FAST MOVING TECHNOLOGY

STÄUBLI

Third Party Testing to Meet New Guidelines for Pharma Robots

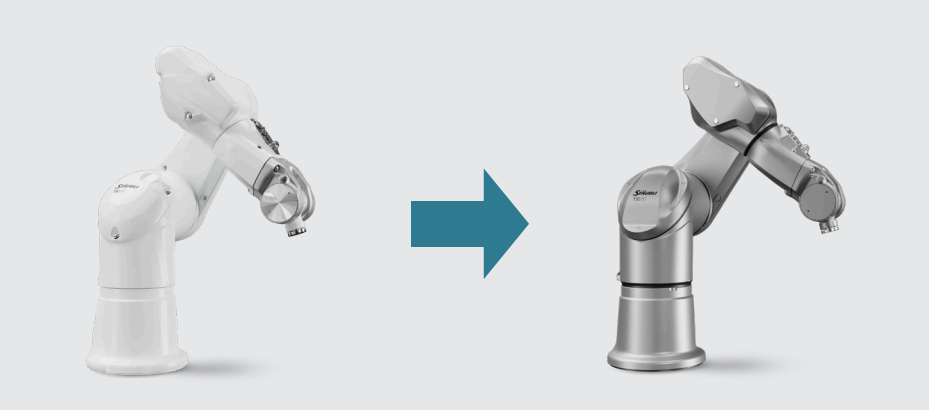
The pharmaceutical industry has been slowly but steadily shifting from a human-centric environment to a fully automated industry. Hygiene, safety, and productivity are all pushing the industry away from manual production. The arrival of the Covid-19 pandemic accelerated the change.

The requirements just got even more restrictive with the draft GMP Annex 1 revision and FDA regulations. Robots are finding their place in this sensitive area. Stäubli Stericlean, launched in 2009, was the first range to fulfill aseptic requirements, particularly inside isolators and RABS.

An Opportunity for a more complete Validation and Documentation Package

To stay in line with these new requirements, Stäubli partnered with SKAN, the world leader in manufacturing isolator systems, and specialized in pharma and aseptic environments, in August 2021. "SKAN's analytical services (SKANalytix) are helping Stäubli improve its aseptic robot design. They also provide robots with the much-needed validation and documentation package that clients ask for. We've done our homework," smiles Rudolf M. Weiss, Stäubli's Global Head of Pharma & Medical.

"Through our SKANalytix service, we provide our customers with analytical support for their questions and concerns around aseptic processing," continues Gregor Hommes, Head of Research and Strategic Business Development at SKAN. "We offer studies around all aspects of isolators, and run tests regarding product, process and operator safety with regard to isolator and cleanroom technology."



Stäubli and SKAN's collaboration has resulted in the development of new features for the Stericlean+ package that ensure that the robots are suitable for aseptic manufacturing conditions.

