a range of different criteria? A global manufacturer of pharmaceutical products posed this question to Ward Automation and got a perfect solution.

Here are some details of the specification: The syringes arrive in tubs containing 100 samples at six tubs per minute. They have to be inspected, labelled and palletized in

> “With the fully automated machine, our customer is able to fulfill 100% checks of syringes, labels and tamper seals.”

Kenny Ward
Business Development Manager

accordance with regulations concerning medical device production (21 CFR Part 11). An important issue was to eliminate the risk of damaged syringes, missing syringes and missing anti-tamper seals. For reasons of production safety and traceability, the robot cell had to be integrated into the company’s SCADA system. All process steps have to be executed in a very small envelope.

Three robots in one cell

Based on these specifications, Ward Automation engineered a robot cell with three Stäubli robots. The fully automated process runs as follows: First, a Stäubli TX2-60 robot removes the nest of syringes for inspection. With a “flash” of two vision systems, the content of the nest is checked for damaged flanges, missing PRTC caps and the correct number of syringes.

Tubs with incorrect syringes are diverted to a reject drawer. The HMI shows which syringe is to be removed from the nest, and the vision system verifies that the correct syringe has been removed. After this, the tub is released to the operator to allow it to be replenished and reintroduced to the machine.

Labelling – inspection included

Good tubs are conveyed to a label station where inner and outer labels are printed and inspected. Incorrect labels are automatically rejected and reprinted. Good labels are applied to the inside and outside of the tub. The inner label is placed using the same TX2-60 robot. At the end of this process, the labels are checked for presence and position.

For the sealing of tubs before palletizing and shipping, Ward Automation has invented an innovative lid separation station. This station presents a single lid to the second robot, which is also a Stäubli TX2-60. After a vision system has verified the presence of one single lid, the robot places this lid on a tub. A custom application head applies a tamper-proof seal to the lid, folding the label around this lid flange. The tub is rotated 180° and a second label is applied. The robot then lifts the tub and places it on the buffer conveyor.

Robots designed for hygienic applications

The processed tubs are stacked on a pallet using a Stäubli RX160L robot. This robot offers the required reach in a small footprint. 200 tubs are placed on each pallet.

A crucial factor for the customer is the hygienic design of the complete process. Here, Stäubli robots have a clear advantage, being available in an “HE” (Humid Environment) version, denoting that the robot can be installed in cleanrooms and production zones where extensive washdown processes occur on a daily or shift-based rotation.

The robot cell, which is 21 CFR Part 11 compliant, can handle both 3” and 4” tubs with 100 or 160 syringes per tub. Compact design is not only required, but also ensured: The cell fits a 3m by 3m footprint and can handle 600 syringes per minute.

The machine is already in operation and the customer is very satisfied with the new fully automated solution. The manufacturer of pharmaceuticals is able to fulfil 100% checks of syringes, the cell can easily be adapted to new recipes and requirements, and the complex process takes place within a very small envelope.

Video Ward Automation

Dedicated grippers are used for handling the tubs.

The third robot covers the tubs with a lid and applies two labels.

PRIMARY FILLING

Vial handling, smartly automated

Dessl Maschinenbau in Schwaz, Austria, has created a fully automated vial handling system. A 6-axis robot from Stäubli's RX160L range handles around 320 vials per minute and is in constant operation.

Display of the deployment area at Dessl Maschinenbau GmbH. (Image rights: Dessl Maschinenbau GmbH)

While utilizing a total floor space of only 9 m^2 (97 sq. ft), the Collector by Dessl Maschinenbau loads around 320 bottles per minute into Euronorm containers, which are un- and reloaded in the machine beforehand. The core element and centerpiece of the machine is a Stäubli RX160L long-armed robot. (Image rights: Dessl Maschinenbau GmbH)

Robots: A core element of any pharmaceutical plant

Packaging vials requires a lower cleanroom classification and longer cleaning intervals than their production. For this reason, one pharmaceutical company decided to separate these processes to limit the packaging of vials to one area, thereby increasing operating efficiency. Dessl Maschinenbau GmbH in Schwaz, Tyrol, was responsible for managing the construction of a machine to both load and unload the vials.

The requirements were vast: The machine must be capable of loading 320 vials per minute into Euronorm transport containers under fully automated conditions. This includes removing the empty containers and palletizing the loaded ones. It is also possible that the height and diameter of individual vials will differ, meaning that containers with different heights are to be used during subsequent processing to ensure optimal use of space. Furthermore, the total floor space of the machine, including pallet storage, was limited to 3x3 m (around 10x10 ft).

