

passive and active RABS. A closed RABS has all the appearances of a true isolator, but requires manual cleaning and manual decontamination. A passive RABS has its HEPA (high-efficiency particulate air)-filtered air provided by the facility, not by the barrier itself. An active RABS has its own integral heating, ventilating, and air conditioning (HVAC) and HEPA system with an interconnected control system with the processing line. All RABS, like the true isolator systems, use glove ports and rapid transfer ports (RTPs).

Recent isolator development has been significant and such systems are now better specified than ever. In advanced aseptic processing facilities, it has been proven that isolators can provide zero colony-forming unit (0 CFU) contamination in process operations, while the background environment is only at ISO 8-EC grade D level. However, cost savings in clean room construction and operation may be offset by the construction and validation costs of the isolator system.

Isolators are enclosed, usually positively pressurized units with HEPA filters, supplying ISO 5 airflow in a unidirectional manner to the interior. Air recirculates by returning it to the air handlers through sealed ductwork. Cleaning can be manual or automated (clean-in-place). Bio-decontamination occurs through an automated cycle typically using vaporized hydrogen peroxide. Access to an isolator is through glove ports and sterile transfer systems. Isolators can be located in an ISO 8 or better environment.

Figures 23-4(A) and 23-4(B) illustrate the adaptation of a large-scale filling line to isolator technology. A smaller version of an isolator used for sterility testing is shown later in Figure 27-3. The operations are performed within windowed, sealed walls with operators working through glove ports. An example of the interior of an isolator is shown in Figure 23-5. The sealed enclosures are presterilized, usually with peracetic acid, hydrogen peroxide vapor, or steam. Sterile supplies are introduced from sterilizable movable modules through uniquely engineered transfer ports or directly from attached sterilizers, including autoclaves and hot-air sterilizing tunnels. Results have been very promising, giving expectation of significantly enhanced control of the aseptic processing environment.

Traditionally RABS operate in clean room environments of ISO 7-EC grade B. They can provide further zoning via screened barriers and HEPA clean-air filtration, such that an ISO 5-grade A critical zone can be established. One key consideration, particularly where process operations require "open door" access and manual intervention, is that RABS provide a high level of protection against contamination from operator intervention.

Some of the key differences between RABS and isolators are (6):

1. RABS offer a combined physical and aerodynamic barrier, ideally controlled by positive pressure with clean-air filtration providing air exchanges and particulate cleanup for an ISO 5 critical process zone.
2. Disinfection is typically manual in a standard RABS involving interaction with the process for cleaning.
3. Traditionally, RABS come in two types (Fig. 23-3): "passive" where there is no in-process open door access; and "active" where, under certain validated system configurations and control conditions, access may be included.
4. With RABS, if component entry is needed after disinfection, then aseptic transfer devices are used to prevent recontamination of the critical process zones.
5. RABS should include environmental monitoring of critical zones to ensure operators are alerted to deviations from performance levels of particulate and microbiological contamination, so that action can be taken.

### **ISOLATOR CONTAMINATION CONTROL ATTRIBUTES**

1. The physical barrier is typically controlled at positive pressure with clean-air filtration providing air exchanges and particulate cleanup for an ISO 5 critical process zone.
2. The ability to bio-decontaminate to a high level with a combined cleaning and sporicidal process often validated to achieve 6 log reduction of *Geobacillus stearothermophilus* biological indicator challenges using a sporicidal gassing process, for example, hydrogen peroxide vapor.