Helium Mass Spectrometry, for high sensitivity CCIT

Instructor:

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PDA Parenteral Drug Association

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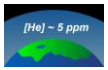
Helium an ideal gas for leak detection

Small molecule (M=4)



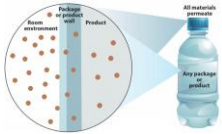
Helium in earth atmosphere
[He] ~5 ppm

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

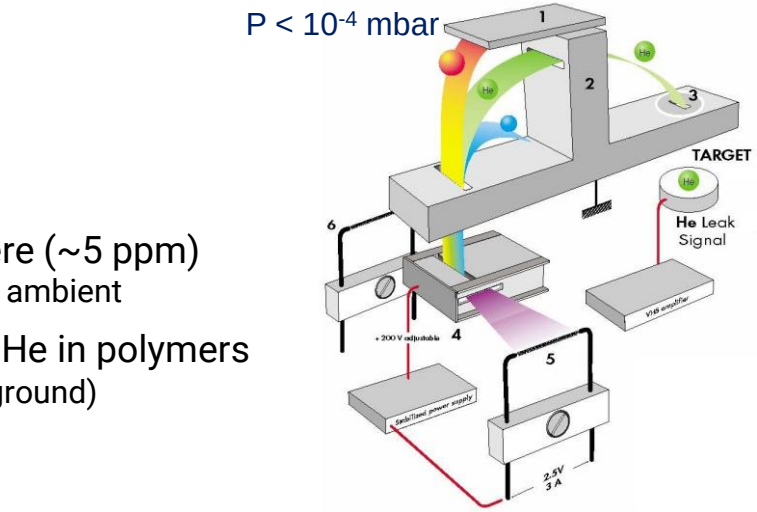
Risk of asphyxiation

Limited resource
5% in natural gas

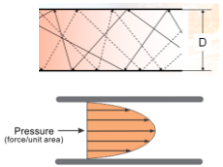
Cost ~8-12 €/m^3

Helium Leak Detection – Operating principle

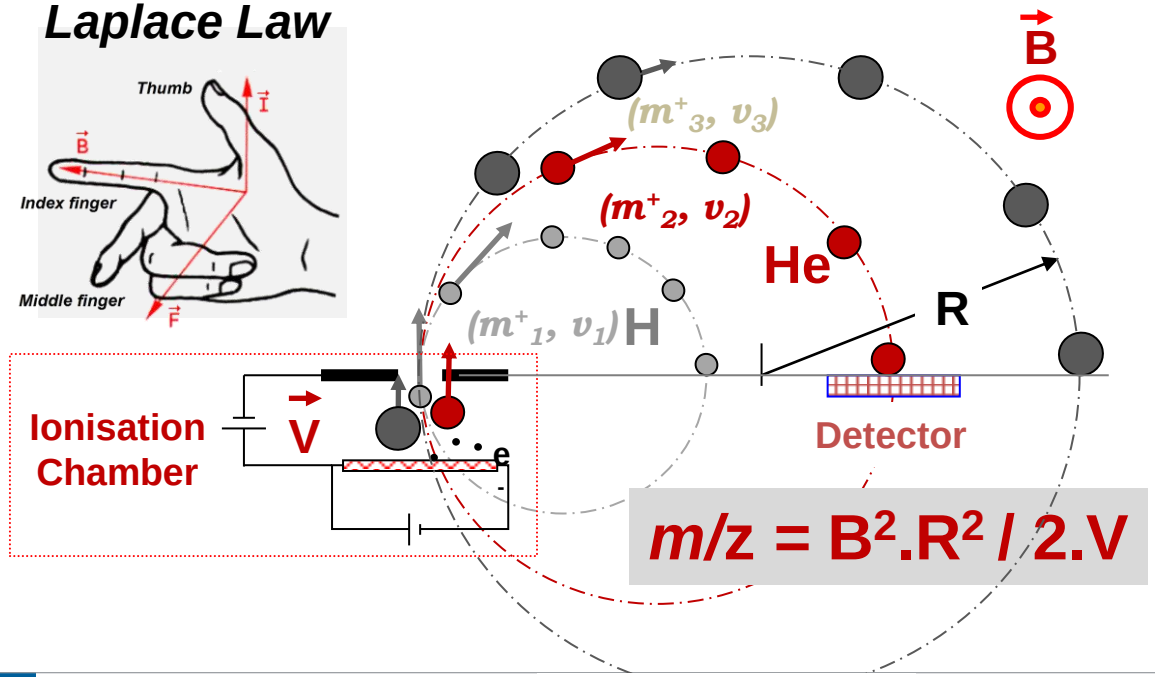
- High sensitivity and Quantitative
  - Magnetic deflection mass spectrometer
  - Down to 10^{-10} mbar.l/s (sub-micron orifice)
- High Selectivity
  - Low Helium concentration in the atmosphere (~5 ppm)
    - Do need to minimize He concentration in lab ambient
  - High permeability, diffusivity & solubility 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



