Optical Emission Spectroscopy, an innovative technology for CCIT

Instructor:

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PDA Parentral Drug Association

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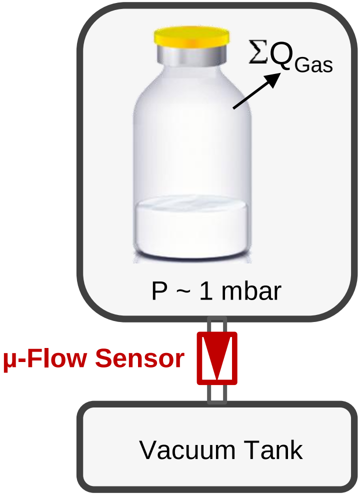
Structure

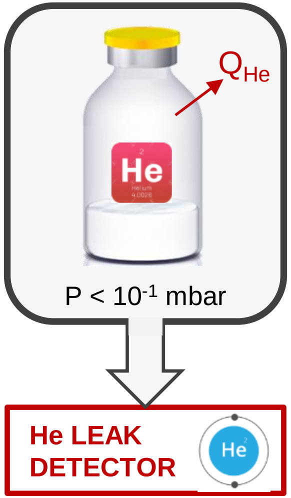
1. Pfeiffer Vacuum 3 CCIT technologies/equipment's
2. Optical Emission Spectroscopy :
   - How does it work ?
   - Influence and limiting factors
   - Advantages
   - Detection of gross leaks
3. Case study #1: Low temperature measurements with O.E.S.
4. Case study #2: Test of Auto-Injectors.
5. Conclusion

Global leak test under vacuum

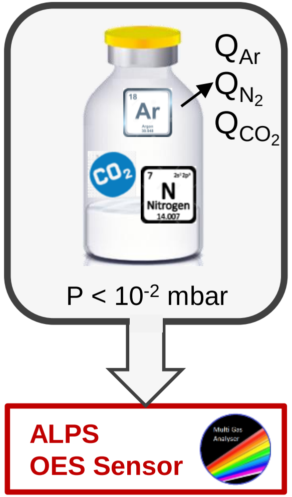
MICRO-FLOW AND MASS EXTRACTION
Micro-flow sensor



HELIUM MASS SPECTROMETRY
Magnetic deflection spectrometer



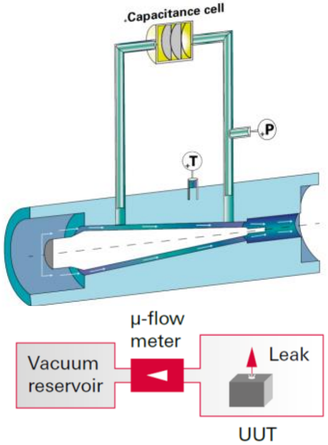
OPTICAL EMISSION SPECTROMETRY
Multi-gas analyser (N_2, CO_2, Ar, H_20,..)



3 technologies for CCIT Solutions

MICRO-FLOW AND MASS EXTRACTION

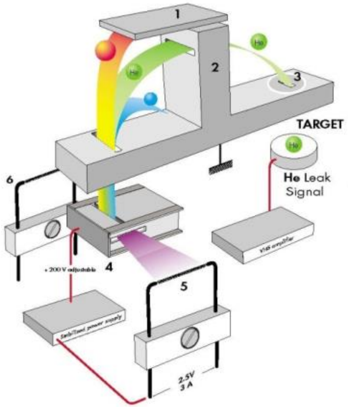
Micro-flow sensor



ASTM F3287-17

HELIUM MASS SPECTROMETRY

Magnetic deflection spectrometer



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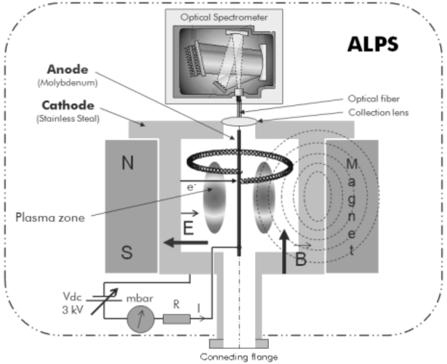
OPTICAL EMISSION SPECTROMETRY

Multi-gas analyser (N_2, CO_2, Ar, H_20,..)



Emerging Technology

3 technologies/equipment's in our CCIT portfolio

MICRO-FLOW AND MASS EXTRACTION

Micro-flow sensor

USP ASTM **ASTM F3287-17**

HELIUM MASS SPECTROMETRY

Magnetic deflection spectrometer

USP ASTM **ASTM F2391-05**

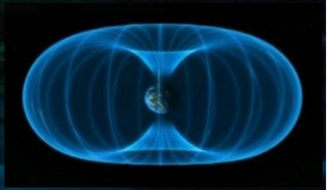
OPTICAL EMISSION SPECTROMETRY

Multi-gas analyser (N_2, CO_2, Ar, H_20,..)

