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To evaluate whether cleanrooms are the best method of protecting today’s products and operators in set environmental conditions, one must consider the cleanroom classifications. Cleanrooms are classified according to the number and size of particles permitted per volume of air (see Figure 1). For a typical cleanroom, the relevant particle size is 0.5µm and this is directly related to the bacterial contamination levels. Along with the classifications come the requirements for hypergeometric distribution sampling, utilities consumption and cleaning that has to be both validated and repeatable.

Cleanroom technology sets out to minimise particulates and maintain set environmental conditions – but why not consider the alternative, containment technology?

Containment, barrier isolation and isolator (or glovebox) technologies are all based on the same basic method of enclosing an environment. The International Society for Pharmaceutical Engineering (ISPE) defines containment technology as a ‘leak-tight enclosure designed to protect operators from hazardous or potent processes or protect processes from people or detrimental external environments or both.’

A basic containment system consists of: a solid cabinet, usually 316L stainless steel; viewing window; gloves and glove port assemblies; supply and exhaust with microbially retentive filtration system (high-efficiency particulate air (HEPA) minimum); input and output openings (equipment-door airlocks, rapid transfer ports) etc. and various other penetrations; extract that provides a negative environment for operator protection; and built-in safety features.

There are two types of isolators as defined by the ISPE – closed or open. In this article closed isolators will be the focus as they represent the best alternative solution to cleanrooms (see Figure 2).

In comparison with a cleanroom, the advantages of such a closed type of enclosure are numerous (see panel on next page). Overall, the benefits of containment technology provide a superior sterility assurance and cost savings. With the trend towards higher potency and purity of pharmaceutical and biopharmaceutical compounds, containment technology is becoming the norm. Because operators need to limit their exposure to these products, handling operations must be carried out inside the isolator.

Containment technology has changed vastly over the past five years and these systems can accommodate integrated equipment, providing set environments and operator and product protection for a very competitive investment (see Figure 3).

With cleanroom technology, every element has to be cleaned and disinfected, including HEPA filters which are the most complicated components to clean and maintain their integrity. Cleanroom cleaning operations traditionally consist of wiping down and mopping walls and flooring, which can take hours to complete. By using containment technology, clean-in-place (CIP) or steam-in-place (SIP) operations are fully automated and the operator only has to push a button to run a full wash-in-place cycle. The system can spray one or multiple detergents that provide a set cleaning recipe for each type of compound processed for repeatable operation.

ARE CLEANROOMS AN OBSOLETE TECHNOLOGY?

Cleanrooms have long provided environmental control for operations or tasks where the products need protection, but Michelle Frisch, PSL, asks are they the best choice for today’s requirements of cleanliness and limited operator interference?
The cleaning time for a typical isolator can be less than an hour, depending on the size of the unit, representing a huge time- and cost-saving.

Cleanroom technology requires 95% confidence that the classification required has been achieved. With an isolator or glovebox, containment is guaranteed and can be proven as it is normally monitored and proven with a particle counter at qualification. The classification can then be validated and maintained over time as it is repeatable.

The utility consumption is vastly different between a cleanroom and an isolator. An isolator, being typically smaller, uses less energy to operate and because it can be operated by only compressed air, eliminates any electrical consumption. Furthermore, another consumption reduction is achieved with HVAC systems, in that isolators have reduced flow rates compared with cleanrooms, and they can be vented directly into the atmosphere. Some systems can even re-circulate up to 99% of air or nitrogen, greatly reducing utilities consumption. Therefore containment technology consumes far less energy to maintain the set environmental conditions than a cleanroom.

Figure 4: This dual isolator for high containment and aseptic processes has a compact and mobile design with low utility consumption.

Benefits of containment technology

1. Achieving set environmental conditions that are repeatable and easy to control, such as relative humidity (RH) control with set points, as well as setting and maintaining oxygen levels
2. Achieving lower ISO Class than cleanrooms with a containment down to the nanogram range or a non-detectable level – thanks to pre-filtered air or nitrogen, HEPA pre-filtration and air pressure differential
3. Easy cleaning within a small area and no floor to wash; simple to validate as operations are repeatable. Isolator systems allow the use of solvents for cleaning and can be sterilised to reduce any bacterial contamination
4. Reduced cross-contamination and the removal of operators within the same environment as the materials
5. It is more effective and ergonomic to contain the operation rather than wrapping the operator in suits and head covers, while handling products and instrumentation easily through glove ports
6. Improved operator safety by removing the operator from the environment in which operations such as filling occur
7. Fully automated system to control all utilities and environmental conditions
8. Lower capital expenditure with a greatly reduced footprint and in many cases containment technology has a lower capital outlay compared with buying and installing a cleanroom
9. Up to 35-50% lower energy costs because the reduced space that isolators require means smaller air flow capabilities are needed, which in turn leads to lower utility consumption
10. Overall lower operating costs with less maintenance but also reduced or even eliminated gowning and de-gowning time

Using glovebox technology eliminates any possible operator contamination of the compound or process, as the operator never has direct contact with the product. This is one of the main advantages of such systems as human interaction is the most difficult parameter to control. Recently, major improvements have been made in containment technologies. Containment systems such as isolators and gloveboxes can be more and more polyvalent, circulating air or nitrogen and working under negative or positive pressures. Such advanced technologies allow the use of a single, compact and mobile isolator to integrate a full aseptic filling line for potent materials, for example. The product is therefore protected from bacterial agents, the operator and environment remain safe and operating costs are lower than cleanroom facilities (see Figure 4).

So why would anyone consider putting in a large, energy-consuming, cleanroom that is complex to clean and maintain when one can achieve better environmental control and reduce operating costs with a smaller, more effective footprint?

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