

Pharma Flash

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EDITORIAL

Robotics: The key to intelligent production



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Industry 4.0 and the accompanying digital transformation is one topic that is dominating debate and activity in the industrial environment. As a manufacturer of high-quality robotics solutions, Stäubli are making great steps towards the Smart Factory which, in the pharmaceutical production environment for example, will soon also incorporate predictive maintenance concepts. Other industries will also start to undergo similar changes as the pharmaceutical sector in the coming years, and this is a change that we are living through with our customers. Trends such as aging demographics, ongoing globalization and personalized medicine are key issues on the agenda. Digital technologies will make lasting changes to the medical and healthcare industry, to the extent that diseases such as cancer may one day be efficiently combatted and general life expectancy increase.

With more people come the increasing need for more medicine and with this the added requirement for it to be personalized. The demands raised with personalization include the need for more package sizes and for these to also be individual. In the event

that smart drugs such as Alzheimer's medicines were equipped with sensors/individual barcoding, this would change the entire production process. These former large batch production lines will be replaced by combined systems and the whole production chain will shift its focus towards the individual patient. Suppliers from mechanical and plant engineering will be brought in to profitably integrate their own digital advances into the customer-side automation of the pharmaceutical companies. No area is more associated with robotic solutions than automation, whether in sensitive laboratory work with cell cultures or handling heavy secondary packaging. As a globally established manufacturer of versatile robots for the pharmaceutical industry, Stäubli are already shaping the future of the pharmaceutical industry today.

Christophe Coulongeant
Executive President Robotics

HOSPITAL AUTOMATION

How ARxIUM meets the requirements of the future



Hi-tech with minimal footprint:
the RIVA™



Video

Stäubli guarantees high precision of the compounding process and a long service life. The robots are virtually maintenance-free and optimise even the smallest workspaces.

The aseptic preparation of drugs such as infusion solutions is one of the more complex tasks in pharmaceutical dispensing. In addition to creating the right conditions for production, the right technology for automation of the process has to be identified and implemented. ARxIUM is a multinational company that offers clinics and pharmacies around the world a highly efficient automation solution for the filling and compounding of infusions that meets the highest standards in terms of quality and quantity. RIVA™ is

a fully automated infusion compounding system that incorporates a TX60L robot arm. The pioneering technology that has gone into RIVA™ means that it is already future-proofed to meet the regulatory requirements of tomorrow's pharmaceutical industry with regard to safety, efficiency and, above all, precision.

Automation is on the rise and Industry 4.0 is steering the way ahead. ARxIUM has set out to establish a technology that would be synonymous with Pharma 4.0 and be able

to operate within ISO Class 5 or higher. As a leading developer of automation, inventory, workflow and consulting solutions for pharmacies, the company has always set the technical bar high. Positioned with headquarters in North America and Canada, ARxIUM has made a name for itself by embarking on new and innovative ways to achieve quality, flexibility, speed and productivity. One important component of this has been a Stäubli robot which, in this case of the RIVA™ production system, is more specifically a Stäubli TX60L. As a

fully hydrogen-peroxide-resistant machine, the TX60L is not only equipped with special gearing but also has specially treated surfaces. Even more significantly, the enclosed structure of the Stericlean model and its IP65 credentials made it the perfect choice for the demands imposed by ARxIUM on the robotics solution for the RIVA™ compounding system.

In its central role on the production line, the Stäubli TX60L Stericlean robot transfers the products via different stations within the RIVA™ compounding cell. It utilizes the space and contributes to the smooth running of the RIVA™ cell during a three-shift operation. Stäubli is the only robot manufacturer to equip its machines with gearboxes that are manufactured in-house. For ARxIUM, this meant a significant reduction in maintenance costs with an associated extension of service life. Durability and advanced technology were key requirements for ARxIUM, even if changes are made in the future to the cell design. This well-established robotics solution can be adapted to any circumstances, the TX60L robot arm can be floor, wall or ceiling mounted, and

“So far, RIVA has produced millions of infusions and hundreds of thousands of sterility tests without error.”

Dr. Niels Erik Hansen
President and CEO of ARxIUM
(Source: Press release)

the scope for reconfiguring the cell is virtually unlimited. Using a robot to automate a repetitive and complex process is the modern way of doing things, also in this specific instance, it reduces the risk of error or contamination in the manufacture of syringes and infusions. The success of the system speaks for itself: as to more than 50 TX60L robots plus controllers have been installed by ARxIUM alone. The number of infusion doses so far compounded on RIVA™ systems is an impressive 9 million. The RIVA™ robotic cell has proven so successful with some customers that a second and often third system has been installed and is now delivering excellent service.