USP *Emerging Technology*

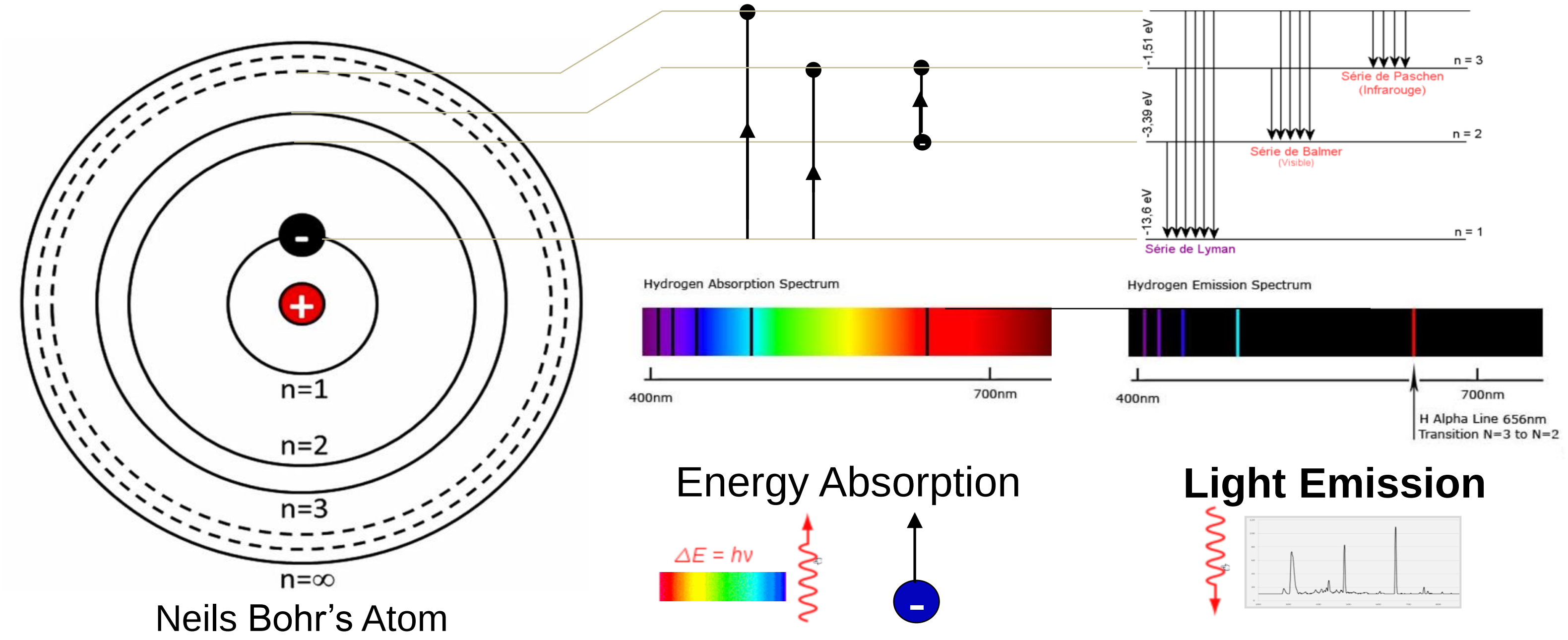
O.E.S. – Operating principle

The Earth's invisible magnetic barrier prevents the energy given off by the Sun from boiling away our oceans and dissipating our life-sustaining atmosphere.



The northern lights (aurora borealis) are caused by solar wind and storms *can generally be seen at about 70 degrees of latitude, near the Arctic circle.*

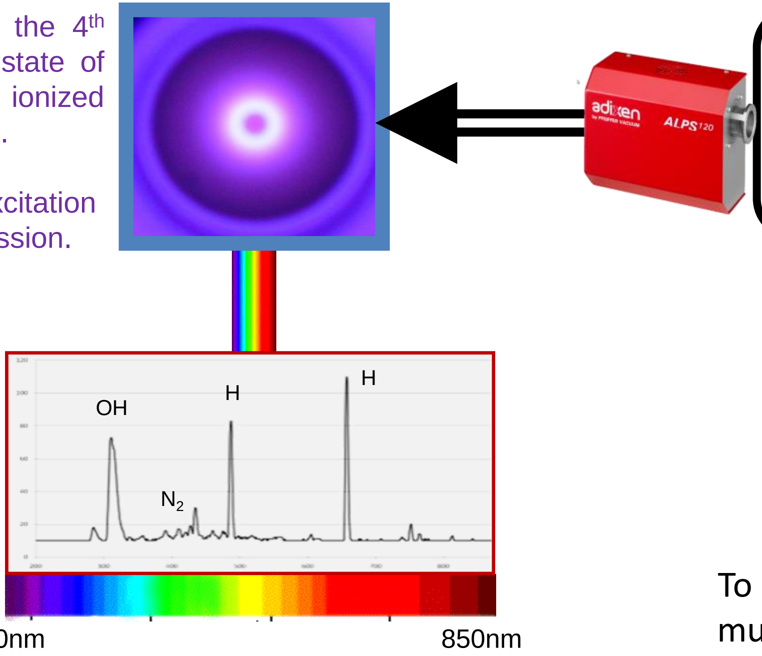
O.E.S. – Operating principle



O.E.S. – Operating principle

A Plasma is the 4th fundamental state of matter = hot ionized gas (instable).

Plasma de-excitation give light emission.



