Modern Problems, Part 1

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Manufacturers of parenteral drugs face a host of challenges. Among the biggest issues are cost and competitive pressures, as well as stricter regulatory demands. One way to meet these challenges is through the use of Restricted Access Barrier Systems (RABS) in aseptic filling. RABS solutions provide high quality and safety standards and enable flexible and efficient production processes.

Pharmaceutical and biotech companies are increasingly under pressure. Reasons for this are highly competitive markets due to sustained globalization in the pharmaceutical and biotech world, the loss of patent protection for many blockbuster drugs, and competition from generic drugs and biosimilars. They have to reduce costs, optimize processes and at the same time develop innovative drugs and get them to market quickly and successfully. By the same token, official agencies like the FDA and EMA are demanding higher reliability and quality from drugs. One option is optimizing processes and conditions in production. For instance, using Restricted Access Barrier Systems (RABS) for the aseptic filling of parenterals offers considerable advantages.

New Solutions

Many modern drug substances made using biotechnological processes are extremely sensitive to environmental impact and require highly classified areas for manufacturing. One reason, terminal sterilization is not possible in the case of these parenterals. Nevertheless, for a high level of sterility assurance, sources of contamination must be excluded as much as possible. One convincing approach is to separate production staff physically from the manufacturing processes. Two solutions have emerged since the mid-1990s: the isolator and RABS.

Favoring Isolators

The isolator, which kept processing completely separate, seemed to be the way to go early on. However, technical issues and long discussions about how to validate the sterilization or decontamination of isolators meant teething problems for the isolator as a system. These issues have now been overcome and safe and proven processes have been established. The filling machines form a separate ISO 5 cleanroom or higher, which is operated in an environment class ISO 8. Gowning procedures are simpler and costs in time and money can be saved in daily operations. Today there are approximately 2,200 production lines worldwide operating in conventional cleanrooms and about 430 isolators lines, say the experts. From the mid 90s until the nearby past far fewer filling lines were equipped with RABS. In contrast to isolators, the physical barriers with RABS are somewhat limited. Hence, RABS lines have to be installed in at least ISO 7 class cleanrooms. Until recently, only about 70 systems of this type were operating world-wide.

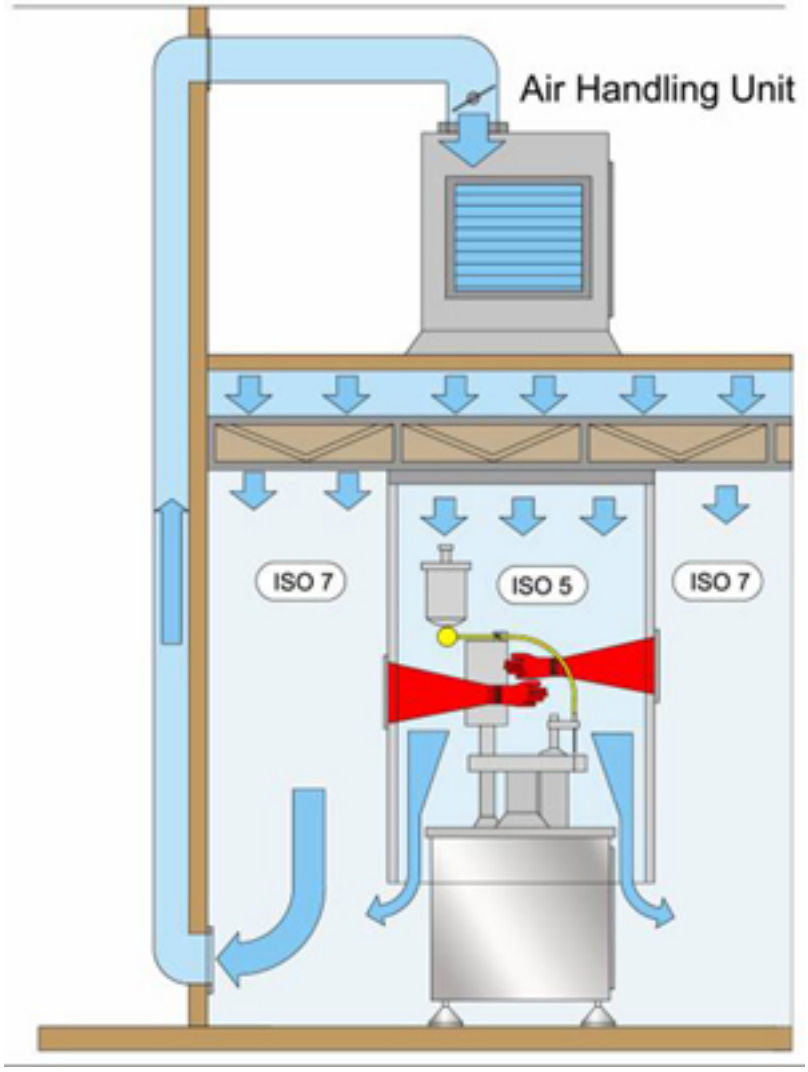

Illustration of a passive RABS system.
Source: Robert Bosch GmbH, Packaging Technology

RABS is Flexible

Lately, however, demand for RABS lines has increased noticeably. Currently, about 250 systems in facilities are operating with RABS. One reason for its growing popularity is its greater flexibility compared to isolators. One of the design features of the isolator systems is an automized bio-decontamination of all machine parts and surfaces in the aseptic processing area before each production. As a rule, the physical separation must be lifted for product change-over. For decontamination, automatic systems usually with hydrogen peroxide vapor are used. This is aseptically safe, but depending on the system, it can last from three to ten hours. Isolators, therefore, are well suited for products manufactured in large quantities or high potent drugs like cytotoxic drugs. Large quantity products allow for longer production runs and campaigns, favoring isolators, while for high potent drugs, operator protection becomes equally important as product protection. For smaller batches as well as lines that are not geared towards manufacturing of a single product, isolators will not be very economical. What’s needed, instead, are plants that are flexible regarding formats and numbers of filled drug-delivery systems and

can be equipped quickly. RABS lines are a solution, because they do allow for rapid change over from one product to the other in as little as 6 hours, when done properly.

As with all operations, the replenishment of stoppers into conveyers is done through gloveports installed in the machine cover.
Source: Vetter Pharma International GmbH

Please tune into Friday's Chem Insider Daily for part two of this two-part series. For more information, please visit www.vetter-pharma.com *[1].*

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