Modern technology: From robot to user level.
A chemist works out the production parameters.



Sensitive handling calls for highly developed gripper tools.

ASEPTIC FILLING

Continually running: Robotic modules



Room to work in even the smallest cell: two Staubli robots in one module.

In the future, pharmaceutical manufacturers will have to make their Pharma 4.0 production processes even more flexible in order to remain competitive. With the upgrade of the VarioSys production system, machine manufacturer Bausch+Ströbel is already responding to the demand of the pharmaceutical industry for space-saving systems that can be quickly converted to other packaging and medicines.

In order to implement the concept, the Bausch+Ströbel design team were looking for a robotics solution that could become part of a complex and modular design. The aim was for the finished machine module to be capable of opening tubs and de-nesting these ready-to-use (RTU) vials in a fully automated and smooth process. To ensure this the engineers of this highly reputable company opted for proven Staubli technology, the TX2 Stericlean robot. The compact

TX2 in combination with the KSF5105 bulk fill-and-seal module provides the ability to fully open tubs, de-nest, fill, close, crimp and stack RTU vials. Thanks to the small footprint of each robot and the extensive reach of their arms, the module occupies a space only 4 meters in length. In addition, the customer can process the nested vials with 100% in-process control (IPC) at full machine output (up to 60 tubs per hour). The Stäubli TX2 that has been integrated in VarioSys is part of an aseptic and toxic fill-and-seal process with state-of-the-art drive and control technology.

VarioSys is an innovative production system in which custom-fit, slimline modules are connected to an isolator system. The system uses a lock-and-key principle, ensuring that the right machine module is connected to the isolator and enables operator safety during aseptic work process. The Stericlean technology of the Stäubli robot is contributing to creating a diverse range of applications in an innovative production process, from the initial clinical trial to the production of complete batches.



Video

The integration of a Stericlean robot arm contributes to safe aseptic production (Class A) in clean rooms, even where toxic products are involved.



Small batch production of the future: compact, mobile modules with integrated robot.

“For us, VHP resistance was important because they are used in the isolator. We also appreciate our strong and constructive working relationship with Stäubli.”

Lukas Bindewald

Product Manager for VarioSys at Bausch+Ströbel

Where isolators are used, companies place even higher demands on robots. The engineers at Stäubli have therefore built the Stericlean robot series for optimal cleanability. They designed it to combine maximum arm reach with minimum footprint and enclosed all electrical connections and supply lines inside the arm. It's this precise detail that made Staubli's Stericlean robot range the ideal solution for Bausch+Ströbel.

The machine manufacturer has developed modern machine modules that impress not only in terms of high dynamics and increased productivity but also ease and speed of cleaning. Wherever isolators are used, it is not uncommon for highly toxic substances to be present, which requires sterilization and cleaning at frequent intervals. Not every construction material can withstand that sort of treatment. The Stäubli Stericlean robot arm integrated into VarioSys is a good example of this germ-free process, with a large number of systems that can withstand this Vaporized Hydrogen Peroxide (VHP) sterilization.

On request, Stäubli can supply arm variants with a special surface treatment that is designed to withstand the extreme stresses and strains of operating in an aseptic processing environment. The robots fully enclosed design complies with IP65 pro-

tection classification and the electrical connections are concealed under the robot pedestal. The plant engineers positioned the TX2 robot arms in the cell in such a way that they are never above the object they are handling, which results in an optimal laminar airflow. The Stäubli robot is an integral part of the VarioSys systems and contributes significantly to stable, precise, safe and quick processes.



A modular system allows variations; modules can be combined and, if necessary, supplemented by sterilization tunnels.



The nature of the challenge: getting a firm grip on delicate products.



Flexibility even with different seals.

PACKAGING GLASS AMPOULES

The TX60 takes center stage

Whenever glass is used as a primary packaging material in pharmaceutical production, it requires delicate handling. The senior management at Nordfels were looking for an automation solution that could package glass vials in 100-unit lots in cardboard boxes. The filled ampoules were subsequently to be labelled, packaged and then removed from the line. For Stäubli and Nordfels, there were two different sets of criteria that were crucial in selecting the right robot. It had to assure the handling of the complicated gripping and handling processes and also be capable of sustaining high performance levels.