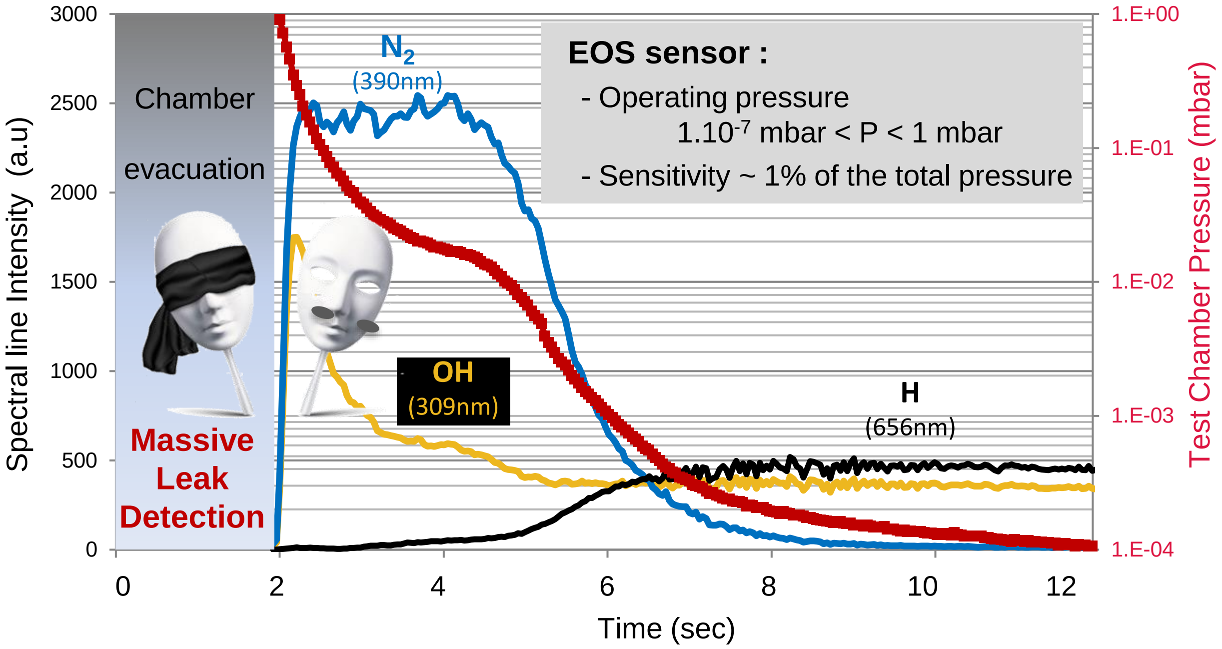
Test chamber (P<5.10^{-2} mbar)

Sealed component (N_2, Ar, CO_2…)

Q_{N2} (atm.cm^3/s)

To detect leaks we are using our patented multi-gas "ALPS" sensor which is based on O.E.S.

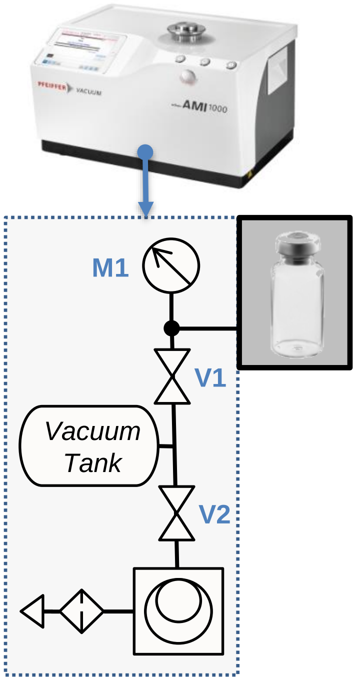
O.E.S. – Real time measurement



The air (N_2) inside the test chamber can be easily evacuated using vacuum pumps.

Moisture (H_20 → H & OH) is much more difficult to evacuate because it is coming from out-gassing of materials in contact with vacuum.

Massive leak detection prior to OES



- **AMI includes a Massive Leak Detection module (>100µm)**

  - GO/NOGO test = qualitative measurement.

- **For Dry Filled Products, based on a volumetric method:**

  - Pressure equilibrium between a vacuum tank and the test chamber.

  - The test chamber is designed in order to minimize the free volume around the sample and the vacuum tank is sized accordingly.

- **For Liquid Filled Products, based on deep vacuum decay:**

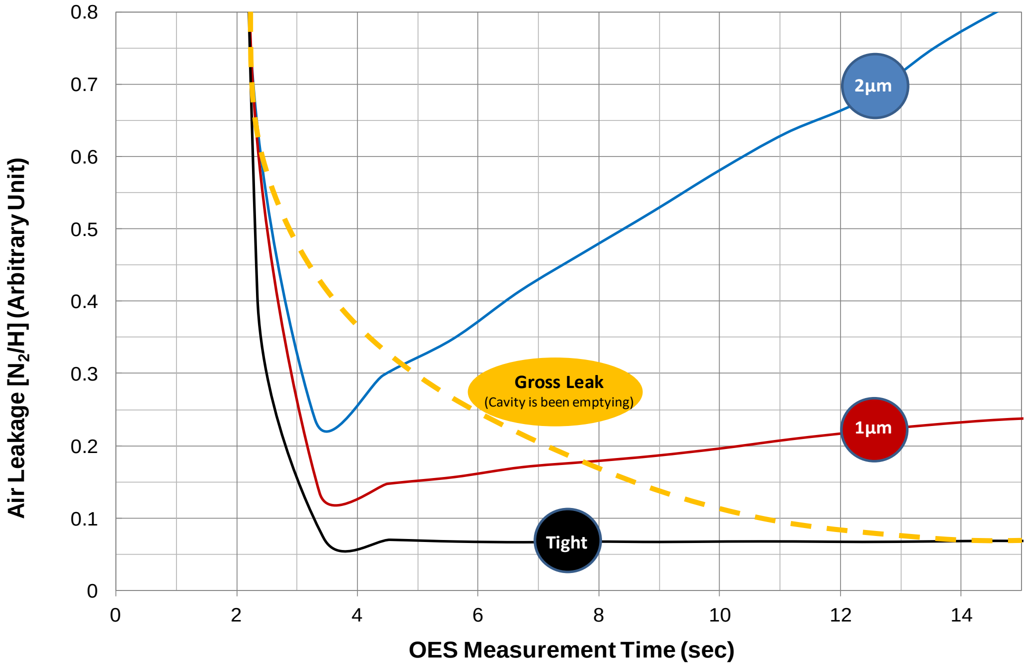
  - Pressure must be below the vapor pressure of liquid.

