Automation upgrade

Robotics solution for pharmaceutical production

In general industry, robots are typically defined by their reach, payload, and speed needed to achieve the desired cycle times for production. Pharmaceutical manufacturing is more exacting, and as such, additional features must be taken into consideration. Principally these include cleanability, compatibility with decontamination media and processes, and particle emissions as defined by cleanroom classifications.

We see four distinct levels of requirements for pharmaceutical production equipment, including robots, in different production areas. The first and most restrictive area, namely closed environments within isolators, is critical and reserved for highly aseptic needs. Here automation equipment and robots that comply with VHP decontamination procedures have been the norm for decades. The second area, also considered sterile, allows limited manual interventions inside RABs or Grade A/B, where product containers are still open and the risk of cross-contamination remains high. H2O2 is used to mitigate this risk and all equipment must be selected accordingly.

In the third area, typically Grade C, robots handle closed containers for inspection and secondary packaging. Cleaning with alcohol wipes is employed here, and limited human intervention is allowed. In the fourth area, dedicated to final packaging and logistics, the environment is comparable to that of a standard factory, although appropriate cleaning measures must still be taken in pharma.

Robot sales data reveal some eye-opening trends. We have seen marked growth in the number of pharmaceutical robots – about 70% – deployed in the third and fourth areas, with the remaining 30% in the sterile areas. The same growth pattern is expected in the coming year. And, in a comparison of robots procured for existing plants versus new ones, we see a clear trend in favor of upgrading automation in existing production lines.

Robotics is well established in containment isolators

The automation of fill-finish tasks is recognized as a must, and this is unlikely to change. The trend toward gloveless isolators will encourage the wider use of six-axis robots for both repetitive and unplanned tasks. The volume of robots sold in this area will continue to grow in response to demand in small batch production, driven in large part by personalized medicine. Biotherapies developed in the early 2000s will reach certification as well as industrialization in the coming years. Manufacturers will need to be prepared.

Another requirement that will encourage the pairing of isolators and robots is the call from regulatory authorities for R&D and clinical trials to be conducted in the same conditions as drug production. This is expected to lead to a proliferation of small isolators and related equipment, including robots.

Grade A (ISO 5) Robotics in containment isolators. The trend toward gloveless isolators will encourage the wider use of 6-axis robots for both repetitive and unplanned tasks.

GMP Annex 1: Automation for loading and unloading freeze dryers

The revision of GMP guidelines is leading to new automation opportunities in pharma. This can be seen in the set-up of production lines, particularly between fill-finish and freeze drying, where containers remain open and the risk of contamination remains high. When a new factory is set up, filling and freeze-drying stations are usually placed next to one another. Existing plants have additional considerations, as this Grade A area needs to be upgraded in 2024 to lessen human intervention. Because each plant is unique, robots are preferred for this upgrade due to their flexibility. Robots easily adapt to existing equipment and different containers. And depending on the overall integration, they are generally more cost-effective.

There are also space considerations related to the way vials are loaded, which can vary from loading the full tray into the freeze dryer to pushing the vials into a ring. There are always empty rings or trays as well as racks to manage, and robots tend to be more compact than specialized machines.

While the complete solution should be designed to avoid glass-to-glass contact, the movement of the robot should also be optimized in a way that keeps the liquid stable and avoids sloshing. The challenge of anti-sloshing is common when using robots in isolators for filling processes. The entire line up to the freeze dryer must ensure the stability of the liquid, limiting sloshing to the deposit of the vial's contents onto its interior walls at most, which creates a milky effect after lyophilization.

The automation of loading and unloading processes also depends on the type of freeze dryer, particularly its doors. This factors into the robot's reach requirement. It may need to access all four sides of the machine or only one entry point, as with a so-called "pizza door" freeze dryer. In some cases, a linear axis in addition to six-axis robots can be used to enable accessibility.

There is a compromise to be made between the complete system's footprint and the cycle time to guarantee the cleanability of the equipment near the robot. Indeed, the robot tool used depends on the loading process, which may require the addition of an actuator to push the vials from the entrance of the freeze dryer to the back. This would enlarge the tooling on the wrist and magnify its impact on laminar flow.