An innovative robotics solution

The machine, currently on offer to customers under the name “Dessl Collector,” is equipped with a Stäubli RX160L robotic arm that ably carries out its duties. Once the containers have been fed into the ma-

Thanks to its increased reach, the RX160L can access both pallet storage areas regardless of their height, so containers can be removed before they are loaded and subsequently palletized elsewhere. (Image rights: Dessl Maschinenbau GmbH)

chine on a pallet, they are measured and removed, positioned, and then loaded with vials before being palletized once more, ready for further transport. To avoid breakage, Dessl engineers designed containers with a patented spring system that keeps the vials in place. This means that vials of varying sizes can be stored in the same container.

A conveyor precisely positions the vials, ensuring they are equally distant from one another. The robot then uses a proprietary vacuum gripper to place a row of vials into a container, which is set to an inclined position to allow for loading. When the container is fully loaded, the RX160L palletizes it.

Using a counterpart unloading machine, the system then unloads the containers. A patented spring system stabilizes the position of the vials during transport and guarantees a smooth unloading process. Both machines combined also offer an interim buffering mechanism should problems arise during subsequent vial processing. This prevents downtime in upstream systems – typically filling systems in sterile environments with correspondingly high downtime costs.

Suitable for use in pharmaceutical environments as standard

All Stäubli robots are easy to clean thanks to their enclosed structures, as per protection classes IP65 and IP67. Furthermore, their standard cleanroom classification is ISO 5, meaning they are particularly well built for use in pharmaceutical manufacturing. ISO class 5, which does not permit particles of 5 µm or larger to be in the surrounding air, corresponds to cleanroom grade A as per EG-GMP guidelines.

Alongside loading and unloading, the robot is also required to reach both pallet storage areas regardless of their height, making the Stäubli RX160L the perfect robot for the job. The “L” in its name stands for “long arm version,” which lends the RX160 a total reach of 2010 mm (6.6 ft) with a payload of 20 kg (44 lbs).

Integrated development

Stäubli’s robot controller, CS8C, is connected to the entire machine via Profinet. Programming takes place offline via the Stäubli Robotics Suite. After importing CAD models of robot, machine and gripper, a realistic simulation of robotic movements is carried

> "We don't need to worry about reliability issues or high maintenance when it comes to the Dessl Collector thanks to its core element and centerpiece – the Stäubli RX160L. Being able to test the machine's 'digital twin' in the Stäubli Robotics Suite meant a shorter startup with only minimal adjustments needing to be made."
>
> **Daniel Angerer,**
> Deputy CEO, Dessl Maschinenbau GmbH

out to determine cycle times and exclude potential collisions during development.

Being able to test the machine's 'digital twin' in the Stäubli Robotics Suite meant a shorter startup with only minimal adjustments needing to be made. Thanks to the successful integration of Stäubli's RX160L as the machine's core element and centerpiece, customers no longer need to worry about reliability issues or high maintenance when it comes to the Dessl Collector.

Stäubli's robot controller, CS8C, is connected to the entire machine via Profinet. Programming for collision control including machine simulation takes place via the Stäubli Robotics Suite.
(Image rights: x-technik)

Video
Stäubli Customer Voice
Dessl Maschinenbau GmbH

PHARMA PACKAGING

Coating under aseptic conditions

Stäubli 6-axis Stericlean robot picks up one of the diminutive sMTS devices within the ISO 5 aseptic dip coating system built by Keller to scale production.

Robot for the surface teatment of drug delivery devices

A manufacturer of drug delivery devices cooperated with a sytems integrator to find the ideal automated solution for applying a dip coating under aseptic conditions. At the heart of this highly specialized production system: a Stäubli robot.

Kindeva Drug Delivery, based in Minnesota, is a contract development and manufacturing organization (CDMO) specializing in complex drug formulation and delivery. Among the company's innovations is a proprietary solid microstructured transdermal system (sMTS) platform. The microneedle-based device is highly patient-friendly, making it ideal for self-administering abaloparatide, a biologic that stimulates bone formation for patients with osteoporosis.

Since abaloparatide is a biologic API, it cannot be terminally sterilized. Therefore the processes involved in coating and packaging the abaloparatide-sMTS combination must take place entirely within an ISO Class 5 environment. The goal was to use a fully automated system, completely housed in an aseptic isolator.