  - Free volume around the sample is not anymore an issue.

- **Massive Leak Detection prevents equipment contamination**

  - In case of Gross Leak (air/liquid), the high vacuum circuit and OES sensor are not contaminated. Only few components can be easily cleaned and dry.

OES – Typical air leakage signal (raw data)

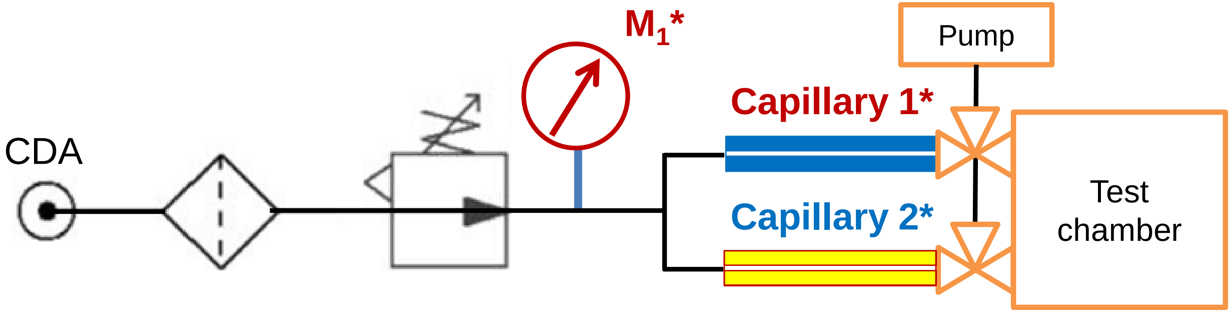


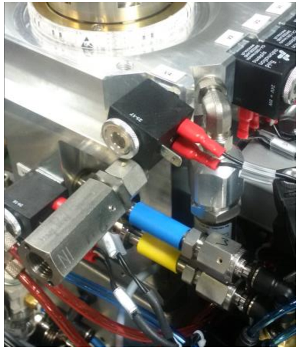
The air leakage corresponds to the intensity ratio [N_2/H]

In case of fine leak, the air leakage signal (N_2/H) increases as out-gassing (OH & H) is decreasing with time.

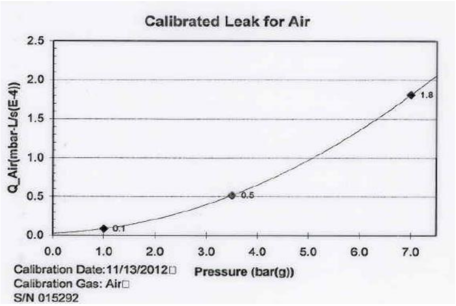
In case of gross leak (>100µm for 1cc headspace), depending on the headspace volume we can see the container being evacuated.

