Modern Problems, Part 2

JOERG ZIMMERMANN, Vetter

This is part two of a two-part piece. Part one can be found here *[1].*

What Is RABS?

RABS lines make a lot of sense in light of the ever-growing need for efficiency. Companies with no RABS experience can still rely on proven technology. Thanks to their flexibility, RABS lines found favor in the mid-1990s with contract development and manufacturing organizations (CDMO) like Vetter. Official agencies started demanding a more precise definition, however. The FDA commissioned a study group made up of industry experts to make a determination. The group included representatives from the FDA, Bosch Packaging Technologies, Pfizer, GSK and Vetter. In 2005, it published its definition within the framework of the ISPE. A RABS line had to include the following:

1. A barrier to prevent human intervention directly into the critical zone
2. Air flow for an ISO 5 environment at least in the critical zone
3. Glove ports and transfer ports used for interventions
4. High-level disinfection = sporicidal disinfection
5. Highly automated processes and proper procedures for rare open-door interventions

The aim of RABS is to combine the high aseptic safety of an isolator with the flexibility of a conventional cleanroom. The definition shows that RABS solutions go beyond merely encasing the production lines. As the illustration of the passive RABS shows, a barrier keeps the production line isolated from the environment. Air flows downward around the machine. It blows through orifices from the ISO 5 area underneath the barrier into the ISO 7 area. From there it is redirected, filtered and steered back into the air circulation system. As with the isolator, intervening with the machine is only done using installed gloves.

How to Run a RABS Cleanroom Successfully

A dividing wall separating the operator and the aseptic production area does not suffice. Four main points are necessary to use a RABS line flexibly and safely and make it a best-practice.

1. During operations, the barriers may not be opened. This applies to the line set-up stage as well. All machine parts and formats have to be installed with the barrier closed and using the gloves. Lifting the separation can lead to contamination. The filling would then have to be interrupted and a complete cleaning and line clearance carried out. The filling can then proceed as a separate batch only.

2. After filling, disinfection with a sporocide must be carried out. Once the manufacturing and monitoring of the microbiological environment has been completed, the barriers are opened for cleaning. This is followed by a high-level disinfection, for example using a peroxide suspension, which generates oxygen radicals and thus avoids build-up of resistance.

3. Gloves have to be tested for integrity and sterilized. After production is finished, the gloves are removed and tested for integrity for example using a pressure decay test. This allows one to spot the tiniest holes. If the gloves are airtight, they can be cleaned, sterilized and mounted back into the gloveports.

4. Using aseptic transfer systems for zone transisition. Materials and formats are only carried into the ISO 5 area using aseptic transfer systems: All parts and raw materials (e.g. syringes and stoppers) are sterilized in steam or dry heat and doubly packed. Prior to being transferred to the ISO 5 area, the outer packaging is sprayed with an alcoholic agent. They are then transferred to the ISO 5 area through a lock, and the outer packaging is removed. All following steps are performed using the gloves. Packaging materials are also put into sterilizable bags and placed in Steriset-containers. These boxes are also sprayed down prior to introduction. When they are opened inside the barrier, their content is exposed to ISO 5 only.

RABS separates production staff physically from the manufacturing processes. During operations, the barrier may not be open and all interventions take place using the gloves.
Source: Vetter Pharma International GmbH

Successful Handling

Complying with these instructions can produce a high level of aseptic safety. For example, in the past 8 years, about 3 million units have been filled at one of the Vetter RABS lines with zero contaminated units. The result is the aseptic safety of an isolator but with high flexibility. Therefore RABS lines are able to serve as an

effective response to current and future challenges in aseptic manufacturing.

For more information, please visit www.vetter-pharma.com *[2].*

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