Flexibility and cost-effectiveness for advanced aseptic production

Sergio Mauri
Manager, Global Integrated Projects, Fedegari Group

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The use of robotics and automation in the industry is not new. For several decades now, many assembly lines have utilized production robots in different functions to increase productivity. Although human operators result in a potentially risky activity in sterile areas, pharma manufacturing remains heavily human. This article discusses how to apply current isolation technologies with robotic systems to reduce the risk of microbial contamination in aseptic processes caused by human intervention.

Key words: Aseptic manufacturing, isolators, robots, contamination control.

Introduction

In the last 50 years, aseptic manufacturing has evolved slowly. In the mid-1950s, the high-efficiency particulate air (HEPA) filters started to be adopted to perform most of the aseptic processing activities. The use of isolators for sterile processing was firstly introduced in the 80s. Since then, a critical point in isolators has been the reliability of gloves as manual operations were still required (1). The automation of aseptic processing and the creation of gloveless systems to avoid direct human activities can be considered a real revolution. An advanced aseptic process can only be achieved if the industry is able to take personnel out from its processing. This automated approach aims to remove human interventions responding to the US Food and Drug Administration's 2004 Guideline on Sterile Drug Products Produced by Aseptic Processing as well as the agency's report on Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach (2). In this perspective, Fedegari has presented at the last year PDA Parenterals conference in Munich, Germany, a gloveless fully sealed isolator that uses a robotic – GMP compliant - arm. This solution is currently in an advanced development phase and offers a flexible and modular solution for small-scale manufacturing of personalized, cytotoxic materials used for clinical trials.

The revolutionary isolator is completely sealed and based on a batch system with no operator required. It supports a completely automated fill/finish process - without the need for gloves and the resulting glove ports and gauntlets - guaranteeing a greater level of sterility assurance. The system includes Cleaning in Place (CIP) capabilities to remove the contamination generated by the process. Single-use material such as ready-to-use primary containers and closures, beta bags and disposal waste bags can be used within the system.

To ensure airtight construction, Fedegari's seven-axis robot arm is made in stainless steel and designed for the lowest particle shedding. It is also resistant to high pressures and temperature wash downs, fully compatible for decontamination using H_2O_2 vapors. The system can also support both positive and negative pressures. An electronic motor controls the strength of the arm's grip. External parts and tubs surface are decontaminated with steam sterilization since an autoclave is connected to the isolator with the robot. The isolator is equipped with the built-in FHPV- Fedegari Hydrogen Peroxide vaporizer, totally engineered and manufactured in-house by Fedegari. With control loop (PID based), the FHPV provides

superior reliability and repeatability for easier validation.

The first isolator produced for a European pharmaceutical industry is currently configured for small-scale manufacturing. Nevertheless, there is room for the use of this technology in larger-scale manufacturing, especially for those manufacturers moving to smaller parallel systems.

Taking examples from other businesses on how to manage the cost-effectiveness of the pharmaceutical industry, we can refer to a semiconductor assembling line that has achieved greater results by using parallel smaller clusters. This way, even if one of the clusters runs out of operation there are another 50 working to give out all the outputs. On the other hand, in traditional big-scale pharma manufacturing, when the line stops for two or three hours the company loses the total production during that time.

There are many benefits of automation in pharma manufacturing including efficiency, saving operators from hazardous environments, reducing training overhead, eliminating human error, increasing process repeatability and reproducibility, and removing the potential for human contamination (3).

A research by the Association for Packaging and Processing Technologies (PMMI) says that robots should be responsible for 34% of primary pharmaceutical packaging operations in North America by 2018, compared with 21% in 2013 (4). Robotic systems represent greater speed and accuracy, in addition to higher flexibility and reliability than hard automation. As the risk for microbial contamination generated by personnel is driven out by advanced aseptic production systems, traditional back-end processes and manual operations will soon become part of the past also for the pharmaceutcial industry.

References

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