A set of 2 capillaries is used for calibration

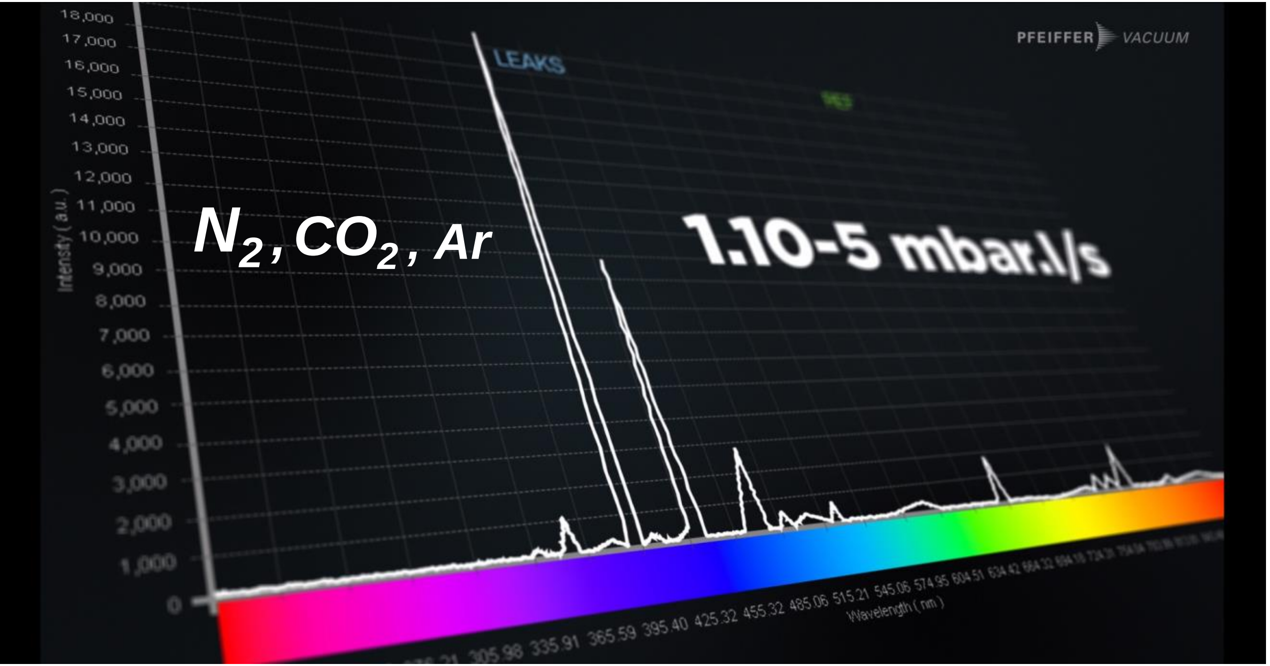




- A set of 2 capillaries allows to generate a calibrated air leak into the test chamber in the range: 2.10^{-5} – 1.10^{-3} mbar.l/s.
- The air leakage provided by the capillaries depending on the CDA inlet pressure set up by the automatic pressure reducer.
- The M1 gauge measures the exact pressure just among the capillaries
- Calibration certificates are delivered for capillaries & pressure gauge



A quantitative and **calibrated** leakage measurement !



OES – Influence & limiting factors

For all vacuum test solutions: **Detection limit ↘ when Test Duration ↗**

– Out-gassing limit the sensitivity of the test, it can be minimized by:
  - Design of Container and test chamber (material, surface, roughness)
  - Controlling operating conditions: temperature (°C) and humidity (<30%RH)
  - Increasing the test duration…

– Gross leak detection can be challenging in case of small gas headspace volume combined with a low out-gassing solid drug.
  - Specific Massive Leak test can be performed prior to O.E.S measurements

No sample preparation – Automatic test sequence

1/. Part loading (manually or automatically)

2/. Chamber evacuation (1000 → few mbar)
(Massive Leak detection)

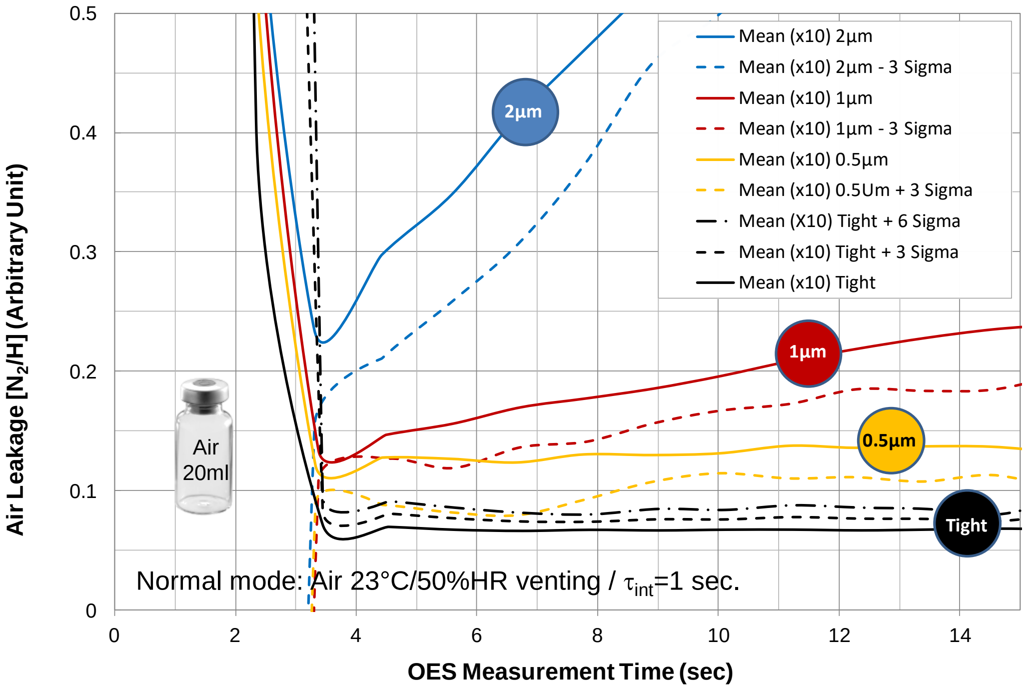
3/. Chamber pumping (few mbar → $<10^{-4}$ mbar)

4/. O.E.S. measurement start when pressure is $< 10^{-2}$ mbar

5/. Chamber venting (with Ambient air, dry N_2 or Argon)

