

High Voltage Leak Detection (MicroCurrent). HVLD^{MC}

- Case Study: HVLD with Albumin Solution
- Case Study: HVLD Vs. Vacuum Decay with Albumin Solution

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PDA, Copenhagen 2024

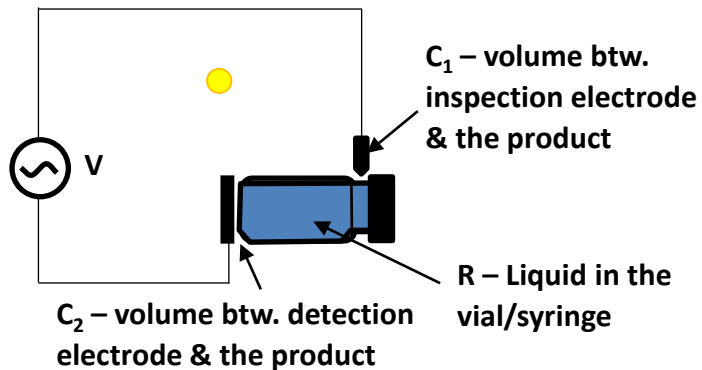


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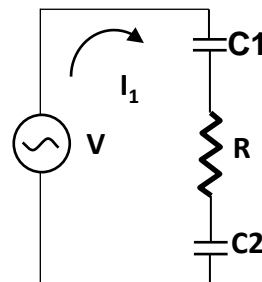


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Functional Principle of HVLD^{mc} Test

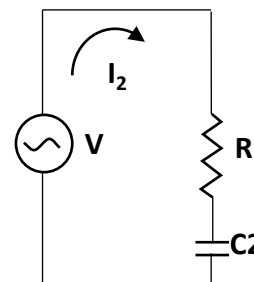


Good Sample



2 capacitors

Leak



1 capacitor

V – High Voltage Source

R – Electric Resistance of the product

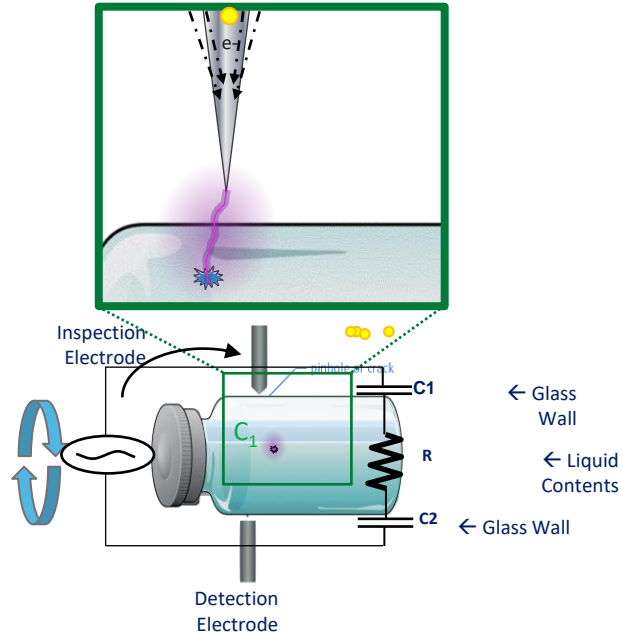
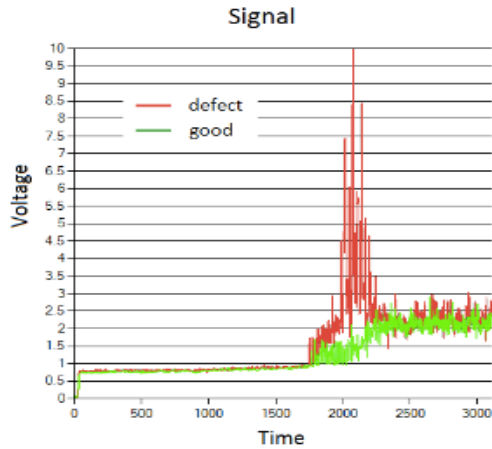
C₁ – Capacitor 1: Glass between the inspection electrode and product

