PALL Biotech

Integrity of Single-Use Systems

Test Methods to Check a Single-Use System (SUS) for Leaks

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Integrity Checking

Visual inspection must be conducted on receipt of a single use system (SUS) as it can identify the risk of gross physical damage to the equipment which has been sustained during transportation and storage. For example, damaged transportation boxes, signs of water exposure, deep marks on film. It is a quick and inexpensive check and product exhibiting such damage should not be used.

However, in some instances, the location of the defect in the SUS is not visible. Additional tests, less subjective, or with a better detectability and/or sensitivity, might be required to identify this type of issue. Many test methods exist (e.g. ultrasonic testing) which can be used for this purpose and the method selected based on a process of risk assessment that goes beyond the scope of this article. As here we have limited our description to the methods known to be used with SUS.

The most commonly used non-destructive test methods for checking a SUS for integrity are:

- Pressure decay: SUS is inflated with gas at a given pressure and the drop of the pressure is measured after a given time.
- Flow measurement: SUS is inflated with gas at a given pressure. The flow required to keep this pressure constant is measured over time.
- Gas tracer method: SUS is placed into a vacuum chamber and connected to the gas tracer (typically helium for SUS) line. The gas leaking out of the SUS is detected and quantified.

The above methods can be applied on 100% of the SUS.

Some destructive methods can also be used during qualification steps, routine destructive sample testing, for investigation or for post-use testing. Here are some methods used for SUS:

- Gas bubble leak detection: SUS is inflated with gas, immersed in liquid and the leaks (gas bubbles) are visually detected.
- Soap leak detection: SUS is inflated with gas, soap is sprayed outside. Leaks (soap bubbles) are visually detected.
- Water leak/dye tests:
    - Ingress test: the SUS is dipped in a bath of dye, then subjected to pressure cycling, and checked for dye ingress after a defined duration. This is the exact same principle that is used for the dye ingress testing of primary packaging components.
    - Egress test: the SUS is filled with water (or water with dye), pressurized, and checked for egress after a defined duration. Absorbing (colored) paper is often used to enhance detectability.

  Water leak test sensitivity can be enhanced by adding product to lower surface tension, typically detergents.
- Microbial challenge tests:
    - Aerosol test: the SUS is filled with a growth media, placed into a chamber where a liquid microbial suspension is aerosolized. After a defined exposure time, the SUS is incubated to promote microorganism growth. The media is then sampled and analysed or checked for microbial growth, or a direct "reading" is done through the SUS transparent surface.
    - Immersion test: same procedure as for the aerosol test, except that the SUS is immersed in a liquid microbial solution.

  Test results highly depend on the test parameters, which should be defined to cover the full range of conditions of the SUS's usage.
- Leak test with reagents: the SUS is pressurized inside with a specific liquid or gas. The outside of the SUS is sprayed with another liquid, reacting with the pressurizing fluid when it comes out, hence revealing the leak location (typically by a color change).

The choice of a test method is made according to following considerations:

- Can the test be destructive or not?
- What sensitivity needs to be achieved?
- Can test be applied to the SUS? (e.g. is the SUS too large or too complex?)
- Is the equipment required for the test available?
- Test time, costs, risks associated to the test itself, etc

Table 1 shows a summary comparison between two key non-destructive test methods (routine industrial parameter setting) applied on a SUS:

Table 1. Comparison between non-destructive test methods: Pressure Based and Tracer Gas

Consideration	Pressure Based Test (Pressure Decay or Flow Measurement)	Tracer Gas (Helium) Test in Vacuum Chamber
Sensitivity	Greater than 10 µm	Greater than 2 µm
Impact of environmental conditions (e.g. temperature) on sensitivity	Medium	Low
Impact of volume of SUS on sensitivity	Medium to high	Low to medium
Impact of materials of SUS on sensitivity	Low to medium	Low*
Handling	Simple to medium	Complex
Test time	Medium to long	Short *Cycle time is much longer than test time*
Cost of equipment	Low to medium	High
True point-of-use test	Possible	Not possible

* providing adequate parameters are selected

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