6/. Part unloading

O.E.S. - Fast and sensitive

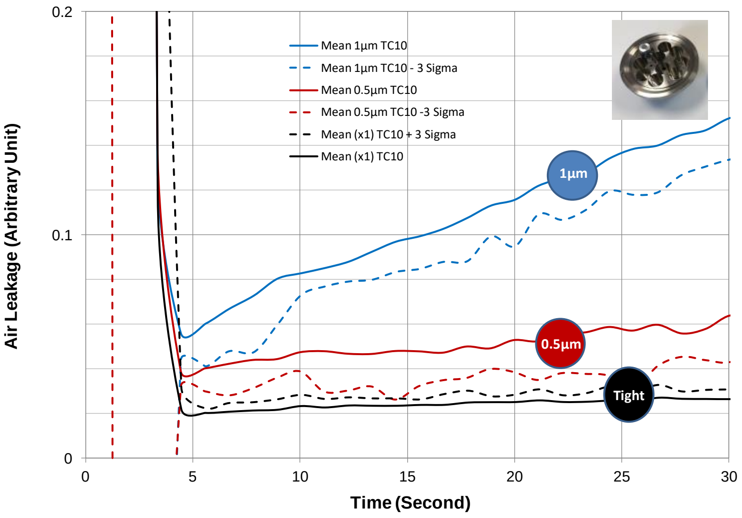


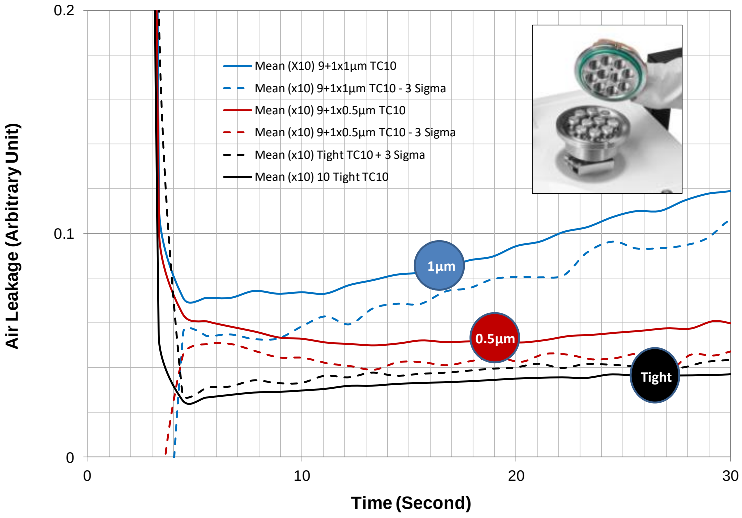
The Air Leakage raw signal corresponds to the intensity ratio $[N_2/H]$.

OES (Ambiant air venting) 23°C / 50% RH		
Detection Limit	Total Test Duration	
	Leak-3σ Blank+**3σ**	Leak-3σ Blank+**6σ**
2 µm	10 sec	10 sec
1 µm	10 sec	10 sec
0,5µm	10 sec	14 sec

O.E.S. – Method is volume independant

→ 0.5µm defect (sharp edge orifice) can de detected in a batch of 10 vials and/or on 1 vial in the same test chamber.





O.E.S. – Measurements are volume independent

Sensitivity are is not impacted by:

- container expansion during the test

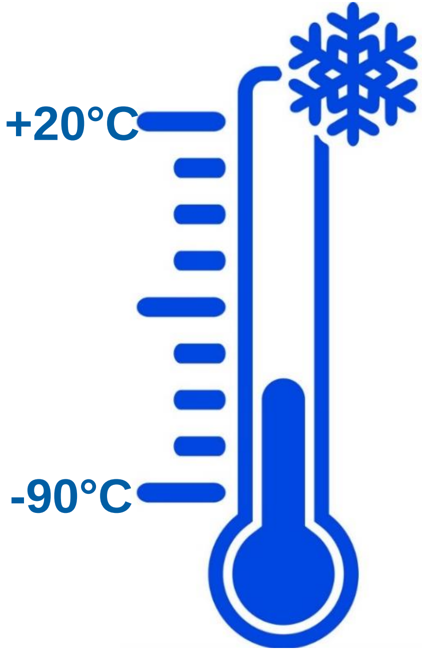
→ Tests can be performed on semi-rigid containers

- free space in the chamber around the container

→ Test of complex design devices (i.e. AI)

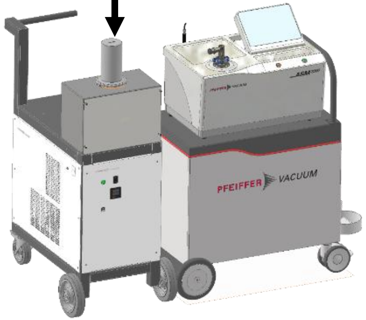
→ Possibility of batch testing to increase the throughput

Case #1: Low Temperature Test (-80°C)



Low temperature Module
to test **closed containers**

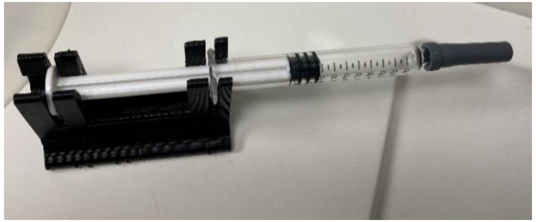
(tracer gas pre-filled containers)



