



AMI INTEGRITY TEST SYSTEM

Innovative solutions for the pharmaceutical industry

PFEIFFER  **VACUUM**

 **伯東**

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Our know-how

Pfeiffer Vacuum is one of the world's leading providers of vacuum and testing solutions. The product portfolio comprises vacuum pumps, measurement and analysis devices, components, as well as vacuum chambers and high performance detection systems. Thereby our customers benefit from over 50 years of experience in helium leak detection.

Integrity challenges

Contamination such as humidity, oxygen or microbiological ingress can impact drug stability throughout the product life cycle. To prevent the risks of stability failure of highly moisture-sensitive drugs (e.g. dry powder for inhalation), or the risk of biological ingress of parenteral drugs, integrity tests with a high sensitivity are required. Most test methods are very challenging in regard to time effort, complexity or the limitation of sensitivity and detection range.

An innovative solution

Our patented method does not require any specific tracer gas. Instead, the gas mixture present in the container headspace of the primary packaging is used to perform high sensitivity tests over a large detection range. Therefore, our method is non-destructive, easy to use and to set up and has higher sensitivity than other conventional methods.

Packaging



Blister packs



Glass vials



Plastic bottles



General customer benefits

- Improves sensitivity, capability and reliability of your integrity test.
- Large detection range – can replace gross leak and helium test.
- Improves manufacturing productivity with equipment that is easy to use and to set up.
- Lower cost of non-quality thanks to advanced process monitoring and feedback control.
- Fast return on investment.

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Ease of use

The products can be sampled directly from the production line and loaded in the test chamber without any specific conditioning.

At the end of the test sequence, the result is clearly displayed and a PDF report is automatically generated at the batch closure. Full automation of the test cycle including loading/unloading of the samples can be easily implemented for in-line tests.

Dedicated to the pharmaceutical industry

AMI equipments have been qualified by leading pharmaceutical companies as in-process control (IPC) leak testing for blister packs. Our software is 21 CFR part 11 compliant.

Large detection range

Different detection methods can be combined in order to cover the complete detection range. Gross leak and fine leak tests are performed within a single test sequence, any additional gross leak test (e.g. blue dye ingress) can be omitted.

Deterministic test method

As no operator intervention is required, the measurement results are totally objective. High accuracy measurements can be achieved thanks to a calibration-validation sequence of the equipment based on certified calibrated leaks.

Therefore, high sensitivity tests combined with high throughput enables trend analysis to early indicate production issues and to avoid the loss of valuable pharmaceuticals.

Operation



AMI INTEGRITY TEST SYSTEM

Packaging types

Blister packs



Sensitivity

Down to $2 \cdot 10^{-5}$ mbar l/s
(Equivalent to $\sim 2 \mu\text{m}$ pin hole)

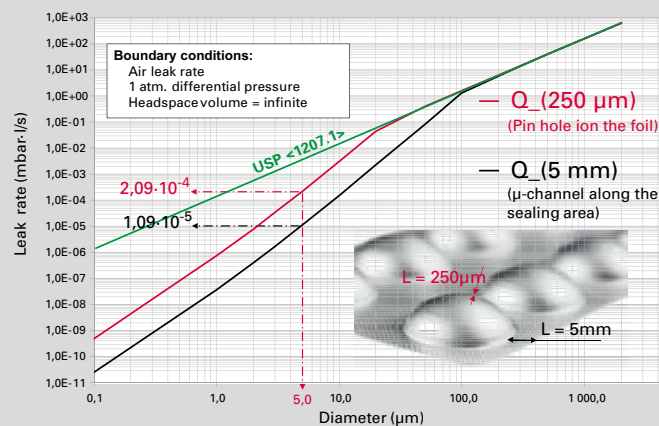
Test duration

Down to 20 sec per test
(Depending on the pack format)

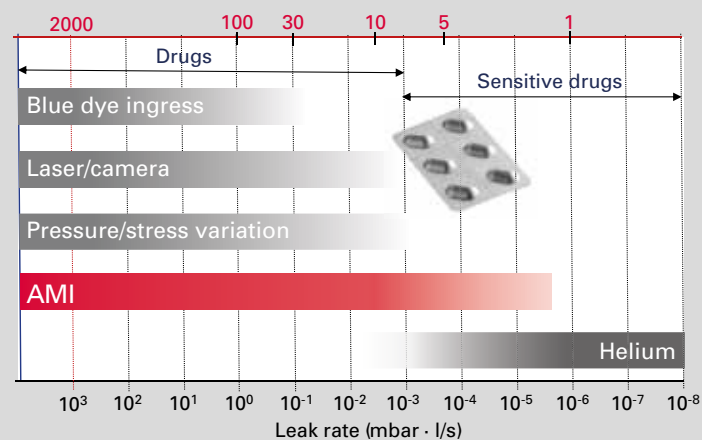
Advantages at a glance

- Widest detection range available on the market
 - Higher sensitivity than conventional methods
 - Blue dye test no more needed
- Can test packs that contain tablets / capsules in multiple material / design formats
- Can test multiple packs per test cycle
- Applicable to peeling blisters