The right robot for a sensitive environment

The company turned to Keller Technology with the order to develop a fully automatic robot cell for this purpose. When choosing the right robot, the Keller engineers opted for a Stäubli TX2-40 Stericlean. A variety

of features enable these robots to operate in a Grade A environment and maintain high performance under strict aseptic conditions: A fully enclosed structure with special seals keeps airborne particles to a minimum. The robot's completely smooth surface, protected by a high-resistance coating, eliminates retention areas where antigens can proliferate. This design also enables the robot to withstand harsh VHP decontamination processes. All connections run through the base of the robot, safely outside the isolator.

High precision at commercial scale

The system Keller devised performs precision dip coating as well as primary packaging, all within an aseptic isolator. It begins when the sMTS devices are transferred into the isolator on trays, while the sterile liquid API is fed into a coating system, designed previously by Keller. The Stericlean's pinpoint accuracy is critical in the dip coating operation that follows. The dexterous robotic arm picks up the individual sMTS devices, each smaller than a postage stamp, and immerses them in the liquid API bath, loading the microneedles with the biologic API.

The robot then lifts the coated sMTS out vertically, places it back on the tray, and repeats the process at a constant speed. Once the tray is full, it is transferred to a tray sealer. The sealed trays are transferred out of the isolator, completing the sterile primary packaging operation.

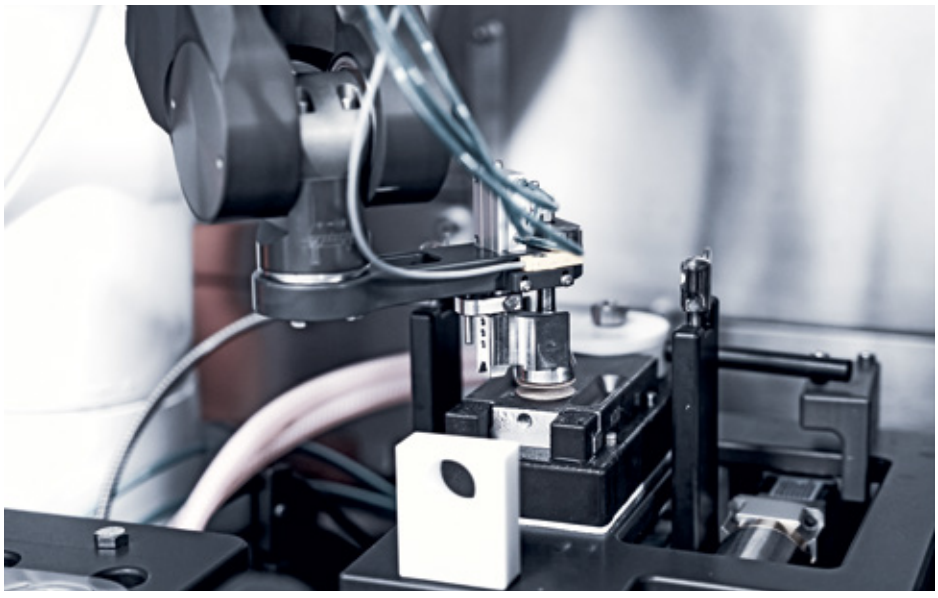
The isolator itself is equipped with a monitoring system to ensure that no septic antigens are present. It also provides laminar airflow, so the entire body of air within the isolator is uniform in velocity and direction. Likewise all system components are designed to minimize airflow disruption – as exemplified by the sleek, fully enclosed structure of the Stericlean robot. This prevents disturbances such as eddies, voids and shadows that could retain antigens.

Dip coating, reinvented

Crucially, the risks that are inherent to exposing a biologic API such as abaloparatide during dip coating are eliminated. Keller engineered and integrated its customized system into an aseptic isolator to maintain sterile conditions and shield the product from contamination. The specialized design of the Stericlean robot brings added assurance. This protects the operators, the product, and ultimately the patient.

While careful precautions are taken at every step of the production process, the automated system also delivers the high speed and efficiency Kindeva needed. These qualities have also enabled the company scale up the product for commercial manufacture. Further, the enhanced traceability provided by the robot's control software optimizes process control, which has the potential to bring long-term benefits for years to come.

Kindeva's proprietary solid microstructured transdermal system (sMTS) serves as an ideal delivery system for abaloparatide, a biologic API for the treatment of osteoporosis.