N_2
CO_2
Ar

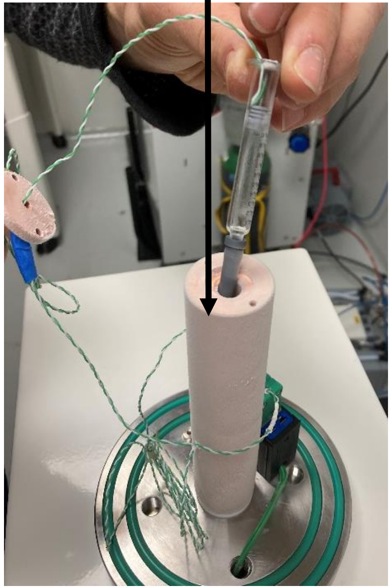
Low Temperature Test – Sample preparation

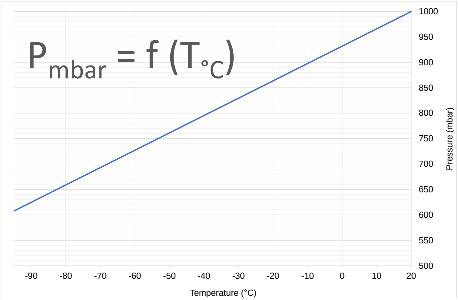
Tracer gas charging procedure



K Type Thermocouple

Copper tooling

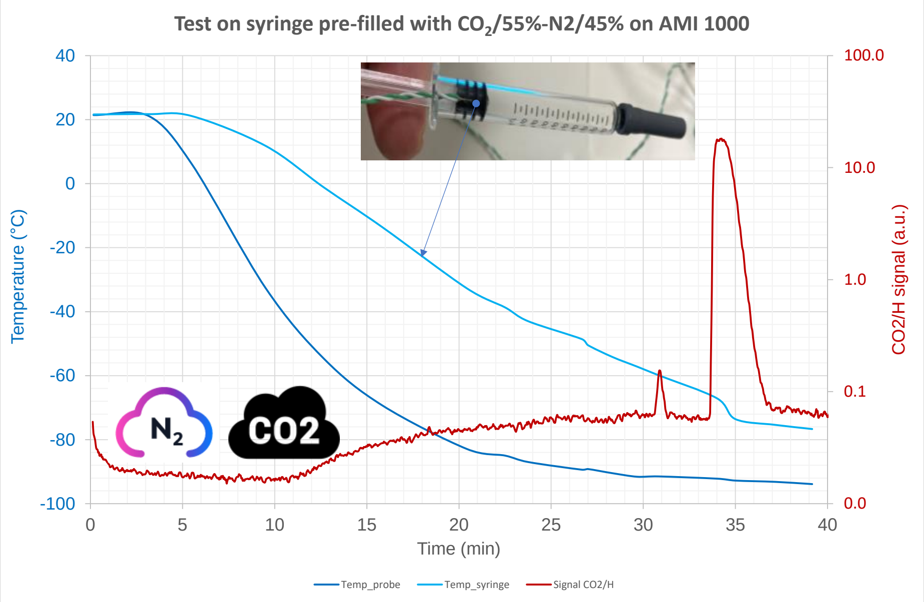


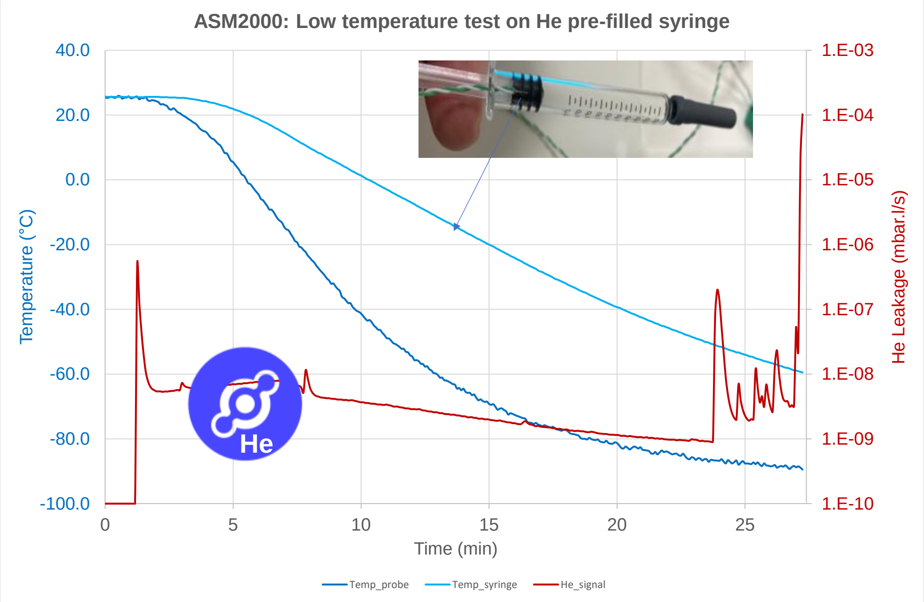


Pressure inside the syringe will decrease during cooling down.

Leakage can be normalized for 1 bar differential pressure equivalence.

