Negative pressure isolators for cytotoxics

Negative pressure isolators are increasingly used for dispensing of cytotoxics. This article looks at whether turbulent flow can be as effective as unidirectional and whether positive pressure isolators might be as safe as negative ones

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The term "unidirectional flow" has superseded "laminar flow" in international standards. Unidirectional flow is defined as follows: controlled airflow through the entire cross-section of a clean zone with a steady velocity and approximately parallel streamlines - Note: this type of airflow results in a directed transport of particles from the clean zone.[1] The following statement in the European GMP amplifies the meaning of grade A: "The particulate conditions for grade A 'in operation' given in the table should be maintained in the zone immediately surrounding the product whenever the product or open container is exposed to the environment."[2]

Envair believes that only unidirectional flow complies with this requirement, by quickly and effectively removing process-generated contamination from the critical zone.

A further point is that a unidirectional flow isolator has an air change rate of 1,800 TAC (total air changes/h), compared with 180 TAC for a typical turbulent flow isolator. In this example, the clean-up time for the whole isolator is ten times faster.

Questions over the use of cartridge HEPA filters

Cartridge HEPA (high-efficiency particulate air) filters are frequently used in turbulent flow isolators. It is not possible to test these filters for single leaks during manufacture or during routine tests in situ, and only the "mixed volume" can be tested for overall penetration or efficiency (volumetric testing). On the other hand, panel HEPA filters can be scan-tested for single leaks. In both cases, testing is carried out using a calibrated upstream aerosol challenge (DOP) and an aerosol photometer with a sampling probe downstream.

The sampling probe is designed to be isokinetic, ie, to draw air in at approximately the same velocity as the unidirectional air passing the probe. This ensures 100% sampling in unidirectional flow systems when the probe is scanned back and forth across the filter in overlapping sweeps. The probe of the aerosol photometer normally samples at 1cfm (cubic feet/min) $= 4.72 \times 10^{-4} m^3/s$. In turbulent flow systems, the probe can only take a sample of the mixed air. For the typical turbulent flow isolator, with an air change rate of 180 TAC and a volume of $1m^3$, the volume flow rate is $180m^3/h = 180/3600 m^3/s = 5 \times 10^{-2} m^3/s$. All leakage through single leaks in the cartridge HEPA filter is diluted into this airflow. Thus, in this particular example, volumetric testing is 100 times less sensitive than scanning. This cannot be overcome by increasing the sample size or the number of tests, because neither of these can overcome the dilution. Therefore even if an isolator is built and tested to a high standard of leak-tightness, there is still a significant risk of microbial contamination (if its air supply is through a cartridge HEPA filter).

Aseptic techniques

Technicians are usually taught aseptic techniques in unidirectional flow. They are trained to carry out critical operations in a streamline of air that is uncontaminated (ie, that has come straight from the HEPA filter). If work is carried out downstream of, for example, hanging bags, technicians have to pay special attention to the prior disinfection of these bags. Technicians have expressed genuine concern about the risks of recontamination in turbulent flow environments.

Positive versus negative pressure

Both types of isolator provide operator protection in most circumstances, due to the physical barrier. The main difference is that, in the (hopefully rare) event of a major leak or breach in a negative isolator, there is no outward flow of potentially contaminated air.

Whatever the technical arguments, the large number of negative pressure isolators being manufactured by Envair demonstrates the preference of pharmacy technicians around the world. When engaged in long-term intensive work with cytotoxics, they need to feel that everything possible is being done to ensure their personal safety. It is important to remember that the isolator is not a magic box – it will only provide safety if properly used, cleaned and maintained. ■

References

1. BS EN ISO 14644-4. 2001.

2. EC GMP Revised Annex. 2003.