Pharma Industry Requirements for Robots in an Aseptic Environment

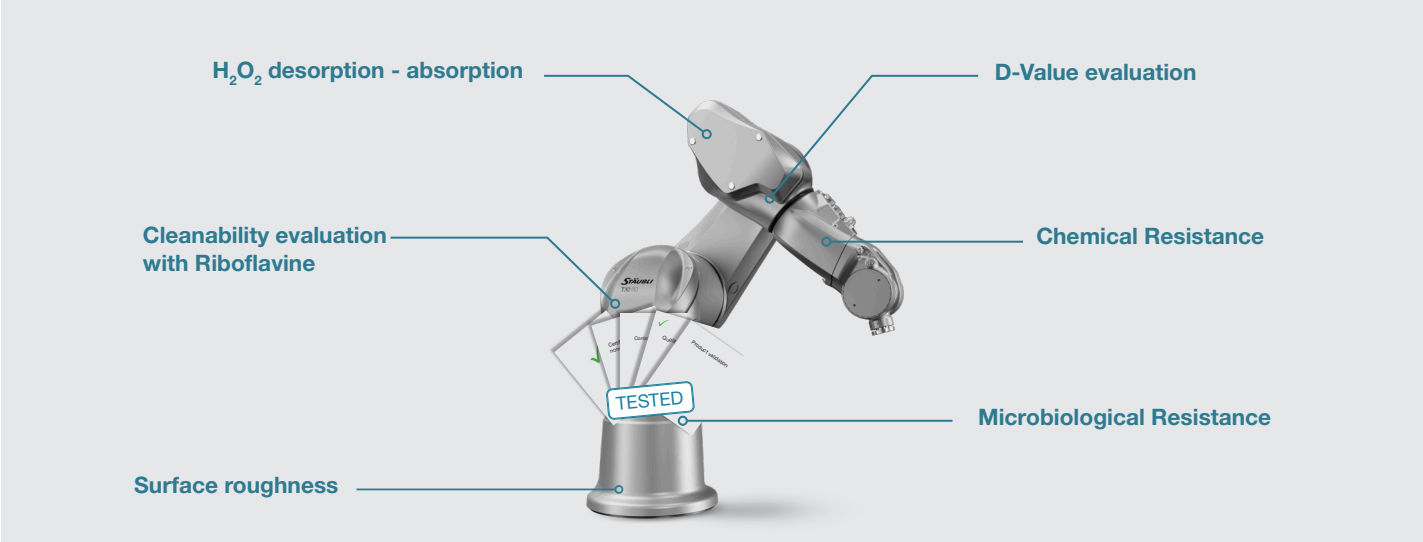
Hygienic design is a central aspect of a robot, establishing that it is suitable for working in an aseptic environment. Design specifics cover a wide range.

"There are two primary factors," states Richard Denk, Senior Consultant Aseptic Processing and Containment at SKAN, and Chairman of the ISPE (International Society for Pharmaceutical Engineering). "First is the entire outer surface of the robot. If this cannot be adequately cleaned and decontaminated, then there is a risk that the aseptic processing conditions cannot be maintained. The materials need to be selected appropriately and the design should allow for easy access. And secondly, of course, moving parts represent the greatest risk of generating particles, so special attention needs to go into the design and sealing of joints."

More specifically, there can be no gaps in joints in the robot's outer shell, where micro-organisms could accumulate and grow. Surface roughness can have an Ra of no more than 0.8µm, again to not harbor fungi or bacteria and enable efficient cleaning. The surface must resist all cleaning and surface decontamination procedures, in particular vaporized hydrogen peroxide (H2O2) which is used for surface decontamination inside isolators.

"A robot should not generate turbulence in the laminar air flow as it moves," Richard goes on. "Particles released during movement must remain at a low threshold, to guarantee that ISO 5 standards are met. And finally, a robot must be easy to clean and decontaminate: all areas have to be accessible and easy to clean. There should be no areas where substances, particles or microorganisms can build up or pool."

Stäubli Stericlean TS2-60 and TX2-40, -60 and -90 robots were run through SKANalytix's intensive tests to determine what improvements could be made to make them even more fit for a clean room or isolator environment.



Intensive Tests for Robot Cleanability, Resistance and Movement in an Isolator

Individually, each test gives information about one aspect of a robot's design. Altogether, they provide a complete picture about a robot and how suitable it is for use in an isolator. Depending on the type of test, each lasts from a few hours to few weeks. Maximilian Mittelviefhaus, Research Manager at SKAN, details the procedure behind each test.

1/ Equipment Cleanability

"We spray the robot with a fluorescent tracer substance, such as riboflavin," he outlines, "before carrying out a cleaning procedure. After cleaning, any residual fluorescence helps identify weaknesses in design, where accessibility is too low and where contamination is hard to remove and/or likely to build up." Testing can go further by a precise spiking of surrogate contaminations, and detecting them down to the nanogram-level after the cleaning procedure.

2/ Chemical and Microbiological Resistance

"These tests focus on ensuring that all materials resist a panel of commonly used cleaning and decontamination agents, including H2O2," Maximilian continues.
All materials must also be inert to bacteria and molds. A standardized set of micro-organisms is inoculated on the construction material, and their growth is monitored over four weeks.