Correspondence: Air leak rate & hole diameter



Leak detection range



Glass vials



Sensitivity

Up to several hundred microns hole
down to $1 \cdot 10^{-7}$ mbar l/s
(equivalent to several 1/10 μm hole)

Test duration

1 – 2 minutes typically

Advantages at a glance

- Global test
- Fast and easy to set up
(no sample preparation, no storage time)
- Flexibility: Unitary test or test per batch
- Applicable to liquid and solid drugs

Plastic bottles



Sensitivity

Up to several mm hole (depends on the inner volume)
down to $2 \cdot 10^{-5}$ mbar l/s (equivalent to several μm hole)

Test duration

40 seconds typically

Advantages at a glance

- Tool-less device
- Fast and easy to set up
- Flexibility (multi-formats)
- High throughput: Unitary test or test per batch
(up to 100 parts can be tested simultaneously)

What other applicable packaging types?

Our versatile method is applicable to:

- All types of drug dosage forms such as tablets, liquid or lyophilized or dry powder filled
- All types of non-porous containers, with gas headspace $> 0.2 \text{ cm}^3$.

Therefore, containers such as blisters, vials, cartridges, syringes, pouches, etc. can be tested with the AML.

The test chamber can be customized according to the product formats and the quantity of products tested simultaneously.

AMI INTEGRITY TEST SYSTEM

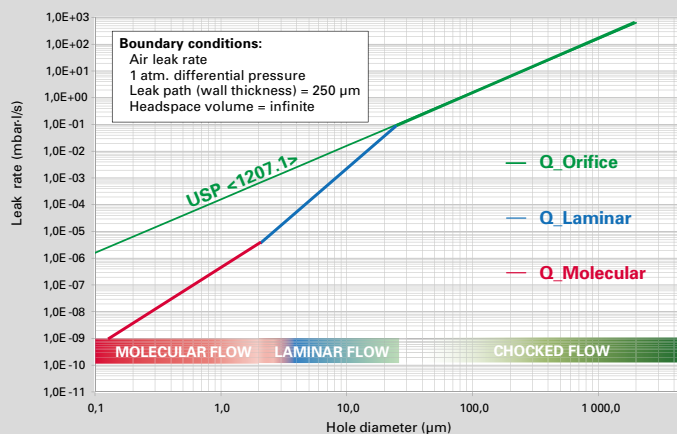
Connection between hole diameter & air leak rate

Leak rate versus hole diameter

Historically, dye ingress testing has been the container closure integrity test of choice. The detection limit of this method is around 20 µm. Since the test is strictly visual the detection limit has been experimentally determined by using orifices of known diameter. As a consequence tightness criteria in pharmaceutical industry are usually expressed as an equivalent hole diameter in µm. However, an equivalent hole diameter is not enough to define the tightness criterion of a packaging. Depending on the diameter of the hole, the leak path (length) must be considered in order to define a leak rate (atm.cc/s) which corresponds to a tightness criterion.

- For large diameters (typically > 100 µm), the leak can be generally considered as orifice (leak path of negligible length) as defined in USP <1207.1> section 3.9. This corresponds to the "CHOCKED FLOW" regime and the leak rate is directly proportional to the surface of the orifice (green curve). For smaller diameters, the leak path (wall thickness) also needs to be considered. Therefore, the hole diameter is not proportional to the leak rate anymore. Moreover, different flow regimes must be considered for calculation of the leak rate.
- In "LAMINAR FLOW", the viscosity of the gas (depending on the gas temperature) is the parameter which determines gas-to-gas variations of media transfer through the leak.
- In the region of smallest diameters there is another flow transition. In "MOLECULAR FLOW" regime the molecular mass of the gas and its temperature are the driving parameters. As shown on the attached graph, the difference between the USP <1207> orifice calculation and the real geometry of the leak is very important for holes with very small diameters.

General introduction (Leakrate / Hole diameter)



$$Q_{\text{Air}} \text{ (mbar} \cdot \text{l/s)} = f [\text{hole diameter (}\mu\text{m)}]$$