Low Temperature Test: O.E.S versus Helium



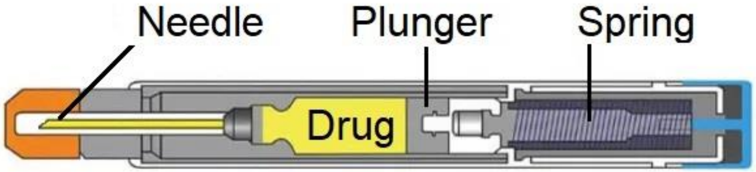


→ Loss of integrity around -60°C can be detected with both test methods O.E.S. and Helium

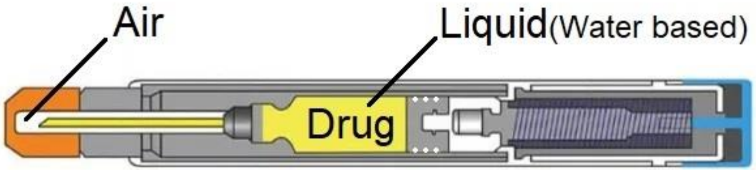
Low Temperature Test: O.E.S versus Helium

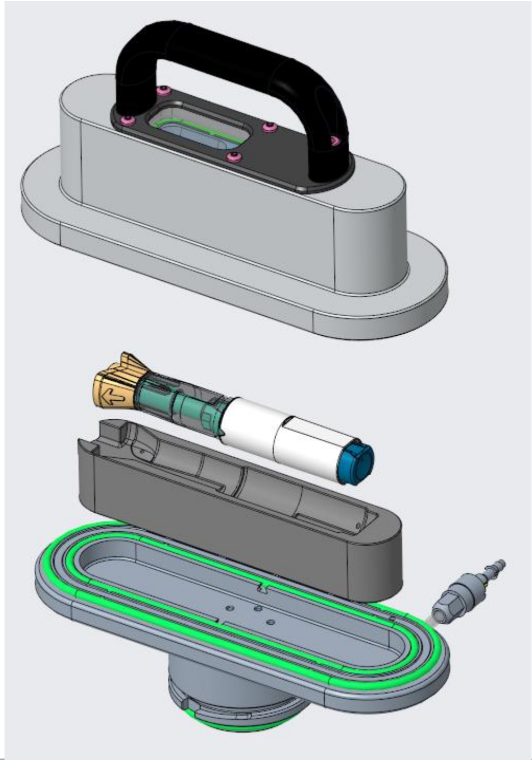
	Helium	O.E.S.
Tracer gas	Helium	Gas naturally present into headspace (N_2, CO_2, Ar, …)
Sample preparation	Need to charge He and to control [He]	No sample preparation
Sensitivity	> 1.10^{-9} mbar.l/s	> 5.10^{-6} mbar.l/s
Measurement	Continuous leakage measurements during temperature drop	
	Do not require any tracer gas bombing stage to speed up the test	
	He permeation need to be considered	Minimum permeation impact
	Destructive	Non-destructive

Case #2: Test of Auto-Injectors



- **Detection of small Air leakage or Large Water leakage at the needle shield → bigger risk during the assembly process !**
- Water leaks at the plunger
  → Difficult to detect with the 3 sealing rings in serie





O.E.S. to test Auto-injectors

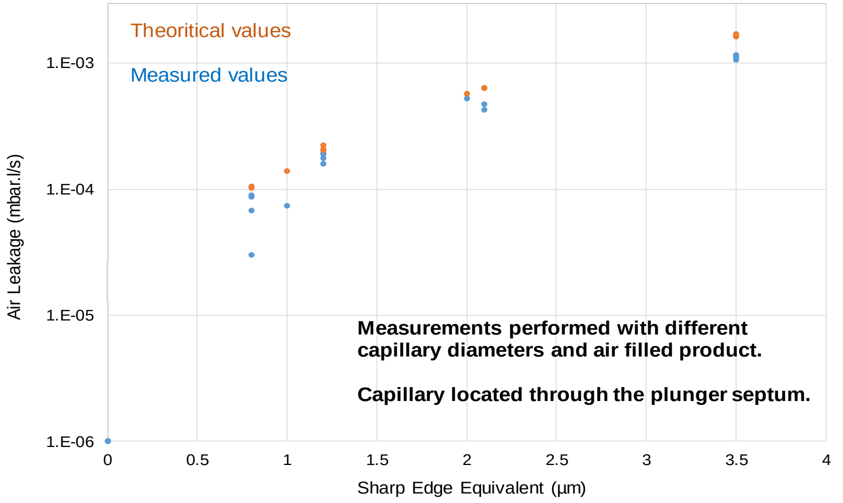
In a single test sequence O.E.S. is able to:

- measure air leakage > 1 µm orifice

and during the same test sequence

- detect water leak > 5 µm (qualitative test)

within about 45 seconds !



Conclusions

General Features

Direct measurement
Specific gas leakage escaping from a container under vacuum

Non-destructive testing

Deterministic method
Deterministic method / Calibrated Measurements

Simple and easy to use
No sample preparation required

Repeatability
Reduces false failures, a very costly issue

Unique features with O.E.S.

Multi-gas analyzer
Optical Emission Spectroscopy sensor, Air, N_2, CO_2, Ar, H_20 can be detected

Selectivity
Can detect air(N_2) and water leaks simultaneously

Speed of test
Much faster than other vacuum tests <15 sec to measure 0.4µm orifice on 20ml vial.

Low Temperature measurements
(down to -80°C and below)

Conclusions

• AMI equipments, using O.E.S. spectroscopy have been qualified as IPC test for blister packs (sensitive inhalation drugs).

• Promising technology to perform high sensitivity 100% in-line leak testing.

→ *0.4µm defect (sharp edge orifice) can be detected in 30 sec on glass vial tested one by one or by batch of up to 10, 50, 100.*

Thank you for your attention !

Links http ://www.pfeiffer-vacuum.com
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