3/ Adsorption/Desorption

Materials should not adsorb H2O2 during decontamination procedures. "When adsorption is strong, or outgassing is slow, it can result in H2O2 concentrations inside an isolator that can be harmful to the product being handled," reveals Maximilian. "The decontamination process can also become unnecessarily long. We practice standardized testing of H2O2 adsorption and desorption kinetics."

4/ D-Value Tests

A D-value in microbiology gives the time required to achieve a 1(log)10 reduction (90% inactivation) in bacteria under a given set of conditions. A low D-value equates to faster and easier decontamination. The efficiency of H2O2 decontamination can vary according to the material. Different finishings on a robot may influence how contamination is deposited on a surface, or how easily H2O2 neutralizes that contamination.

"With this test, we artificially contaminate pieces of sample materials, then decontaminate them and compare the results with stainless steel. Making up most surfaces in an isolator, stainless steel serves as the reference," Maximilian explains.

5/ Particle Emissions

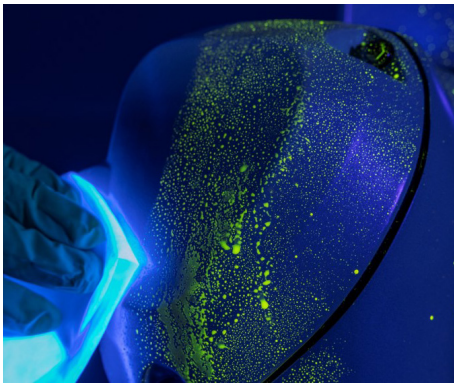
During kinematic movement, the robot should not produce any particles that could contaminate the drug being handled inside the isolator. "This test ensures compliance with ISO 5 requirements for a robot used inside an isolator," Maximilian relates.

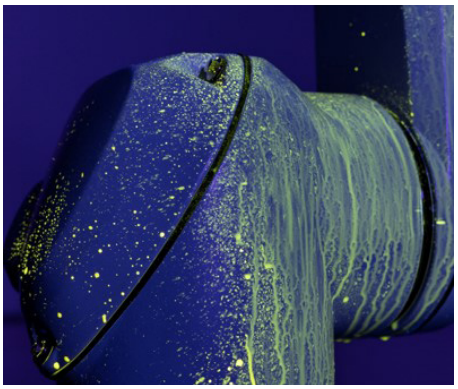
6/ Surface Roughness

"Finally," he concludes, "we evaluate the surface roughness of different spare part materials, as a component of hygienic design." Parameters for both profile roughness and area roughness are determined, "and we compare these values with those according to EHEDG guidelines, and SKAN's internal specifications."

7/ Seal tightness

"In addition to SKAN's tests, we perform our own seal tightness test," adds Renaud Doen, Stäubli's R&D Pharma leader. In keeping with IP65 requirements, seal tightness is measured during dynamic and static movement.





Applying SKAN's Results to Improve Robot Design for Pharma

Testing resulted in two major benefits. For Stäubli, greater progress in R&D design, and for clients, greater transparency about robot performance.

Renaud Doen comments, "When we compare and combine our own test results with SKAN's, we gain a much more detailed understanding of critical deficiencies in our robots. We adapted the design to create smooth, cleanable surfaces, and to improve the decontamination capabilities of all surfaces and all materials."

Richard Denk confirms: "This information helps to improve robot design. The testing is very useful in validating that implemented changes have had a beneficial impact on the suitability of the robot for its intended use."

As for Sébastien Lagarde, Global Pharma and Medical Market Leader at Stäubli, "This approach supports the change in our communication. Clients now have fully transparent and neutral proof about a robot's mechanical and aseptic capabilities. They can make up their own mind about the value of our robots."

Microbiological, adsorption and desorption, and D-value tests are all important for clients. This scientific data is now part of each robot's validation and documentation package, that can be delivered with the robot. "Since cleaning procedures may differ between customers," Sébastien acknowledges, "the tests make it possible to recommend cleaning methods that are adapted to different equipment, activities and required cleaning thresholds."

"Providing test results isn't something we have to do. It's a commitment that we're making," Rudolf Weiss clarifies, "to strengthen trust among our customers and partners." Clients now have neutral documented results that Stäubli robots fulfill their essential role in isolators.