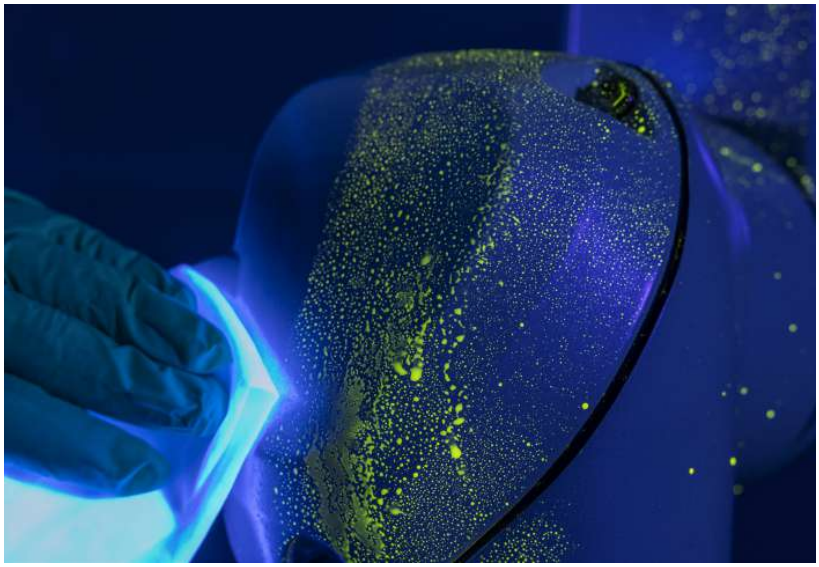
How to Make the Grade in Pharma Manufacturing

The current era in pharmaceutical manufacturing is defined by challenging market demands and stricter regulations, particularly with new, more comprehensive GMP standards codified in the EU's revised Annex 1 and updated CGMP standards from the FDA. Industrial automation pioneer Stäubli Robotics, in a show of foresight, has entered it armed with solutions to bring the efficiency of robotics to more applications while assuring compliance – and delivering the documentation to prove it.



Stäubli Robot with fluorescent tracer substance (riboflavin) and cleaning. (Source: Stäubli/Skan)

Regulations vary around the globe and are often a source of confusion. But their goals are both straightforward and universal: to avoid contamination, chiefly by minimising human intervention, and thus ensure the safety of products and patients. Separating operators from processes is the overriding theme of Annex 1, and any contamination control strategy (CCS) must make this its focus. From this unifying standpoint, Stäubli Robotics has developed a robust portfolio of pharma robots designed to reliably handle processes in aseptic areas and withstand rigorous cleaning procedures.

This mission started long before the EU or FDA set out to enact stricter requirements for aseptic processing. Stäubli Robotics is a pioneer in the field, having served the pharmaceutical industry for decades. In 2009, the company launched its groundbreaking Stericlean series, the world's first robot specifically designed to operate inside isolators and RABS. Today these robots are used in pharmaceutical and biotech labs and production facilities worldwide for a range of tasks in material handling, filling and closing, as well as troubleshooting, inspections and packaging.

Joining Forces to Meet New Challenges

In the 15 years since Stericlean was launched, Stäubli has worked with its installed customer base to learn from their experiences and refine the robot's design. The company has also cultivated partnerships with OEMs and integrators specialising in pharma to expand and adapt its portfolio of robots to handle more applications and meet the industry's changing compliance and commercial needs. The pharma community witnessed the next leap forward at CPHI Frankfurt in 2022, when Stäubli launched its next-generation Stericlean+ series, designed exclusively for use in isolators, with the flagship TX2-60.

In many ways, this is a classic story of evolution through adaptation, specifically to GMP grades and ISO classes. It is also a story of partnership. To fine-tune its aseptic robot design and help end users meet the standards of Grades A/B through D/E and ISO Classes 1 through 8, Stäubli partnered with SKAN, the market leader in isolator systems. Stäubli also sought to proactively provide customers with the validation and documentation packages they would need to prove that their equipment is compliant. SKAN proved an ideal partner for this purpose as well. Through its SKANalytix service, the company conducts comprehensive third-party testing and analysis of isolator and cleanroom technologies.

