Helium Leak Detection for Pharmaceutical Packaging CCIT (MALL Test)

By: Philippe Bunod, Pfeiffer Vacuum SAS

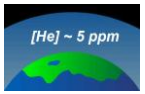
Presentation Overview

- Helium, an ideal gas for leak detection
- Helium Leak Detection – Operating principle
- Helium test methods
- Helium test on empty syringes
- Bombing test of sealed components or closed containers
  - A 4 steps test sequence
  - Detection of large leak detection
  - Summary and conclusion
- Helium charging method in sealed container (vial)
- Summary and conclusion

- Optical Emission Spectroscopy (OES) an emerging technology for CCIT
  - How does Optical Emission Spectroscopy for CCIT work ?
  - Key features
  - Influence factors
  - AMI equipment - Main features

Helium an ideal gas for leak detection

Small molecule (M=4)



Helium in earth atmosphere
[He] ~5 ppm

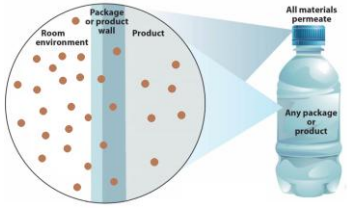
Non-toxic, inert
& non-flammable

Chemically inert
(food preservative E939)

no impact on global warming
and the ozone layer

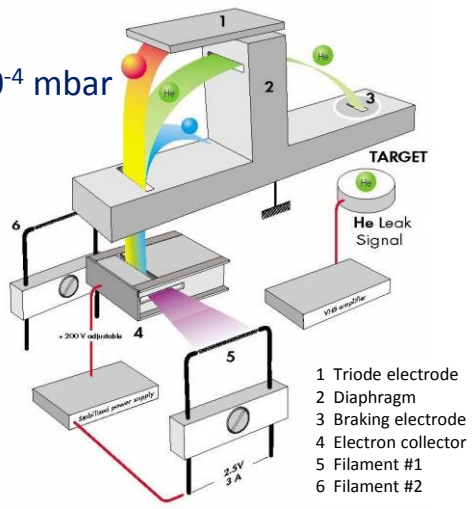
Can be diluted and recycled

High Permeation
& Diffusion



Limited ressource

Helium Leak Detection – Operating principle



High sensitivity and Quantitative

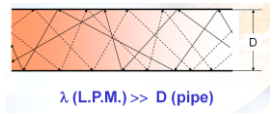
- Magnetic deflection mass spectrometer
- Down to 10^{-10} mbar.l/s (sub-micron orifice)

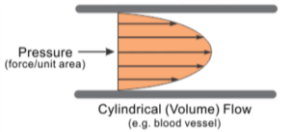
Selectivity

- Low Helium concentration in the atmosphere (~5 ppm)
  - Do need to minimize He concentration in lab ambient
- High permeability, diffusivity & solubility of He in polymers
  - Can limit the sensitivity of the test (He background)

Helium flows through cracks:

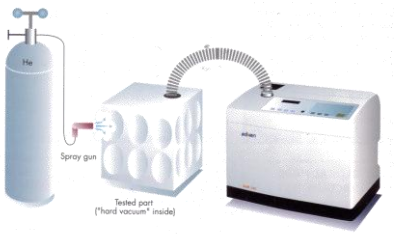
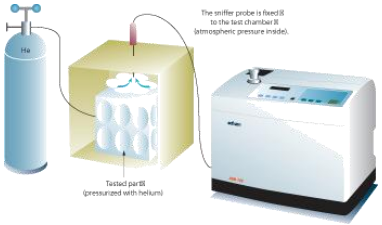
- Molecular flow
  - 2.7 larger than air for sub-micron defects
- Laminar flow
  - 0.93 smaller than air for micro-channel





Helium Test Methods

The HLD can be used in different way depending on your objective:

LOCATION OF THE LEAK - maintenance application - quality control		**GLOBAL TEST** - industrial application - quality control	
SPRAYING TEST (vacuum method)	**SNIFFING TEST** (test is performed at atmospheric pressure)	**SNIFFING TEST WITH ACCUMULATION** (test is performed at atmospheric pressure)	**GLOBAL HARD VACUUM TEST** (Vacuum Method)
- the system or the UUT can be placed under vacuum. - you need to detect very small leaks.	- the system or the UUT : > cannot be placed under vacuum > can be charged with helium - the sensitivity is not a major issue	- the system or the UUT : > cannot be placed under vacuum > can be charged with helium - the sensitivity is not a major issue	- the system or the UUT : > can be placed under vacuum > can be charged with helium - you need to detect very small leaks.
			