1 Triode electrode
2 Diaphragm
3 Braking electrode
4 Electron collector
5 Filament #1
6 Filament #2



Helium Mass Spectrometer – Operating principle

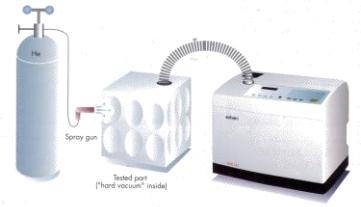
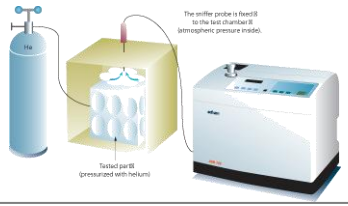


At the exhaust of the ionization chamber, ions have a linear trajectory and a given speed depending on their mass.

A perpendicular magnetic field ion will bend the trajectories of ions and the radius (R) depends on m/z ratio.

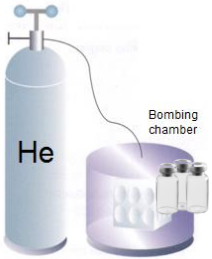
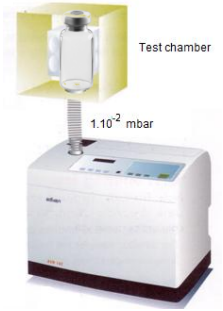
Helium test methods

- 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 performed at P_{Atm})	**GLOBAL SNIFFING TEST** (test performed at P_{Atm})	**HARD VACUUM TEST** (global test)
- the system or the UUT: > can be placed under vacuum. - 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 - to detect very small leaks.
			

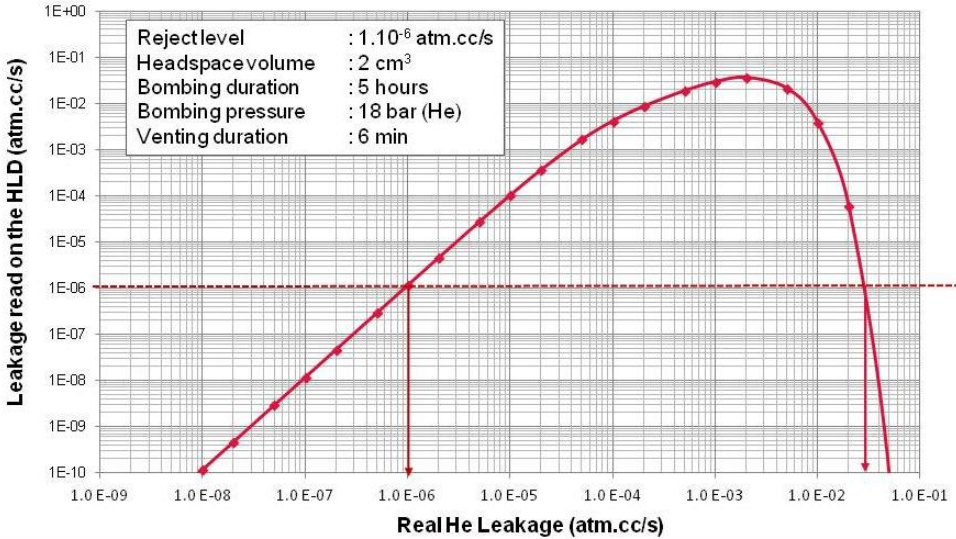
Bombing test of closed containers

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 He leakage (mbar.l/s)	To check that Helium is still present into the part.
1 to Few hours, depending on: - Headspace volume - Minimum detectable leakage - 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 – Challenging to detect large leak

- In case of large leak, the helium inside the container can be evacuated during the initial pumping stage before to be able be measured !



→Risk !

To measured the He leakage for a large leak or a fine line.

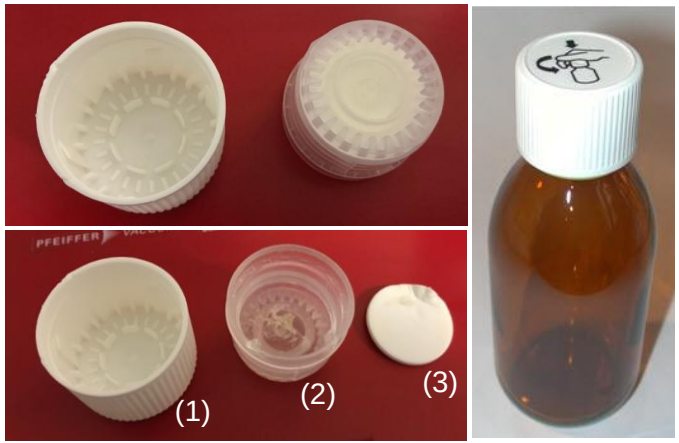
Bombing test of sealed container – summary