Putting Aseptic Robots to the Test

Stäubli and SKAN's collaboration involved putting Stäubli's then-current offering of Stericlean robots through intensive tests for cleanability, resistance, and movement. The object was to determine what improvements could be made to make the high-performance robots even more fit for use in cleanrooms and isolators. These tests, including actual cleaning processes, helped define the R&D roadmap for the new design, which also benefited from testing and validation by a neutral third party.

Ultimately this rigorous process would result in the development of new features for the Stericlean+ robot Stäubli was developing. But first, there was painstaking work to be done. Ensuring beyond a doubt that Stäubli's next generation of Stericlean robots would be optimally suitable for aseptic manufacturing in highly aseptic Grade A (ISO 5) areas was not to be taken lightly. The robots were evaluated inside and out against the highest hygienic standards in terms of design, materials and components.

The robots would need to operate in highly monitored fill-finish lines in the production

Engineer proceeding cleanroom test. (Source: Stäubli/Skan)

of drugs that are not only highly potent and/or toxic, but also very costly. The safety of people and products had to be absolute. And crucially, the robot's entire outer surface would need to withstand regular cleaning and decontamination with VHP (H_2O_2) in isolators. All areas of the machine had to be easy to clean and free of any gaps, surface roughness, or other areas where substances, particles or microorganisms could adhere and accumulate.

Individually, each test provided information about one aspect of the robot's design, specifically equipment cleanability, chemical and microbiological resistance, adsorption and desorption (H_2O_2), D-value, particle emissions, surface roughness, and seal tightness. Together, the tests painted a complete picture of the robots and how well adapted they were for use in isolators.

Applying Test Results to Improvements in Hygienic Design

SKAN's testing, combined with Stäubli's own, resulted in major benefits. The new data propelled and informed many aspects of R&D. Since, for example, cleanability depends both on the materials used and ease of access, Stäubli's engineers focused on simplicity of form. The robot's joints demanded especially close attention, since moving parts represent the greatest risk of particle generation. The robots would need to interact harmoniously with laminar airflow, generating no turbulence despite their rapid movements during operation to keep particles at a low threshold in accordance with ISO 5 standards.

TX2-40 Stericlean+ is designed exclusively for use in isolators with an improved hygienic design on the covers and new FDA-compliant dynamic sealing on each joint

Crucially, Stäubli obtained a much more detailed understanding of the shortcomings in its existing robots in the context of new standards and requirements for aseptic equipment. In the 15 years since the release of the original Stericlean, much has changed commercially as well. The steep increase in demand for personalised medicine and small batch production runs demands utmost flexibility. The new robots must not only handle an expanded repertoire of tasks, but also switch from one to the next with no errors or significant time loss.

The new Stericlean+ series, designed specifically for use in isolators, pushes the frontier of aseptic process automation and helps future-proof production. The range includes four six-axis models with an improved hygienic design on the covers and new pharma industry-approved dynamic sealing on each joint, as well as a new FDA-compliant coating on the entire surface, which is VHP/H_2O_2 compatible for higher cleaning performance and chemical resistance. Stäubli also offers a hollow wrist option with all cables running inside the robot to the flange.

A Validated and Documented Solution

The scientific data based on SKAN's test results is now part of the validation and documentation package delivered along with every Stäubli robot, to the benefit of machine builders and end users alike. For machine builders, it provides support for the qualification documentation of the whole

Unique hygienic robots for pharma aseptic processes

Stericlean+ series of TX2-40, TX2-60 and TX2-90.

machine, helps with global contamination risk assessment, and increases acceptance amongst end users. It gives end users greater transparency as to how the robot was developed and validated, while confirming its mechanical and aseptic capabilities and compatibility with highly aseptic ISO 5 / Grade A environments.