C₂ – Capacitor 2: Glass between the detection electrode and product

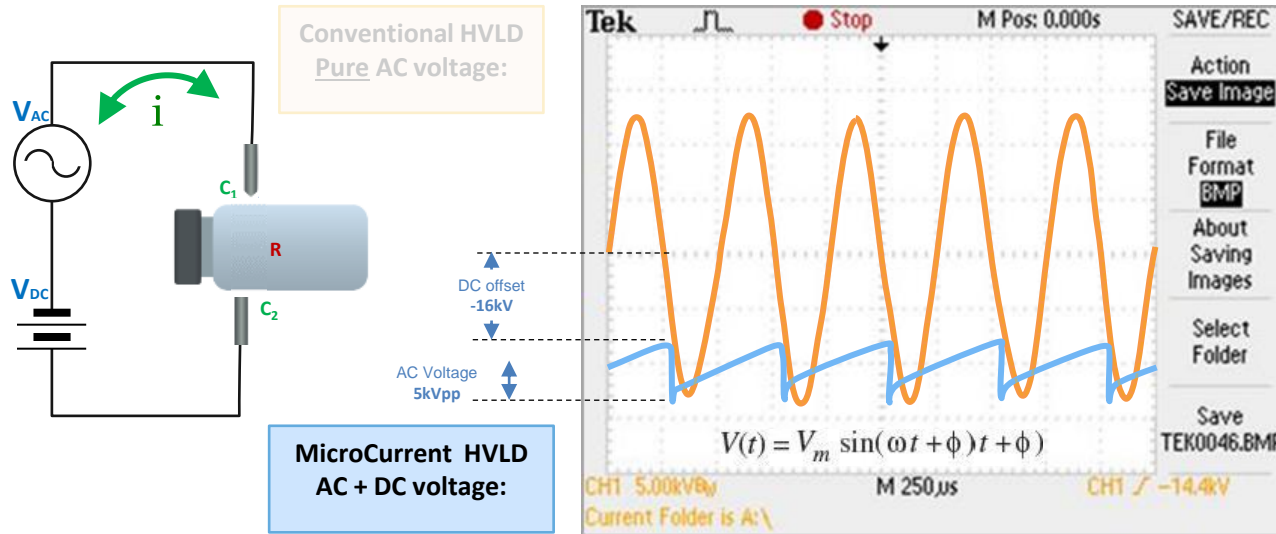
I₁ – current produced when product container is sealed