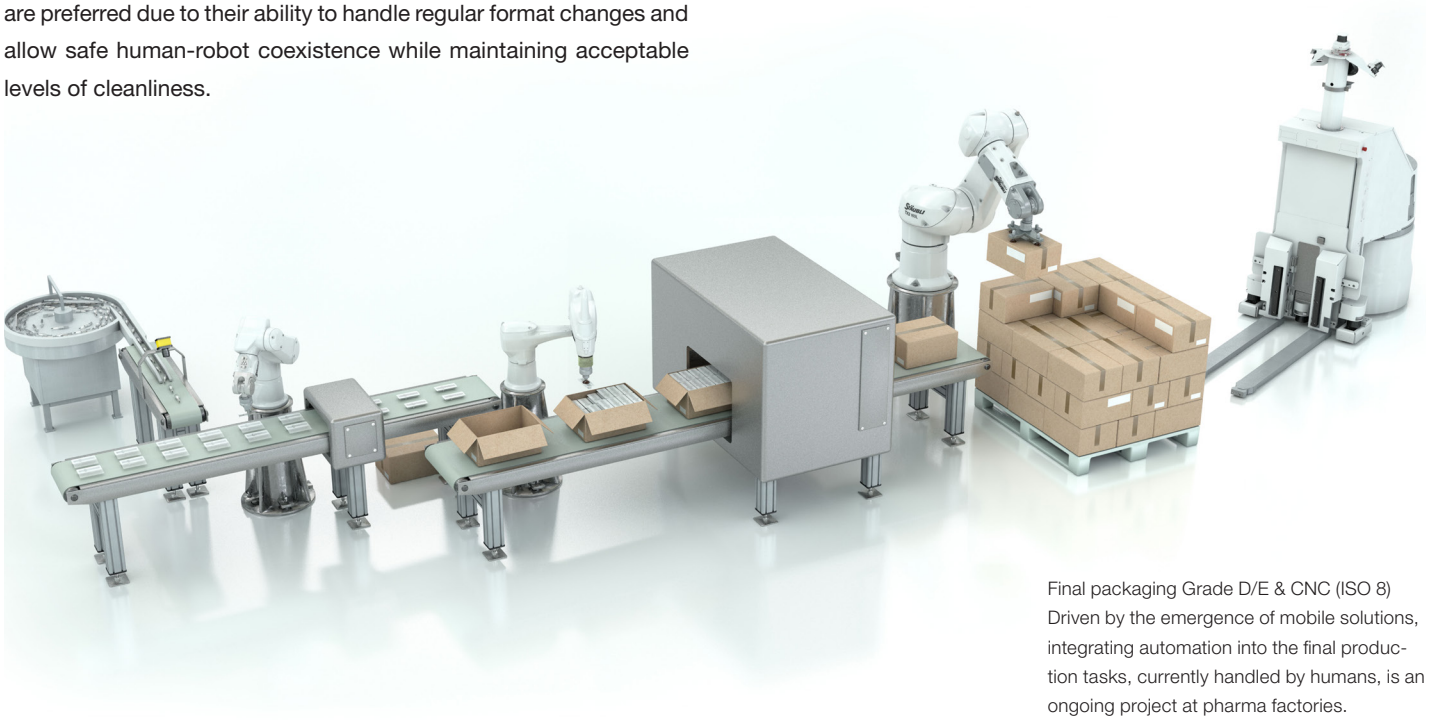
While automated loading and unloading is fairly common in factories, whether using standard or custom freeze dryers, the way vials are transferred from the isolator to the loading system poses a major challenge for many in the industry. Therefore, it warrants special consideration in an automation upgrade. Laminar flow and accessibility for maintenance must be guaranteed, and depending on the distance between the isolator and freeze dryer, conveyors are less than ideal.

As an alternative, mobile robots and automatic guided vehicles (AGVs) are on the minds of all plant managers. The development of a Grade A mobile solution is expected. The success of this approach would require sufficient space on the factory floor. Since trays cannot be stacked, they would need to be transported individually by AGVs. High production output would be maintained by multiple AGVs feeding the freeze dryer with the ability to cross one another unhindered.

Grade A/B (ISO 5) Existing pharmaceutical production lines reveal key trends in automation. Therefore, automating transportation from the end of the fill-finish line to the freeze dryer is currently a major focus of automation upgrades.

Loading and unloading – an endless cycle at the intermediate level

With regard to automation upgrades, the third production area, inspection and secondary packaging, offers big opportunities in pharma factories for various reasons. Europe and America have a lack of workers, and people who work in this sector often suffer from muscle problems. Containers such as Akylux boxes do not facilitate gentle movement. Automation for the endless loading and unloading of machines such as washing machines, inspection machines, and secondary packaging is a priority for investment in factories. Robots are preferred due to their ability to handle regular format changes and allow safe human-robot coexistence while maintaining acceptable levels of cleanliness.



Final packaging Grade D/E & CNC (ISO 8)
Driven by the emergence of mobile solutions, integrating automation into the final production tasks, currently handled by humans, is an ongoing project at pharma factories.

From automation upgrade to mobility upgrade

Driven by the emergence of mobile solutions, integrating automation into the final production tasks, currently handled by humans, is an ongoing project at pharma factories – and the wish to move directly from an automation upgrade to a mobility upgrade is tempting. While cleanable solutions are not yet on the market, the end-of-line production area (logistics and secondary packing) is the first to be considered. It is important to keep in mind the real value of adding mobile equipment to a factory. The first benefit is to collect data that are not available today to optimize workflow management. Further, shifting Grade C and B tasks to mobile solutions is certain to lower the risk of contamination.

The lights out factory

The idea of a “lights out” factory seems to be the goal for some robotics enthusiasts. In terms of risk mitigation, a factory with fewer humans can reduce certain hazards. However, operators will always be needed. There will always be unexpected tasks to perform, and artificial intelligence is not close to being the solution. All equipment should be upgraded with telemanipulation capabilities, allowing operators to take control of stationary and mobile robots remotely when troubleshooting or other interventions are required. This technology enables operators both inside and outside of sensitive areas to feel what the robot and the gripper are handling. They should even be able to precisely identify the robot’s immediate environment, promising a bright future for augmented reality in the pharma factory.

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