"Providing test results isn't something we have to do," says Rudolf M. Weiss, Global Head of Pharma at Stäubli Robotics. "It's a commitment that we're making to strengthen trust among our customers and partners." Customers now have neutral, documented results that Stäubli robots fulfill their essential role in isolators. A comprehensive and well-documented testing package adds value for the pharmaceutical industry and ultimately for patient safety.

Together, Stäubli's original Stericlean and Stericlean+ robot series have every area of the pharmaceutical production environment covered, from the most restrictive isolators in Grade A to logistics, including RABs, freeze dryers, autoclaves, various levels of inspection, and secondary packaging. They are also used in cell & gene therapy (CGT), biotherapy, API research and production, lab automation, auxiliary processes, and other areas within pharmaceuticals.

Extending the Advantages to Diagnostics

Boosted by the pandemic, as well as the boom in personalised medicine, diagnostic tests have come to play a vital role in global healthcare. In personalised medicine, they help curb high costs by enabling pharmaceutical companies to predict the effects of personalised formulations and refine them for patients. Stäubli robots are increasingly being deployed in the diagnostics segment to support the growing footprint of automation and enable efficient high-throughput screening (HTS).

In laboratory settings, robots cooperate safely with humans and take over repetitive tasks. Mobile robots are proving especially valuable here. While no mobile solution exists that is compatible with Grade A/B or even C environments in drug production, laboratories are less restrictive, opening the door to the integration of modular Stäubli robots designed for general industry. This includes autonomous mobile robots (AMRs), which help with the handling and storage of blood bags, for instance. They not only increase productivity, but also collect data that can be used to optimise workflows and traceability.

Reagent production is another key area of diagnostics where robotics is having an impact. The processes are similar to those in drug manufacturing, consisting of pick and place, filling and closing tasks. While an aseptic environment is essential in drug manufacturing, reagent production requires a DNA-free environment. The same technical features that make Stäubli robots safe and effective in drug production apply.

Bench-top cells remain the primary domain of robots in diagnostic testing, delivering safer, more reliable results. Combined with a tool changer, Stäubli robots can perform multiple tasks within a small cell, such as handling a PCR plate for a moment and then moving into vial handling. The Stericlean version is often preferred to control contamination. Both stationary and mobile robots perform these and other tasks such as pipetting and centrifuge loading. Automation is making it possible to meet demand amidst a lack of resources to manage routine tasks while relieving operators of neuromuscular problems resulting from repetitive actions. The safety of both operators and patients is assured.

TX2-90 Stericlean+

Groudbreaking Stericlean evolves to Stericlean+

The flexibility of Stäubli's standard, Stericlean and Stericlean+ robots is also a key factor: Whether in a small isolator or in a complete production line equipped with multiple robots, within highly controlled areas including freeze dryers impacted by the new GMP Annex 1, non-classified rooms, or intermediate levels where cleanability remains essential, they can manage a variety of different RTU containers, making changeovers to different formats and sizes quick and easy, thanks to the Stäubli Connectors division and its variety of tool changers. This is also becoming important as personalized medicine enters the industrialization phase with production scaling up.

CPHI worldwide attendees will have the opportunity to see Stäubli's robots in action at Stand 3T61, Hall H3.0 in the Pharma Machinery and Equipment Zone.

Rudolf-Michael Weiss

Rudolf-Michael Weiss started in the senior management at the Stäubli Robotics Division of the STAUBLI Group in October 2020. He took over the global responsibility for robotic/automation business in pharma and medical devices as Global Head of Pharma and as a Member of the Global Management Team. After his studies in Stuttgart Rudolf M. Weiss started working at Servotech in 1999. From 2001 on, he was working at Groninger where he was responsible as Marketing Director, Senior Project Manager and Sales Director. After experiences at FIMA, he decided to go back to pharma and joining Bausch+Ströbel the global leading company for fill/finish equipment 2018 he was announced to be Authorized Officer and Director Sales & Marketing.He can draw on 20 years of experience in the field of Pharma Fill / Finish.

Email: rm.weiss@staubli.com