At the dipping station, the API is meticulously loaded onto the microneedles. A uniform coating on each unit results in high repeatability.

BIOTHERAPY

Shaken not stirred – robots in the cell factory

Using Stäubli robots to produce vaccines

Chinese pharmaceutical manufacturer Chengda Biotech produces vaccines that are cultured in cell factories – small trays that are shaken regularly to enable the inoculum to propagate naturally. Stäubli TX200 Stericlean robots now carry out this task in one of Chengda's new factories. This marks the first time robots have been used in this way for biopharmaceutical manufacturing in China.

Biotechnology offers new opportunities when it comes to the production of medicines and vaccines, because under specific conditions, a drug will essentially reproduce itself. Among these conditions are stable environmental conditions and processes. Maintaining them requires a high level of automation.

Liaoning Chengda Biotechnology Co., Ltd. has built a plant to manufacture the Hepatitis A vaccine at a pace of around three to four million doses per year. Stäubli's Stericlean robots play a pivotal role in their handling of cell factories.

These "factories" are nothing other than racks of trays containing 160 dishes each. Each dish contains a nutrient solution in which the "mother cells" are inoculated. During this process, the cell culture grows at a continuous rate, although the nutrient solution in the dishes needs to be changed. The second step involves adding virally

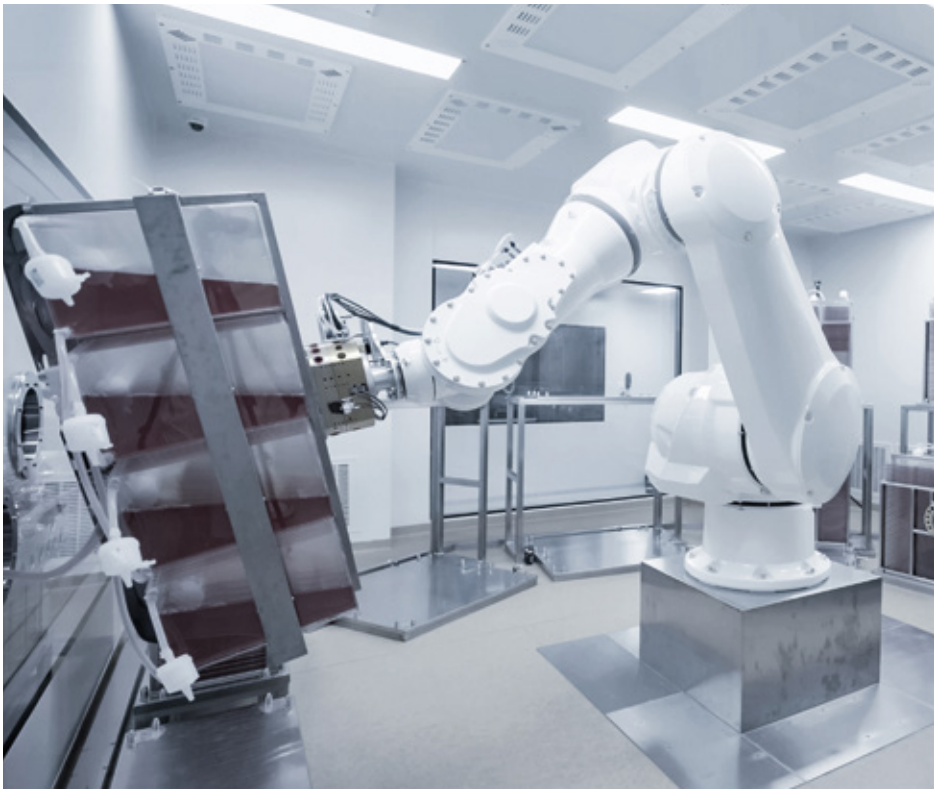
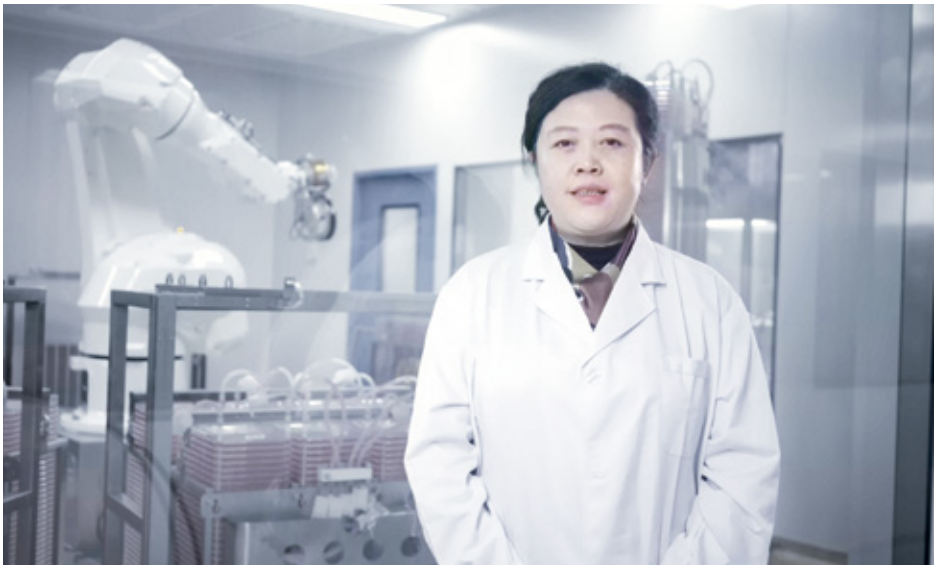