The planning team decided on the TX60, this six-axis robot arm met the specified parameters, with maximum efficiency and minimum space requirements. Their decision was further reinforced by the large number of first-class reference projects in the pharmaceutical industry. All robots of



Precision is a must: gripping process at the syringe nest.



Protective spacer between the vials.

“The hygienic design of the Stäubli machines makes them the benchmark in medical and pharmaceutical applications.”

Bernhard Schaubschläger
Project Manager at Nordfels



Maximum freedom within minimum space: The robot seen from above.

the TX series comply with ISO cleanroom Class 5. The media lines of the TX60 run inside the arm and the cabling enters from below through the pedestal.

The designers positioned the TX60 robotic arm as the central element of the packaging line. The glass ampoules are fed to the plant via a ten-lane accumulation conveyor. The TX60 picks up a complete batch of 100 glass ampoules in a single pass and places them in a carton. In terms of control technology, a lot of expertise has gone into this process. Before the ampoules can be picked up, the robot must retrieve a cardboard lattice with 100 slots from a magazine and gently and precisely place it over the 100 ampoules, one ampoule per recess. This cardboard spacer ensures damage-free robotic handling of the fragile glass elements.

Complex gripping technology

The gripping of the ampoules in their cardboard protector posed a problem for the system engineers. The glass of the ampoule has a predetermined breaking point, which makes sensitive robot handling mandato-

ry. Tests had shown that a vacuum gripper solution did not work with sufficient accuracy. As an alternative, a mechanical gripping system was developed for the TX60. Thanks to this device, the Staubli robot is able to grip the glass ampoules together with the cardboard lattice in a reliable manner and place the entire batch quickly but carefully in the carton without damaging the contents.

Automated stations on the linear conveyor line are responsible for the feeding and unfolding of the cartons and cardboard separators. After the TX60 has gripped the ampoules and passed them on, the next stage is integrated quality assurance by means of a vision system. In a final step, foam padding is placed on the ampoules and the technical information is enclosed and then the carton is closed, weighed and labelled. The decision in favor of the TX60 was justified when the developers were asked to implement a control system with a user-friendly operating concept. Today, a touch screen allows easy access to all essential functions. Employees without ro-

botics expertise can operate this complex system with confidence.

The complete system is made of stainless steel, the TX60 connector is concealed under the base. Furthermore, all the cabling as far as Axis 5 runs within the arm. The innovative packaging line impresses by virtue of maximum availability and meets all requirements of the end user.

HIGHLY AUTOMATED CELL CULTIVATION

The next big thing: Cell production

Whenever drugs are produced by genetic engineering, the one criterion that really matters is that the quality remains consistent. With regard to the manufacturing process, this places the highest demands on automation specifications. It is not a simple formula that is being used, but rather living systems. Once a company has selected the appropriate line in cells and succeeded in producing them in the laboratory, the process can be scaled up to series production.

TAP Biosystems, part of the Sartorius Stedim Biotech Group, develops and manufactures systems that automate cell culture and fermentation processes for biopharmaceuticals, regenerative medicine, and industrial biotechnology. This is managed without separation – the laboratory procedure can be scaled up in a plant they have called Cellmate. The proverbial linchpin of Cellmate is a Stäubli robot, the cleanroom TX60 CR. It is the key to success, because it performs a variety of tasks including the sowing of the cells, the enzymatic and mechanical harvesting and the rinsing of the cell plates. The TX60 CR handles the change of medium, the mechanical removal of the crop and the filling of the bottles with gas.

The processes and technology have since become so well established that the TX60 CR robot arm is a key component in 90 systems that are currently operating in production and research worldwide. The broad spectrum of applications is testimony not only to the innovation of Cellmate but also

to the quality of the Stäubli robot. In addition to cell cultivation, Cellmate is also used for high-speed screening, tissue engineering, therapeutic proteins, gene therapy and veterinary vaccine production. The six-axis robot was built to comply with hygienic design requirements and is now used worldwide in the manufacturing of pharmaceuticals. The cleanroom robot integrated into Cellmate handles all samples and liquids sensitively and with extreme accuracy. The TX60 is perfect for this task. It was designed to mimic the movements of the human arm in terms of speed, fine motor skills and flexibility. For TAP Biosystems, the TX60 CR was the ideal solution for reproducing the



Chemist in protective gear working at a Cellmate with robot.

gripping and processing that had previously been carried out manually by a chemical technician. The TX60 CR performs smooth movements, while ensuring the quality of the organic products.