Test of open container – Glass syringe
Rubber plug / Barrel seal Helium Leak Test

Operator start test cycle on HLD

1/. Gross leak air test on rubber plug

- Vacuum is applied in the barrel volume
- Gross leak detection with air

2/. Helium charging of the Helium/vacuum chamber

- V_{P1} open until pressure M1<1 mbar (to warranty 99.99% of He)
- V_{He} open during 1 sec to charge He at atm. pressure

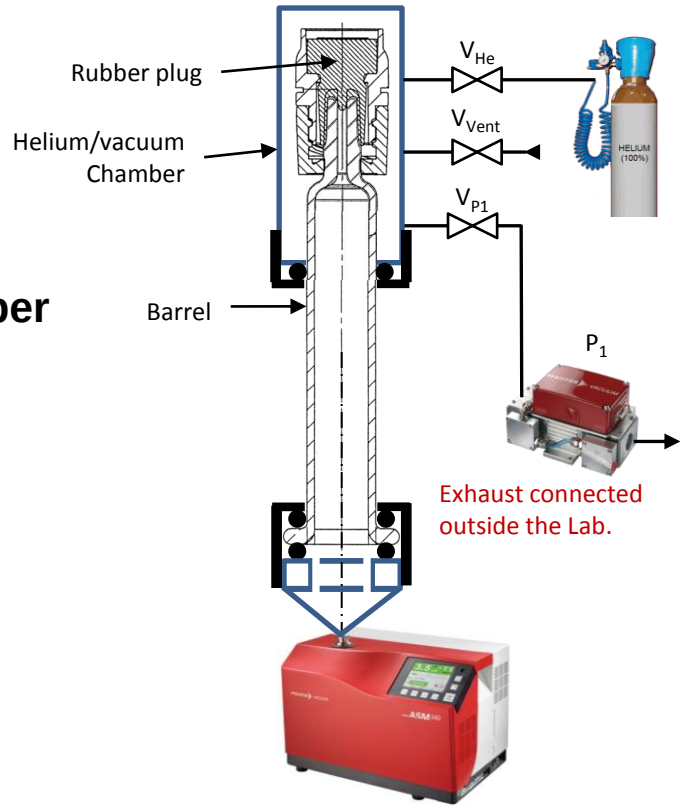
3/. Helium measurement

- If $Q_{He} > 6.10^{-6}$ mbar.l/s → Part is rejected

4/. Helium evacuation

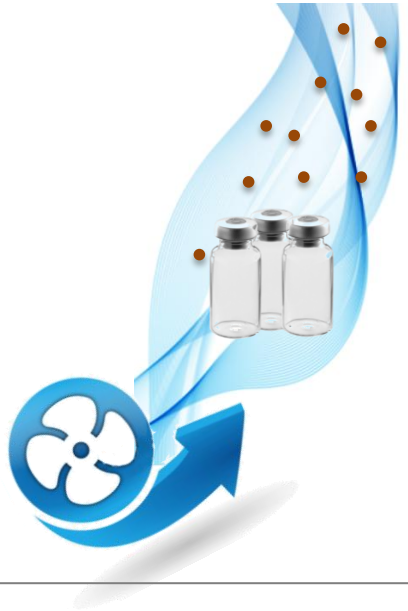
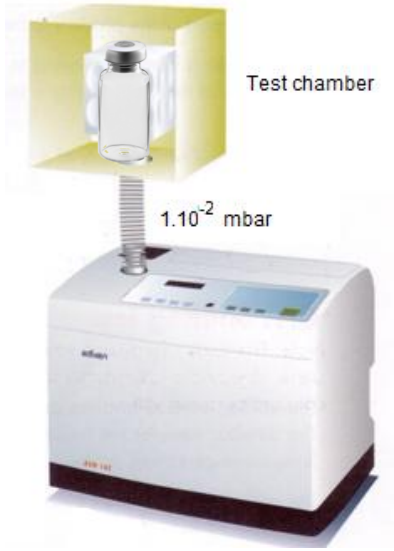
- V_{P1} open until pressure M1 < 1 mbar (to avoid pollution of ambient)
- V_{Vent} open 1 sec to vent the barrel volume with ambient air or N2