Image (left):
Stericlean robots also assist during filling and liquid changeover processes.

Image (right):
Chengda Biotech manufactures vaccines that are produced using biotechnological procedures.



"The Stäubli Stericlean robots offer advantages in precision and reproducibility, and they are the only ones that meet GMP A-level requirements. In addition, there are already many successful use cases in the pharmaceutical industry."

Zhumu Bai
General Deputy Manager, Chengda Biotech

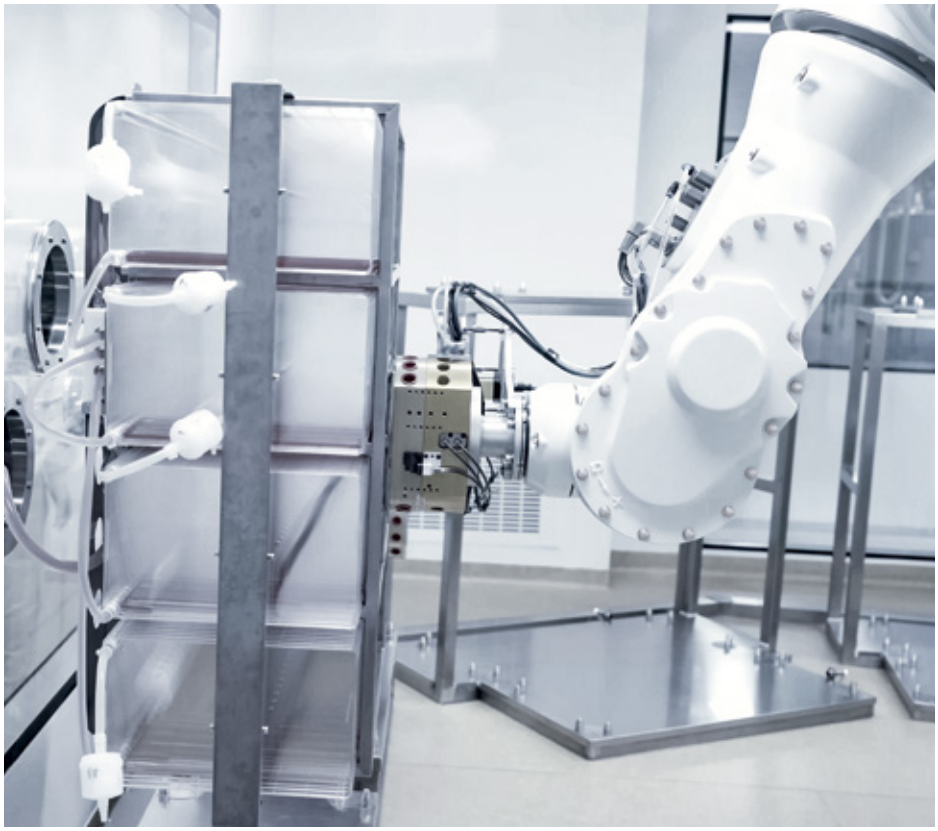
infected cells as well as a growth-stimulating medium. "Harvesting" the virus – now a highly efficient, self-propagating or "self-manufacturing" vaccine – signals the end of the process.