I₂ – current produced when product container is defective

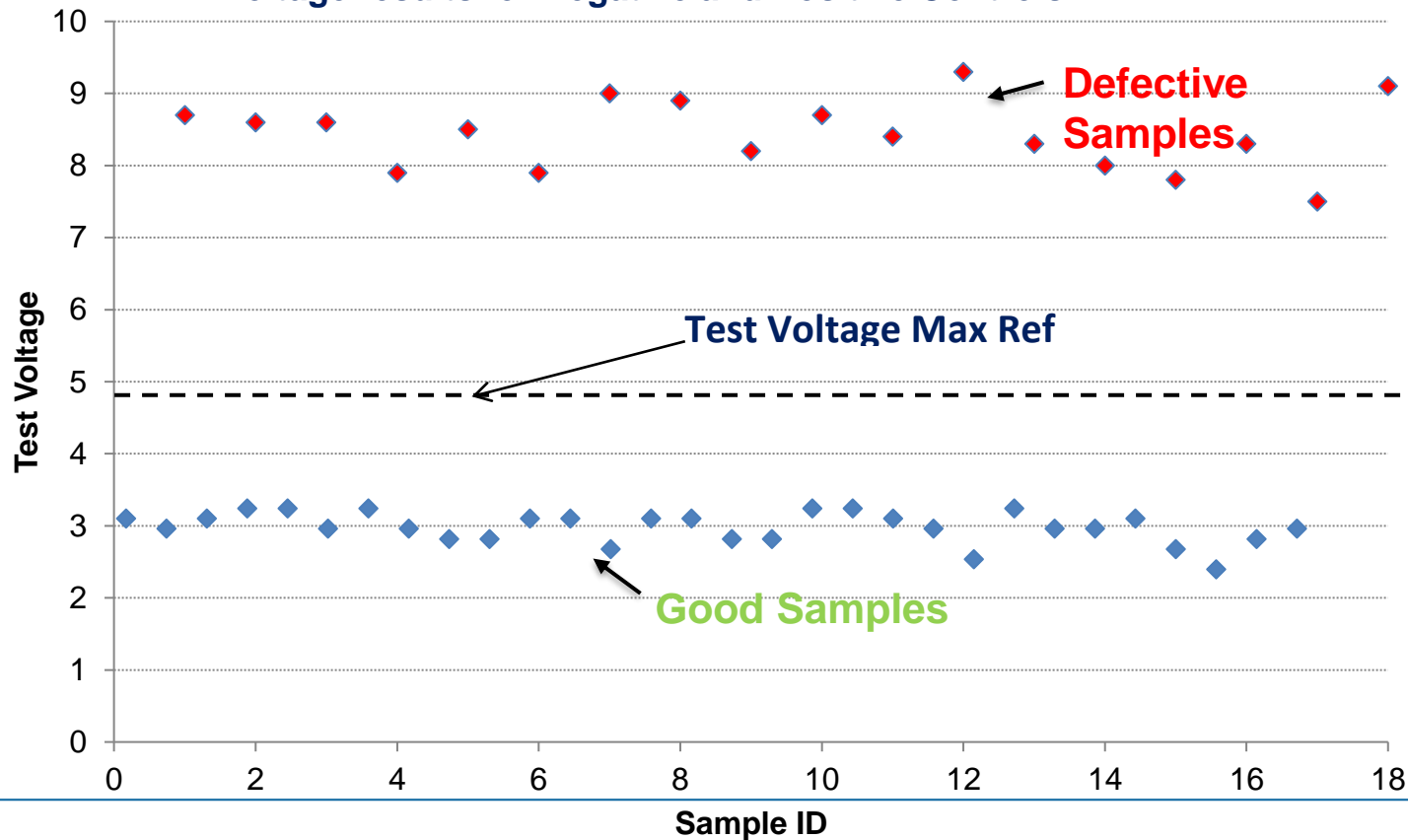
High Voltage Leak Detection (Microcurrent).



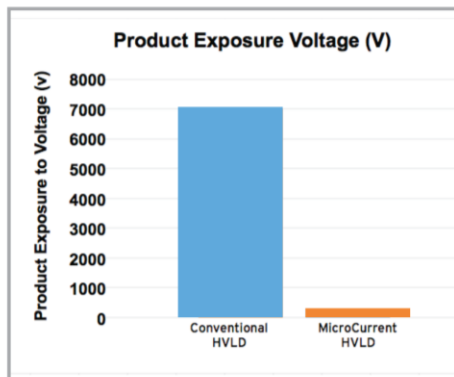
This new technology applies less than **50% of the voltage** used with conventional high voltage technologies and the product its exposed to less than a **5% of the voltage exposure** experienced when testing with comparable HVLD solutions.



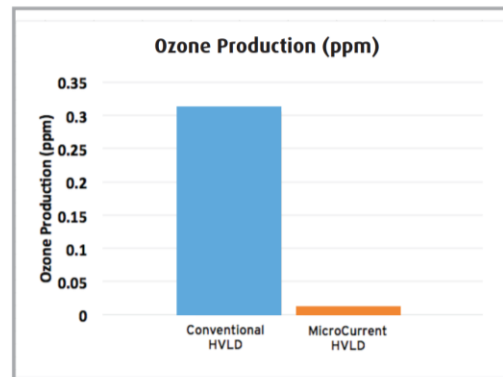
Voltage results for Negative and Positive Controls



Product HV Exposure



Ozone Creation



10 minutes test
Outside the product

	Conventional HVLD	MicroCurrent HVLD
Exposure Voltage (V)	7000	300
Ozone Production (ppm)	0.305	0.006