5/. Barrel venting / End of test



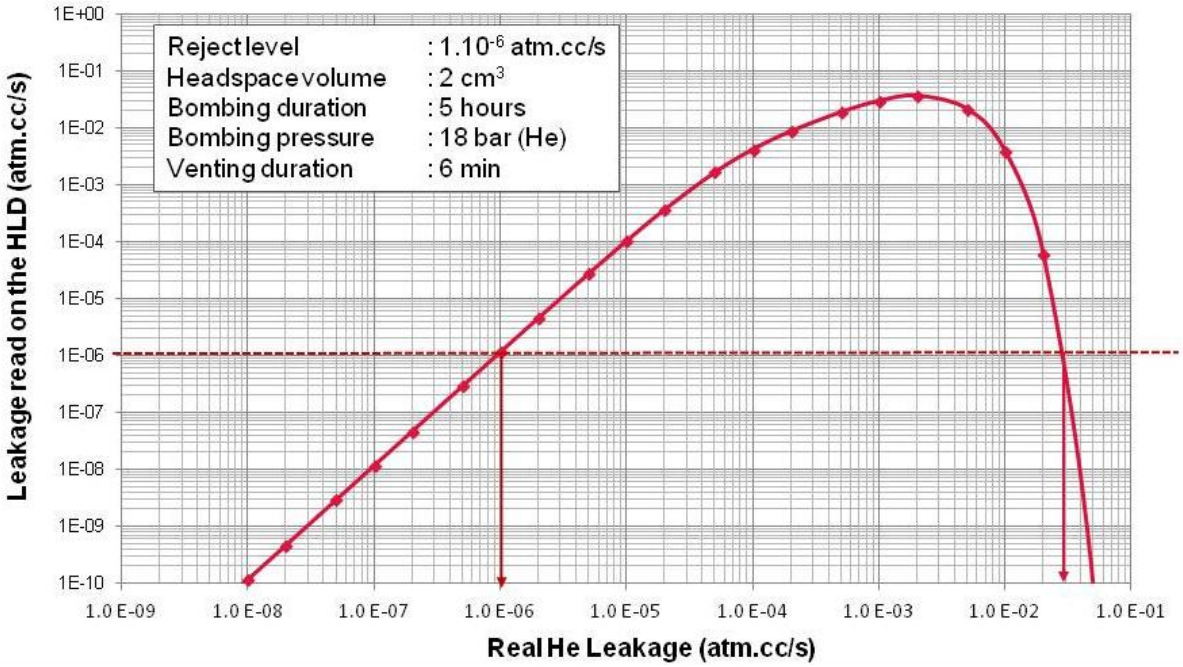
Bombing test of sealed components or closed containers

A 4 steps test sequence :

1/. HELIUM BOMBING	2/. PART VENTING	3/. HELIUM TEST	4/. PLAUSIBILITY TEST
Helium is charges into the part through the leak paths	Helium trapped on the part wall is removed by air flow	Hard vacuum test to measure Helium leakage (mbar.l/s)	To check that Helium is still present into the part.
1 to Few hours, depending on: - Headspace volume - Minimum detectable leak rate - Bombing pressure	1 to Few hours, depending on: - Container materials - Bombing time - Bombing pressure	Few seconds !	To measure [He] and display real helium leakage.
			

Bombing test of sealed container – Large leak detection

In case of large leak, the helium inside the container can be evacuated during the initial evacuation stage before to be able to measure He leakage!



→ In particular cases, the measured Helium leakage could be the same for a large leak or a fine line.

Bombing test of sealed container – summary

Easy to understand but difficult to set-up

Many parameters need to be considered and/or defined:

- Bombing pressure (depending on the container design)
- Bombing time (depending on the headspace volume and the leakage to detect)
- Venting time (depends on permeation of the material in contact with helium)
- Maximum time between bombing and He test (to limit He escape in case of large leak)

Gross leak detection will be very difficult to detect

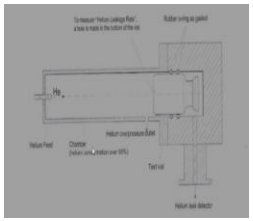
Quantitative measurements require to know the Helium concentration inside the container.

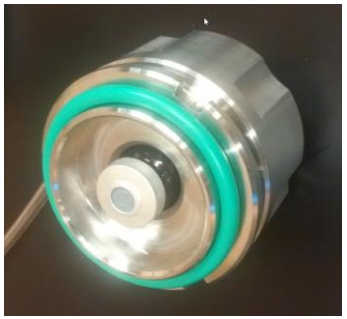
Destructive test (a plausibility test is mandatory to check that He is still present in the container)

How to charge helium in sealed container – Glass vials

1. Through the rubber plug via a needle.
   - ➢ Integral test of the vial
   - ➢ [He] in the vial is known but it vary in the meantime between He charging and test, then:
     - → Plausibility test required to valid tight results
     - → He concentration measurement need to be measured to get quantitative leakage measurements

2. Through a hole made in the bottom of the vial
   - ➢ Integrity test of the cap sealing only.
   - ➢ [He] is known & constant during the test
     - → No plausibility test required
     - → Quantitative measurements





→ Destructive procedures !