Stäubli's TX200 Stericlean robots are used once inoculation of the cells has been carried out and the vaccine is left to develop. Equipped with an image processing system, the robot takes the cell factory and transports it to its required location, gently shaking it to distribute fluid evenly throughout. The cell factory is then taken to a designated storage location to allow the cells to develop. During the 10-day incubation period the robot returns to the racks to gently shake and tilt them.

Highest levels of sanitation reached

One reason Chengda wanted to automate this complex process was due to the stability required when it comes to environmental conditions, including temperature. Since staff are not required to enter the workroom it becomes easier to maintain a constant temperature. This better guarantees the reproducible quality and efficacy of the end product. Additionally, using Stäubli robots allows for GMP A, the highest cleanroom classification, to be achieved.

For obvious reasons, the production environment of the cell factories must be frequently disinfected. Chengda Biotech uses vaporized hydrogen peroxide (VHP) for this process, which would immediately render



The robot docks onto the cell factories, each containing 160 trays of inoculum, all while being guided by a camera.

conventional robots unable to function. This cleaning process is, however, no match for the TX200 Stericlean robots due to a special anti-corrosion coating and their hermetically sealed outer casing.

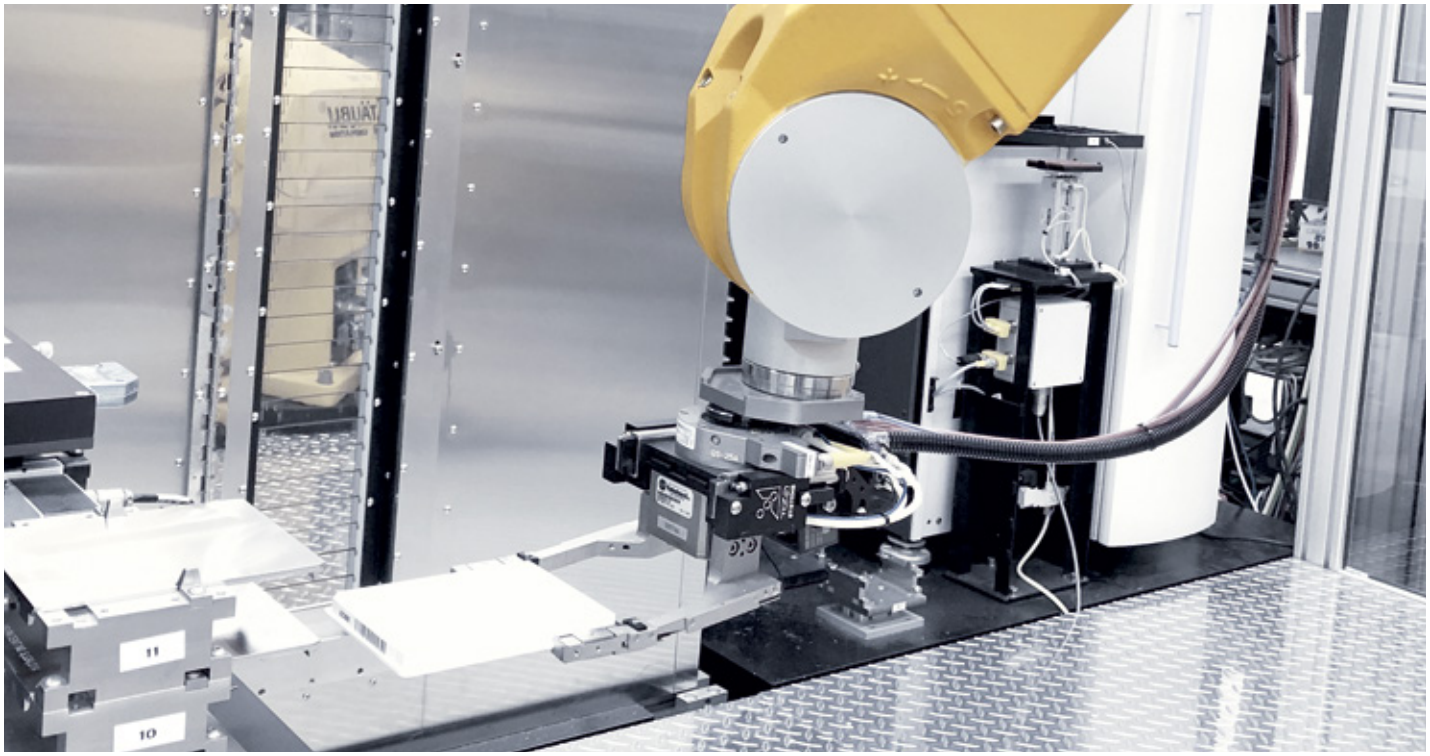
The benefits of automated vaccine manufacturing

According to Chengda Biotech, robot-assisted cell production means reduced investment and operating costs, among other things. Furthermore, the contamination risk during production is considerably lessened due to the lack of human intervention. Since a cell factory that is completely full weighs more than 100 kg (220 lbs), machine assistance would already be required during handling.