Misconceptions between

Conventional AC based HVLD vs. MicroCurrent HVLD^{mc}

- With MicroCurrent HVLD^{mc} the product is not exposed to HV (200-300V vs 7'000 – 10,000V+)
- No Ozone is created inside the package
- The current through the product is 2 - 3'000 times less than with conventional AC based HVLD systems >>> MicroCurrent
- MicroCurrent HVLD^{mc} can measure low conductivity products - < 1 micro Siemens
- MicroCurrent HVLD^{mc} can inspect products containing alcohol
- MicroCurrent HVLD^{mc} is capable of inspecting small Packages with low fill levels
- MicroCurrent HVLD^{mc} does not adversely affect proteins
- MicroCurrent HVLD^{mc} can detect defects under the crimping
- MicroCurrent HVLD^{mc} can detect clogged cracks

Case Studies:

- HVLD^{mc} with Albumin Solution (1,2,3 and 66 days)
- HVLD^{mc} vs. Vacuum Decay with Albumin Solution

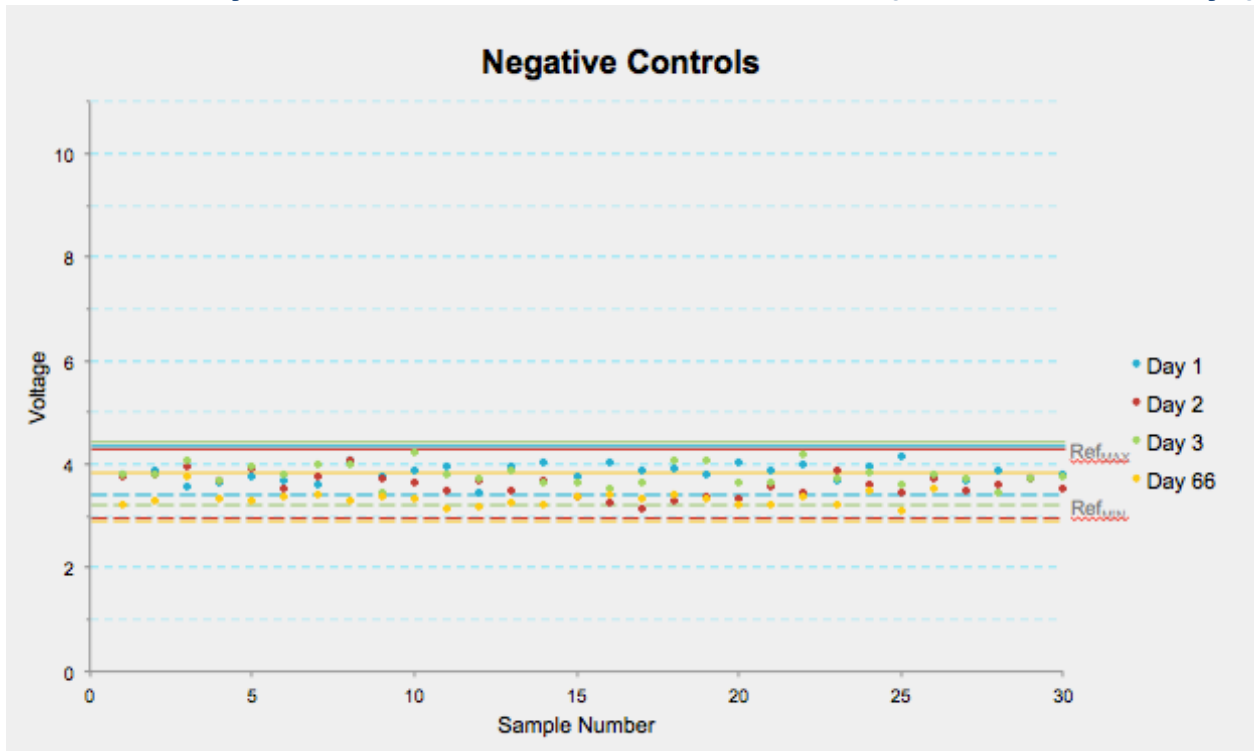


Case Study 1: HVLD with Albumin Solution (1,2,3 and 66 days)

