



Leak Detection for Pre-filled Syringes

*Application
note*

Vacuum Decay method for leak detection of Pre-filled syringes has proven to be an effective method of testing. In this application note, we demonstrate the benefits and its application to better understand how the technology works.

The Vacuum Decay testing method is based on **ASTM F2338-09*** for leak testing containers which is a recognized consensus standard by the FDA and is included in the list of Deterministic Leak Test Technologies of **USP General Chapter <1207>**.

Tested products:

- Carpules,
- Injection Devices,
- Pre-filled Syringes.



BENEFITS

Testing to prove containers integrity for proper sealing and absence of any product leak after packaging ensures pharmaceutical companies' compliance with regulatory recommendations in the use of a deterministic test method for sterility and stability.

Employing a non-destructive method allows for repeating tests also at different times, in order to validate the packaging assembly and components stability; it can also be a good business practice as an in-process control to ensure a robust control of the package container closure integrity (CCIT).

APPLICATION FIELDS

The technology allows end users to ensure efficient and productive manufacturing and packaging while also meeting safety requirements, authorities' regulations, and market quality standards.

The possibility to integrate the technology into different types of machines allows for its application to the various stages of the package lifecycle. This kind of flexibility helps the client to apply it to small scale testing as well as to 100% in-line testing.

TESTING TECHNOLOGY

The Leak Test takes place in an airtight Testing Chamber in which a pressure differential is applied (Patent No. 1225063 of 13-9-1988). The test objective is to detect container leakages by measuring the reached pressure level as well as the pressure change over the test period. The test will result in a Pass, Fail Gross, or Fail differential pressure (ΔP) outcome, and will be displayed on the Human Machine Interface (HMI) screen. The high reliability and

reproducibility of the method allows determining in a few seconds the integrity of the tested container.

AIM OF TECHNOLOGY

Bonfiglioli Engineering lab appliances and automatic machines have been successful in testing for critical defects in individual containers. The technology has been used and implemented for several applications with different types of Pre-filled Syringes, Carpules and Injection Devices, speed, and leak requirements. We offer excellent test capabilities for those looking for machines ranging from small manual units to 100% in-line solutions. Bonfiglioli Engineering test appliances have a long record as a proven non-destructive test method with a fast ROI compared to traditional destructive test methods such as blue dye and microbial ingress testing. Bonfiglioli Engineering solutions take advantage of electronic and pneumatic components state of the art which are a common factor between the entire range of testers for Lab, off-line and in-line applications. This allows end users to utilize the same test method from the early stages in the lab, through clinical trials and into full scale manufacturing with 100% inspection.

* "Standard Test Method for Nondestructive Detection of Leaks in Packages by Vacuum Decay Method".

GMP COMPLIANCE

Bonfiglioli Engineering machines have a SCADA system for full data collection and control capability. The computerized system contains the required technical elements to be compliant with EU Annex 11 and 21 CFR part 11 to meet the latest updates on regulatory requirements in terms of data integrity.

The equipment qualification and validation comply with requirements stated in EU Annex 15. The equipment manufacturing process and materials are compliant with applicable GMP requirements.

LEAK TESTING TECHNOLOGY COMBINATION

Bonfiglioli Engineering leak testing technology can also be integrated and combined with Automatic Visual Inspection and Headspace Gas Analysis to support end user in required testing processes



Bonfiglioli Engineering machines are equipped with a plunger stopper device to prevent any significant plunger movement and ensure product sterility.

HOW TO TEST

The operating principle is based on the insertion of the container into a dedicated testing chamber, then applying a vacuum to the outside of the container, generating a differential pressure between the inside and the outside. Once an equilibrium pressure is established in the testing chamber, a sensor monitors any change in the pressure within the chamber to determine if:

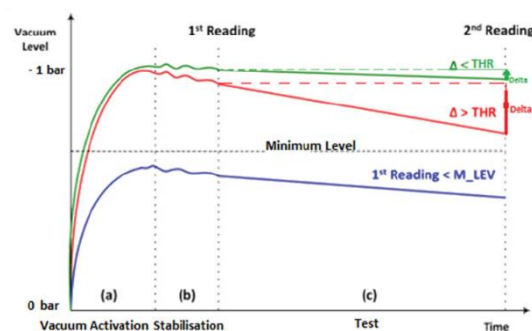
- Gas from the tested pack is leaking.
- Leaking liquid is evaporating into the testing chamber.

One of **3 distinct outcomes** will occur:

- 1) **Pass**: Containers with good assembly and no pinhole leaks will achieve the predetermined vacuum equilibrium for a set amount of time. The testing chamber will maintain the internal pressure level, or, at most, there will be a negligible change which will not interfere with the results if it doesn't exceed the designated threshold during the testing period. This is the expected result for Pre-filled Syringes with no assembly or pinhole leaks.
- 2) **Fail Gross** (absolute): A Pre-filled Syringe with a large hole (gross leak) will fail to achieve the equilibrium pressure during the established test time. Although the test is

completed, the evaluation of the test phase is no longer used as the criteria for passing. This is the typical failure for large cracks.

- 3) **Fail ΔP** : A Pre-filled Syringe with a small leak achieves the predetermined equilibrium for the test time but then fails the ΔP outcome during the test period. The graph below shows the three possible results as they would appear on the Human Machine Interface (HMI). The test in blue failed to meet the equilibrium pressure. The red and green tests both met the equilibrium pressure during the established time (1st reading) but the red test exceeded the maximum ΔP outcome before the test was completed (2nd reading).



Bonfiglioli Engineering provides varied leak detection solutions from lab to inline machines, for pre-filled syringes, cartridges and carpules. The machines include features like quick format changeovers, automatic drying systems for no testing chamber contamination, auto test in real time and Manufacturing Execution System (MES) for remote machine data exchange and download.

LEAK DETECTION SOLUTIONS:

LAB SOLUTION	MULTI-HEAD SOLUTION	IN-LINE SOLUTION
LF-S11 SY	LF-SMH	PK-SY



The [LF-S11 SY](#) is suitable for laboratory applications, statistical purposes, and off-line leak testing. It performs the leak testing process after the Pre-filled Syringe is manually loaded into the test chamber by an operator. Following the testing process, the containers are manually unloaded from the chamber and they are managed according to the results of the test. This equipment is fully compliant with requirements of 21 CFR part 11.



The [LF-SMH](#) is suitable for laboratory applications, statistical purposes, and off-line testing. It performs the leak testing process after the Pre-filled Syringes are manually loaded into the test chambers by an operator. The machine can test up to 5 Pre-filled Syringes at the same time. This offers a time-saving solution in the class of laboratory equipment. While one set of Pre-filled Syringes is being tested, another set can be loaded into the chambers for fast turnaround. Following the testing process, the containers are manually unloaded from the chamber and they are managed according to the test outcomes.



The [PK-SY](#) is suitable for 100% In-Line and off-Line testing. It performs the leak testing process in continuous operation by means of testing chambers under vacuum which are installed on to a rotating central carousel.

Following the testing process, the containers are automatically unloaded from the testing area and they are managed according to the results of the test.