The deployment of robots is not only significantly more economic, but it also takes up less space, making the entire process much more flexible. The most important benefit, however, comes from the guaranteed high and consistent quality of the vaccine product, achievable only by means of innovative automation.

During this project, users began to place their trust in this solution as well as in the Stericlean robots. That is why three were ordered instead of two. It is the first successful application of a Stäubli TX200 Stericlean robot in the Chinese biopharmaceutical industry, and Stäubli China expects other organizations to follow suit when it comes to automation.

Video
Chengda Biotech China



Rapid screening of millions of active ingredients.

LAB AUTOMATION

Robots in search of new medical drugs

The Genomics Research Center in Taipei, Taiwan uses an ultra-high-throughput screening device to test 1536 substances in one cycle. In the center of the machine, which is used 24/7 for developing COVID-19 medicines: a Stäubli robot.

In current times there is no doubt that finding new drugs and vaccines is a crucial task for mankind. The Genomics Research Center (GRC) in Taipei is committed to fulfilling this mission – with high expertise, profound scientific knowledge and also a fast pace.

The public research institute, part of Taiwan's renowned Academia Sinica, enhanced and accelerated its drug-screening capacity as a consequence of the SARS epidemic in 2003. The Academy made a heavy investment of 300 million Taiwan dollars and acquired a professional device for the "ultra-high-throughput screening" (uHTS) of medical compounds. Using this advanced technology has already led to real positive results: With uHTS on board, the GRC developed an effective anti-influenza drug in 2007. It is no surprise and no secret that currently the GRC's uHTS factory is focused on finding remedies for fighting COVID-19. Therefore uHTS marks the front-end process of a complete drug discovery procedure.

Screening drugs by millions – 1536 at once

The machine that is screening the drugs in Taipei was designed and manufactured by

the American company GNF, a subsidiary of Novartis, concentrating on creating technologies for discovering new medicines. Their uHTS system uses a microplate – no bigger than the palm of a human hand – with 1536 drugs each in a quantity of several µl that can be screened in one cycle, taking about 70 minutes but overlapping as the next cycle can start while another one is already ongoing. All in all, more than 50 plates – 76800 different substances – can be screened each day.

Why is such a speed necessary? Dr. PoHsun Lin at the GRC explains: "According to statistics, it is necessary to search for more than one million compounds to have a chance to find a lead compound." These millions of compounds can be tested within 650 cycles (1000 0000 compounds, divided by 1536 drugs per microplate). It goes without saying that the machine is working in 24/7 mode with high speed and very high accuracy: The 1536 wells of the microtiter are extremely small.

Altogether the GRC stores up to 2 million compounds in its library, but not every project requires a complete screening. Dr. PoHsun Lin: "For the most common use, we keep around 100 microplates with 1536 compounds each in our library, including FDA approved drugs, known drugs, bioactives, small molecular, natural products and representative compounds."

In the center: One single robot – precise and versatile

A glace at the uHTS system illustrates the process: Several stations for storing, commissioning, handling and screening build a cycle with a Stäubli RX160 robot in the center. This robot type is not only fast and precise, but also very versatile because it is – as can be seen in the uHTS machine – able to fulfil different handling tasks. This is the process step by step: First, the robot takes a plate from the incubator and places it on the dispenser station. Here, protein is dispensed into the plate. In the next steps, the robot takes the plate with the 1536 drugs to a transfer station, an incubator and two dispensers, where further compounds and substances are added. Then the robots takes the ready-to-screen plate to a reader station for detection and delivers it to the station where the screening starts.

Selecting the right robot

When selecting the robot, the engineers of GNF considered qualities like speed, accuracy and availability. Another advantage is the long lifetime. The GRC acknowledges this benefit. Dr. PoHsun Lin: "Our uHTS system has been used successfully for many years, but it simply doesn't grow old. The Stäubli RX160 robot is still on the cutting edge in terms of precision and dynamics and impresses with remarkable reliability. The system delivers top performance, efficiency, and stability."