- Easy to understand but difficult to set-up
- Many parameters need to be considered and/or defined:
  - Bombing time / Bombing pressure (reject level / container design)
  - Venting time (permeation of the material in contact with helium)
  - Maximum time between bombing and He test (He escaping in case of large leak)
- Quantitative measurements require to know the Helium concentration inside the container.
- Gross leak detection will be very difficult to detect
- Destructive test (plausibility test)

Case study – Glass bottles (180 ml)

Objective: To qualify closure system for different sealing torques :

Closure #1 (plastic liner)



Closure design:

- Complex structure, assembly of 3 parts:
  - a plastic cap (1)
  - an inner cap (2)
  - a liner (3), to ensure tightness (compact plastic plate ~2mm thick)

- The liner is glued on the inner cap.

Test protocol:

- 10 samples for each sealing torque value
- 5 different sealing torques

Test 1: Helium prefilled bottles

ASM 390
(Helium leak detector)

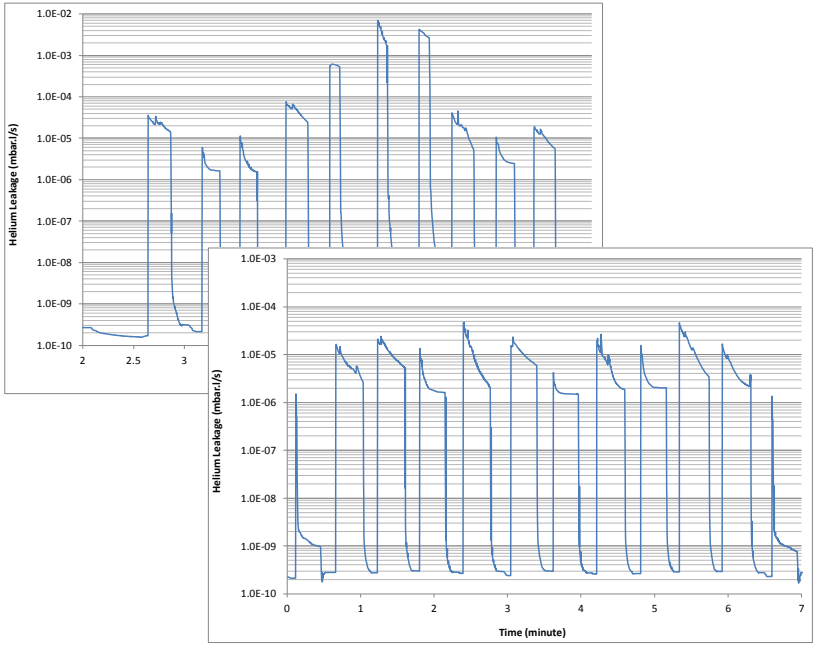
Test chamber

Test protocol:

- Day 1: Preparation of the samples
  - Helium flushing
  - Closing with defined sealing torques
- Day 2: Shipment
- Day 4: Helium test

→ On day 4, the Helium prefilled bottles have been test with ASM 390 helium leak detector…

Test 1: Helium prefilled bottles



What do we observe ?

→ Whatever the sealing torque, most of the helium pre-filled bottles show a He leak rate > 10^{-5} mbar.l/s

→ Helium signal is not stable and decreases

What do we measure ?

- Real helium leakage ?
- Helium trapped inside the cap behind the liner ?
- Helium permeation through the liner ?

What can we conclude ? …. Nothing !