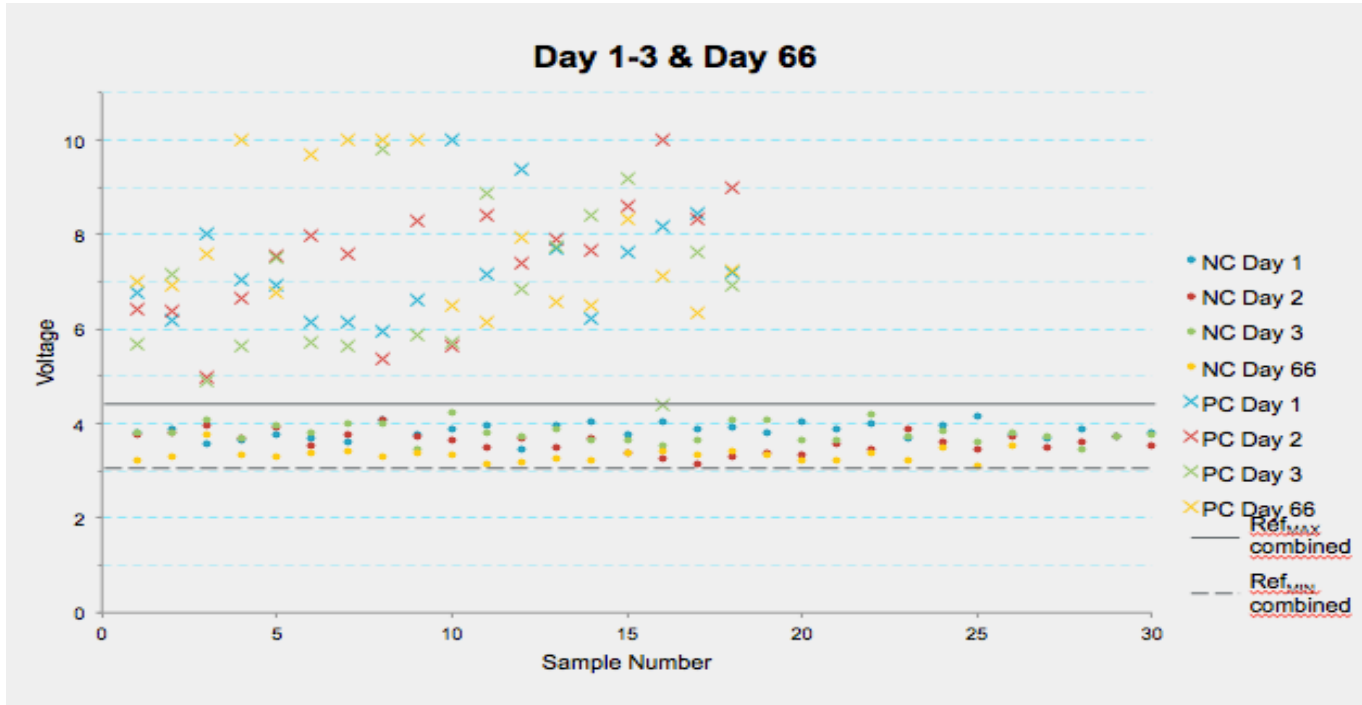
- ✓ 2R (4ml capacity) glass vials
- ✓ 13mm Teflon faced stopper, Flip Off Seal 13 mm
- ✓ Positive Controls: 5, 10 und 15 μm laser drilled holes, neck and bottom
- ✓ 3 positive control samples of each hole size and position
- ✓ 4 rounds of testing; 3 consecutive days, and one round 66 days later in different locations (NY-CH).
- ✓ Fill volume was 3ml 20% Albumin solution for both PC and NC groups. Vials were filled prior to testing, stoppered and crimped.