The technology behind the smooth action is backlash-free reduction gearing in combination with a torque control that allows power to be gradually applied at each joint. The smooth and wipeable sealed surfaces of the cleanroom robot can be cleaned easily and quickly between cell types, which make for greater effectiveness. The plant manufacturer opted for Stäubli because the PC-controlled robot arm can be easily reprogrammed and modified. Companies benefit from this feature, even when no final decision has been taken regarding which cell line is to be produced or where the process still needs to be adapted. The operator can readily save the motion profiles of the robot and store process variables such as volume, temperature and timing. The fact

“Our customer was very specific on the performance criteria of this automated system.”

Richard Archer
CEO

(Source: <http://laboratorytalk.com>)



Video

that a chemical technician can operate the fully automated Cellmate relatively easily after only a short course of training together with the scope for adapting parameters dynamically represents a major step in the direction of greater operator safety and increased efficiency.

Cell production must be absolutely vibration-free. The TX60 mimics the movements of the human arm and contributes to the safety of the staff.



Cell cultures are a highly sensitive product.

ADVANCED ASEPTIC PROCESSING

Robotics for the efficient automation of RABS



The sleeve-glove system that is characteristic of RABS (picture left) allows technician access (picture right).

Today, robots are an integral part of RABS (Restricted Access Barrier Systems) and isolators. Stäubli meets the high demands of Advanced Aseptic Processing (AAP) with its TX range, available in Stericlean and Humid Environment (HE) versions. The robots, which are specially designed for use in wet rooms, are enclosed and compliant with IP 65 protection class. They can be readily reprogrammed and adapted to alternative tasks; integrated tool change systems enable automatic exchange of gripper. The TX60 Stericlean robots, which are integrated into the RABS-specific fixed machine casing, meet the requirements of Class 100 (ISO 5). The doors to the ultra-sterile work environment are locked, and human

involvement is therefore exclusively by means of permanently affixed gloves. The robotic systems are also highly valued for use in isolators where they are a vital safety feature in critical areas of aseptic production. In isolators, their enclosure becomes a protective barrier for the TX60 Stericlean.

The TX series allows manufacturers to clean and sterilize AAP production systems to the highest standards using isopropyl alcohol as well as sporicidal agents or Vapor-Phase Hydrogen Peroxide (VPHP). This is made possible by the internal cabling with moisture-shielded connectors in the robot base and the stainless-steel surfaces in combination with special coatings and gaskets.

PACKAGING OF PARENTERAL ITEMS

Heavyweight machine for safe handling

It is not always sensitivity that is at issue in the handling of products. For example, chemicals giant Bayer needed a robot with a nominal load capacity of 100 kg as part of the automation solution for its parenteral goods line. The task for this integrated robot at the end of the bagging and packaging line was to handle large metal trays. The heavy trays enclosed by a steel frame hold 24 bags per tray and impose tough demands on robotics and gripping tools.

The TX200 was chosen because in addition to the tray it can also bear the weight of the bags and the sturdy gripper tool. The additional components for this fully automated process are two RX160 robotic arms. After they have deposited the bags on the tray, this is picked up and carried away by the TX200. Bayer made specific demands of the robot controller in terms of flexibility, namely that the replacement of one tray with the next should be smooth and uninterrupted to ensure maximum performance and flexibility in filling. This was achieved through the use of a CS8C HP controller, which now directs the entire process.

The fact that the TX200 and the RX160 work perfectly in combination and that they are both cleanroom compatible was another strong argument for equipping the parenteral goods line with Stäubli technology. All robots have a compact design and enclosed surface structures, thereby considerably facilitating the cleaning process. The combination of the TX200 and RX160 and the common control system is part of



Seen here, the TX200 picking up a full tray.

a solution concept that will keep pace with future production demands. With its maximum load capacity of 150 kg, the TX200 also offers the option of increasing parameters such as bag volume or weight without jeopardizing stability of the process.



HANDLING OF SYRINGES

Separating and reuniting

Ciseo S.A. of Belgium was looking for the right robots for its new, fully automated manufacturing plant. The management specifically wanted cleanroom-approved machines to play a central role in the production process for separating and filling syringes. They opted for two TX60L CR (designating Clean Room) robots, a model that already has an excellent track record in many comparable applications in the pharmaceutical industry worldwide for its assured handling of sensitive products. The case for the TX60L was strengthened by the customer's specification regarding the number of cycles: the robots in the twin-cell system were required to handle a daunting 600 units per minute! Plastic containers arrive at the first cell, each holding a tray of 100 empty syringes. The first of the two TX60Ls has the job of picking up the tray with a vacuum gripper in a single smooth pass and transferring it to a feed point where it is approached by the second robot

equipped with a special gripper which lifts out the 100 syringes to place them in rows of tens on a linear conveyor.