AMI 121 INTEGRITY TEST SYSTEM FOR BLISTER PACKS

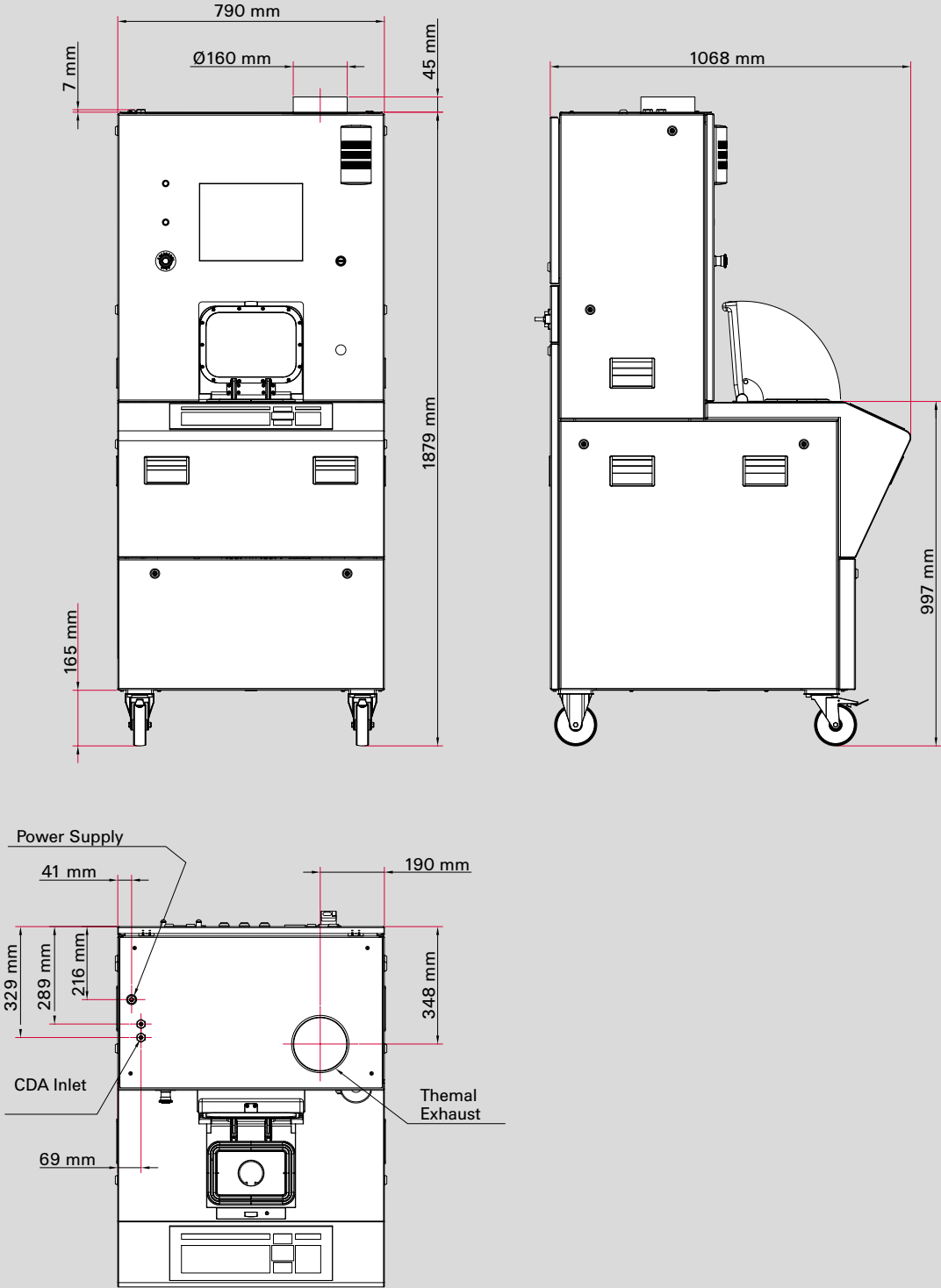
Technical data

	AMI 121
Construction	Housing: 304L stainless steel
Test chamber dimensions (l x w x h) ¹⁾	204 x 132 x 9 mm 8,03 x 5,19 x 0,35 inch
Tooling change over	< 30 sec.
Test type	Non-destructive integral vacuum test based on optical emission spectroscopy
Measurement range	> 1 · 10 ⁻⁵ mbar l/s (Equivalent to few microns hole diameter)
Testing speed	Typically 40 sec. for 1 µm hole size on aluminum blister ²⁾
Operating conditions: Temperature (min./max.) Humidity (min./max.)	20/30 °C 20/65 % relative humidity
Power supply	208-230 VAC, single phase, 50/60 Hz
Typical power consumption	2.3 kW
CDA pressure supply (min./max.) (1.3.1 according to ISO 8573-1)	6/8 bar rel. 87/116 psig
Typical CDA consumption	7 NI/cycle
User interface	15 inches touch screen (1024 x 768) IP65 keyboard with touchpad
Software	21 CFR part 11 compliance PDF GMP test reports LDAP compatible OPC (optional) MES connection (optional)
Network connection	1 x LAN
Interfaces (printer, bar code reader, data export)	2 x USB (ext.)
Dimensions (l x w x h)	790 x 1.068 x 1.924 mm 31.1 x 42 x 75.74 inch
Weight	395 kg/870 lbs.
Noise level	53 dB (A)

¹⁾ Other dimensions available upon request

²⁾ Depending on blister type and operating conditions

Dimensions



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perfect vacuum solution?
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