Helium leak detection for CCIT - Conclusion

Demonstrate conformance to MALL

To preserve sterility and drug stability

MALL <= 6.10^{-6} mbar.l/s (atm.cm^3/s) <USP 1207>

Helium leak tests are widely used during packaging system development and development/qualification phases

Assess critical seal elements, sub-assembly and system design

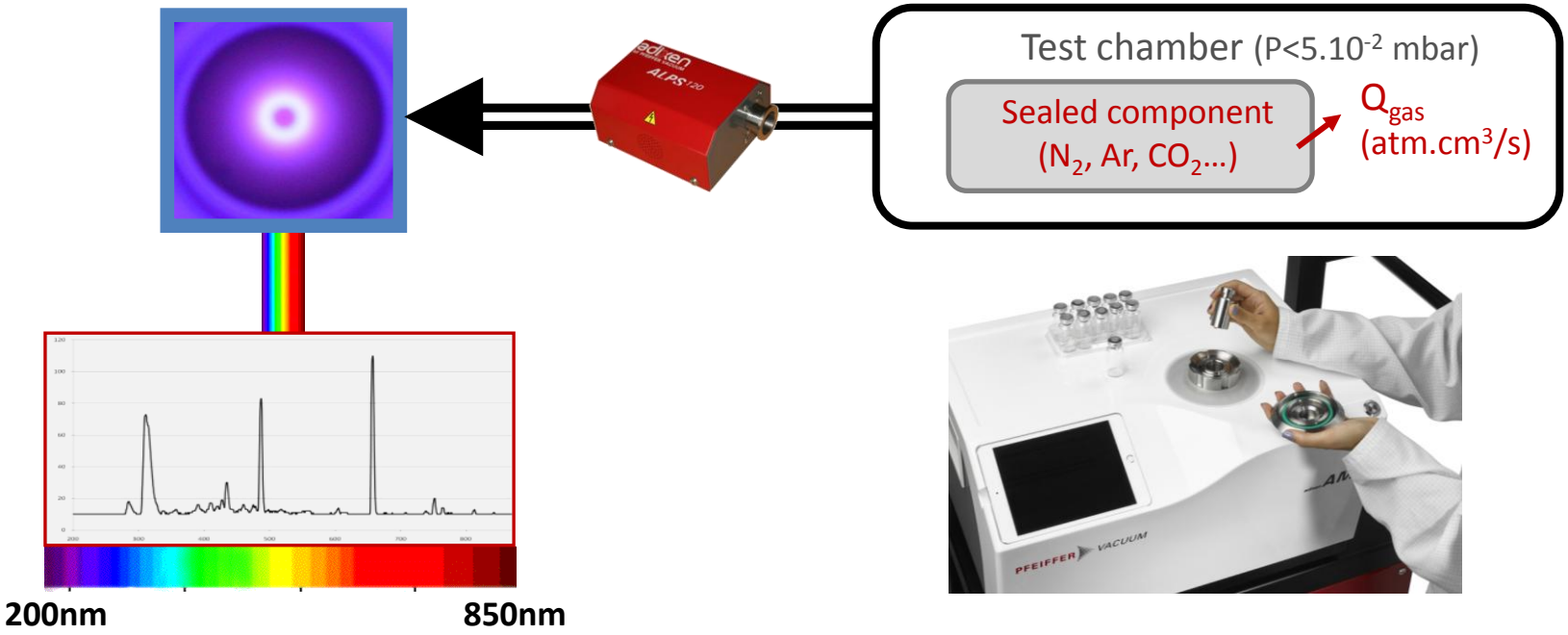
Evaluate sealing robustness (impact of defects on container integrity)

Difficult to set-up in production…and destructive for sealed containers

Optical Emission Spectroscopy (OES) an emerging technology for CCIT

Basic idea: No specific tracer gas is required to performed the leak test. Gases naturally present inside the container will be tracked for leak detection.

Multi-gas sensor based on Optical Emission Spectroscopy is used to measure the gas leakage comming from a container in a vacuum chamber.



OES – Key features

Deterministic test method

- Certified calibrated leaks are used for calibration

Applicable to all types of non-porous containers

High sensitivity & high throughput

- Less than 10 sec to detect 0.7 µm glass µ-pipette on vial
- No impact of the test volume on the sensitivity (test per batch possible, up to 10)

Selectivity

- Air leaks & water leaks can be detected and measured simultaneously
- Possible selection of the tracer gas (N_2, CO_2, Ar, H_20,…)

References: Qualified for highly sensitive (moisture) inhalation drugs in blister packs
: Already used as IPC on production line

OES – Influence factors

Container out gazing may impact the sensitivity of the measurement (global vacuum test)

- Materials in contact with vacuum
- Surface in contact with vacuum
- Temperature

Minimum headspace volume (1 cc) or high outgazing drug (compressed powder, liquid,..) is required.

AMI Equipments – Main Features

Compact & Lightweight

2 leak detection technologies
- Vacuum Decay (Coarse leak)
- O.E.S / ALPS (Fine leak)

2 operation modes:
- GO/NOGO for production
- Analytical tool for development & qualificatio

Modular design:
- Manual test chamber easy to customized
- External roughing pump

CFR 21 Part 11 compliant

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