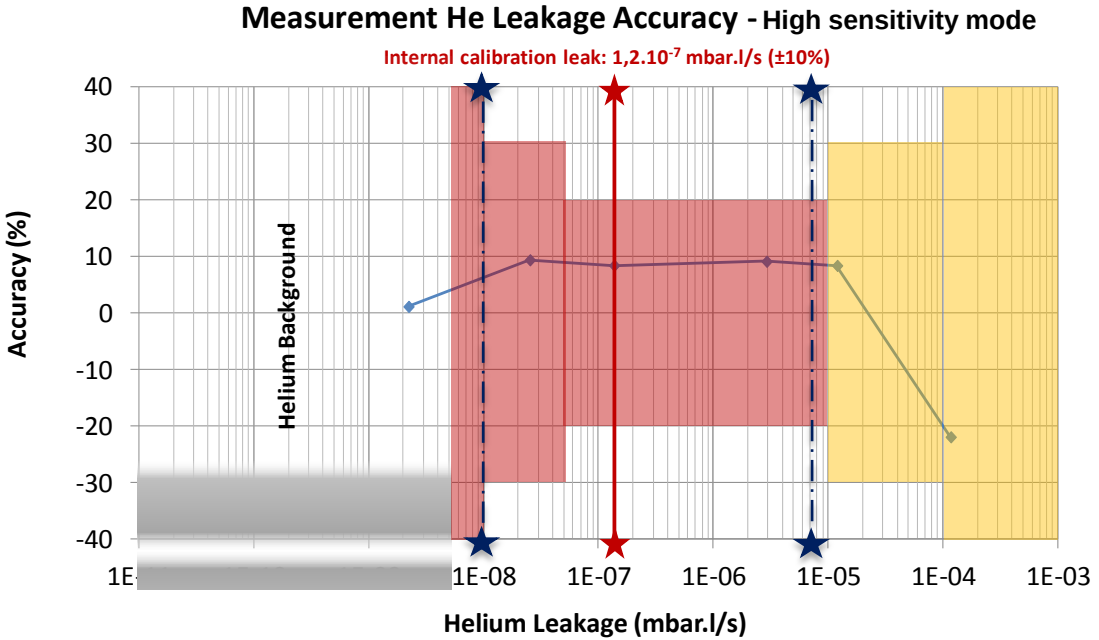
You don't know what you are measuring

How to proceed ?

Test 2: Performed on ASM 2000 (MALL Station)

- Turn-key equipment dedicated for pharma.
- Based on high performance Helium leak detector
- All in one, including Helium charging module
- PLC and HMI (3’’,5 touch screen).
- Customized tooling according to the part to test.
- Trolley includes all vacuum pumps
- Data storage / 3 access level / PDF test reports

Test 2: ASM 2000 - Detection range / Accuracy



★Auto-calibration is performed using the internal calibrated leak ~1.10^{-7} mbar.l/s

★Upper & lower verification points are checked using external calibrated leaks.

Test 2: ASM 2000 and specific tooling

ASM 2000 (MALL Station)

Tooling for glass bottles

Test 2: ASM 2000 test sequence

Tooling for glass bottles

How to proceed ?

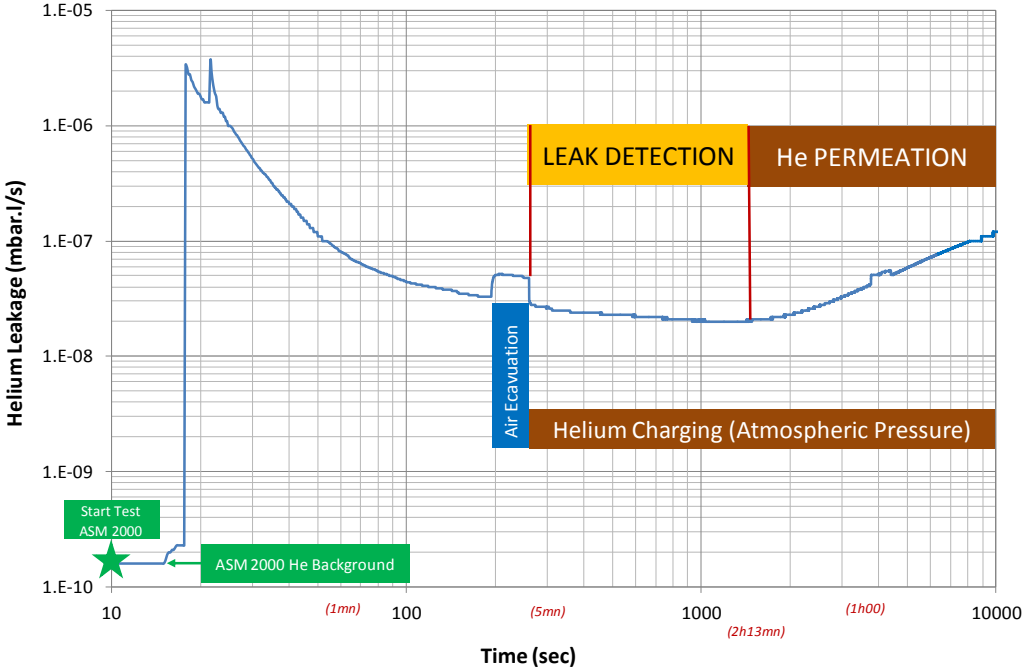
→ Helium injection inside the bottle must be controlled & performed during the test sequence.

→ Leak testing must be performed before helium permeation appears.

Test sequence

1/. Start test on ASM 2000
2/. Bottle evacuation (air)
3/. Helium Charging (Patm)
4/. Helium test
5/. Helium evacuation (Helium)
6/. N_2 venting
7/. Stop test on HLD / Venting

Helium test on ASM 2000



Conclusions

- 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