This is why it can contribute to the crucial goal of COVID-19 treatment research in 24/7 mode – and why GNF today still uses Stäubli robots for their current models of HTS and uHTS screening machines.

"Our uHTS system has been used successfully for many years, but it simply doesn't grow old. The Stäubli RX160 robot is still on the cutting edge in terms of precision and dynamics and impresses with remarkable reliability. The system delivers top performance, efficiency, and stability."

Dr. PoHsun Lin
Genomics Research Center, Taipei, Taiwan

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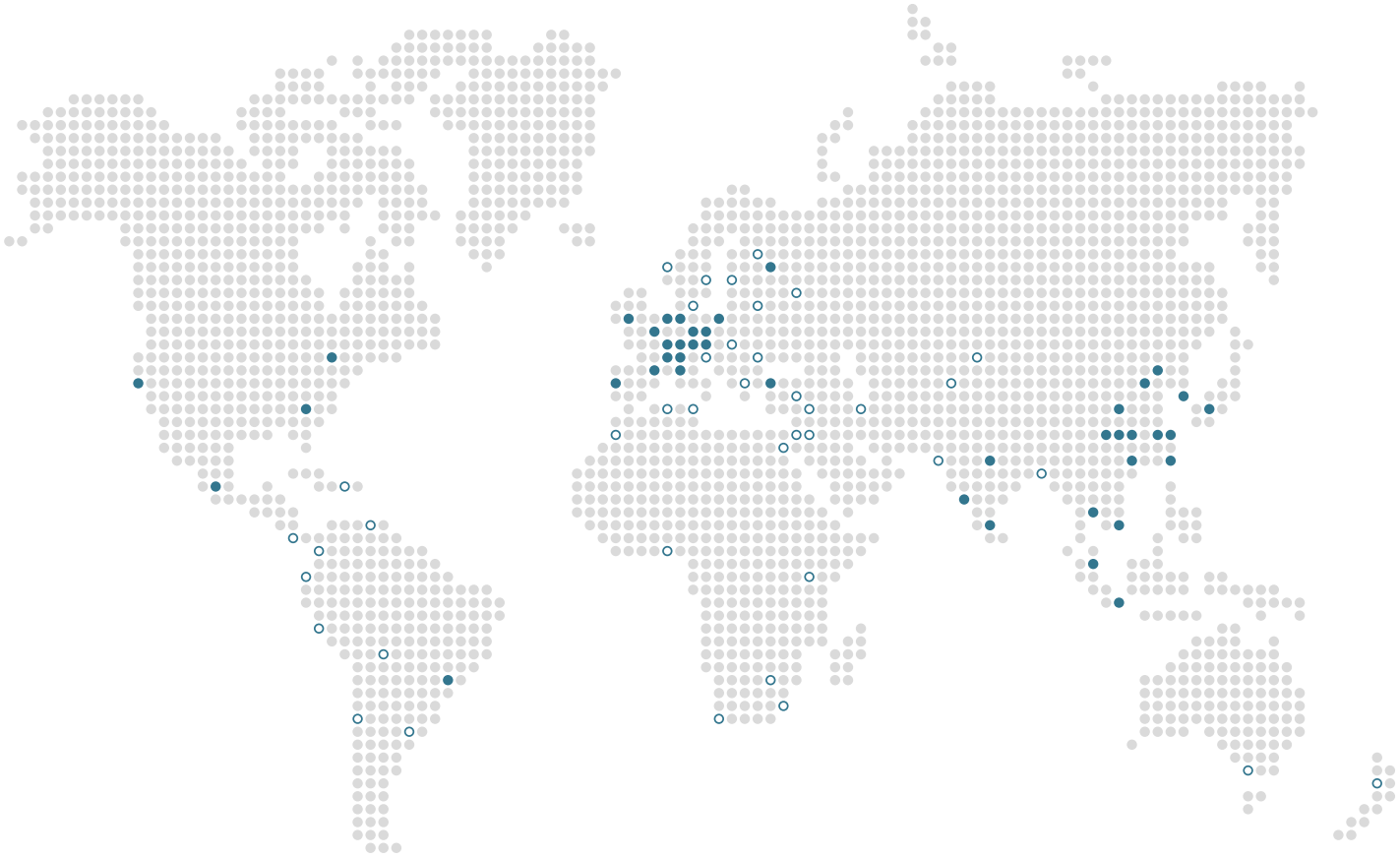

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