“Stäubli is just as flexible in responding to our requirements as we are to the wishes of our customers.”

Grégory Reichling
CEO

The robot then places the syringes in batches of ten on a linear conveyor belt which takes them to be filled. When this highly complex process has been completed, the other TX60L operating in parallel and in reverse order returns the now full syringes in batches of ten from the linear conveyor to the tray.

Its ability to handle vaccines and glass syringes was just one reason why Ciseo chose the Class 5 approved and ISO 14644-1 certified TX60L. The enclosed casing of the six-axis machine and the internal routing of the cables satisfies all hygienic design requirements. The system design team were

Picture left:
Full-on view of robot
with gripper tool.

impressed by the fact that all connections can be concealed under the robot pedestal. Taken together with the compact design and the ability of the TX60L to use its six degrees of freedom to optimal effect in the smallest of spaces, this argument ultimately proved decisive. The fact that Stäubli robots already have a high market penetration in the pharmaceuticals industry made them the logical choice.

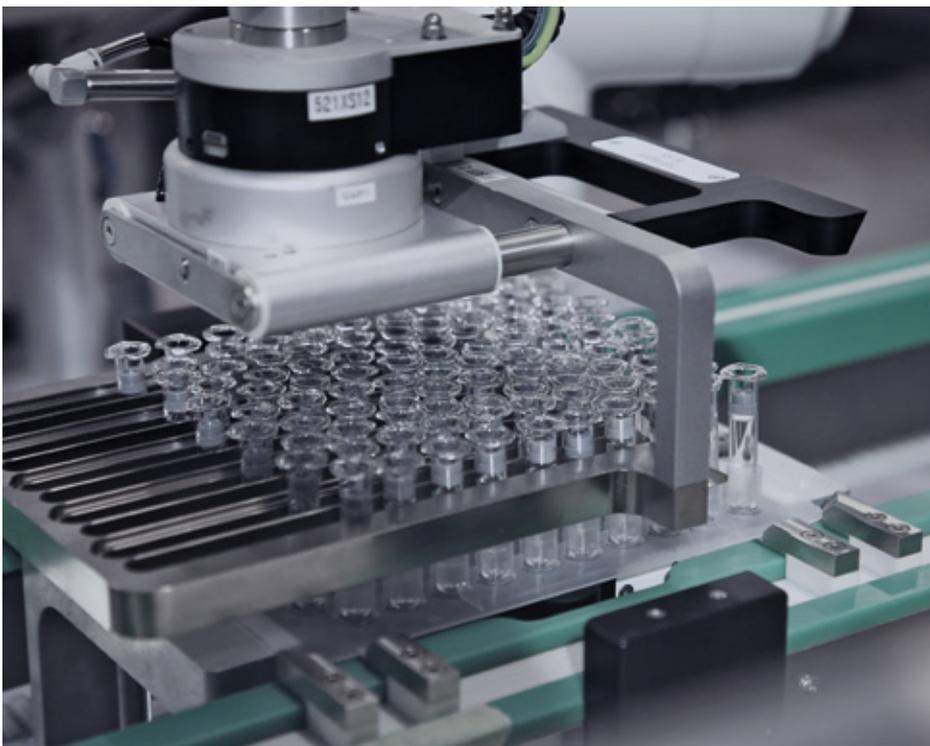
Apart from the ultra-compact design, one very important consideration in system integration was the absolute precision required for positioning the tool between the delicate ampoules, especially with the high speed and short cycle rates at which robots work. In the case of the Ciseo system, the design team were impressed with the TX60L's repeat accuracy of 0.03 mm, because there were two issues that were crucial for the technical implementation: compliance with regulatory requirements and level of performance. The designers had focused on a solution that was viable only with the use of high-speed robots – a format change that

could be effected in only ten minutes. Consequently, the TX60Ls, not only contribute directly but also peripherally to the performance of the syringe filling line.



Video

The TX60L combines the advantages of sensitive gripping processes and high cycle rate to produce an efficient manufacturing process.



Absolute precision is required when positioning the tool between the delicate ampoules.



Despite their minimal footprint, the robots make full use of their degrees of freedom.



High-speed and high-precision gripping of a batch of ampoules.



● Stäubli Units ○ Representatives/Agents

Global presence of the Stäubli Group

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