Case Study 1: HVLD with Albumin Solution (1,2,3 and 66 days)



Case Study 1: HVLD^{MC} with Albumin Solution (1,2,3 and 66 days)

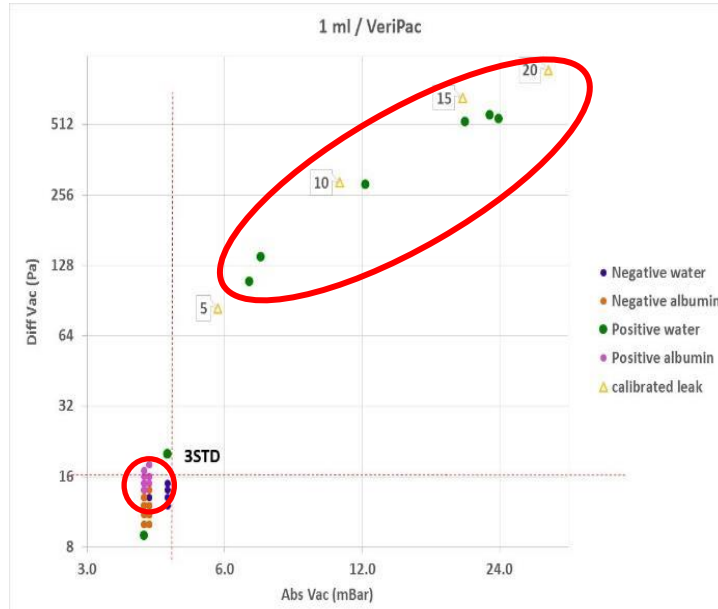


Case Study 2: Vacuum vs. HVLD^{mc} for PFS

- ✓ 1mL and 2.25 mL Syringe (Water and Albumin)
- ✓ Positive Controls: 5, 10 und 20 µm laser drilled holes, barrel and shoulder.
- ✓ 3 positive controls with water for each size
- ✓ 5 positive controls with Albumin for each size
- ✓ Albumin concentration of 17.5%
- ✓ Two test methods: Vacuum Decay and HVLD^{mc}

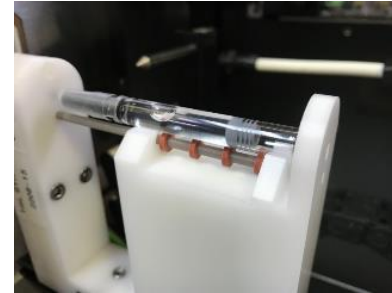
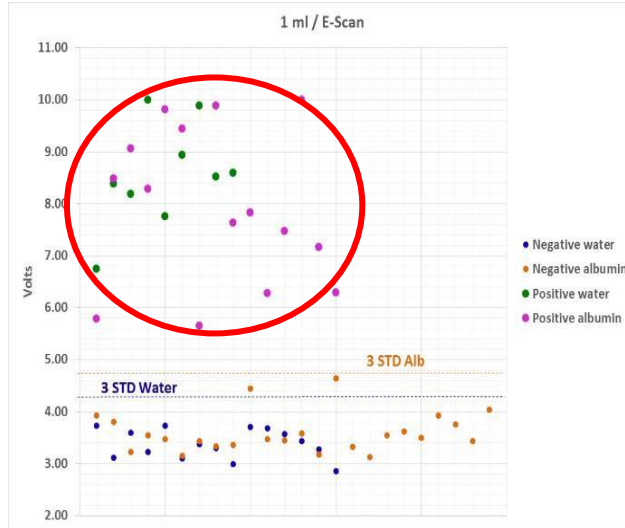


Vacuum Decay



- Vacuum Decay @ <5.0mbar
- Albumin & Water Samples
- Laser Drilled Defects 5, 10, and 20 μ m.

HVLD^{mc}



Conclusion

HVLD shows a clear advantage in detecting defects in parenteral packaging containing large molecule products.

Realistic Defects



Naturally Occurring Defects

Sample	leak rate			Visual	Size um
	mbar-l/s	10^{-5} mbar-l/sec	sccm		
1	0.00095	95	0.05700	Large crack	2.67
2	0.0000021	0.21	0.00013	Medium crack	0.13
3	0.000014	1.4	0.00084	Medium crack	0.32
4	0	0	0.00000	Small Scratch	0.00
6	0.00067	67	0.04020	Large crack	2.24
7	0.015	1500	0.90000	Large crack	10.61
9	0.00000029	0.029	0.00002	Small crack	0.05
10	0.00029	29.0	0.01740	Large crack	1.47
11	0.074	7400	4.44000	Large crack	23.56
12	0.055	5500	3.30000	Large crack	20.31
16	0.0014	140	0.08400	Small crack	3.24
18	0	0	0.00000	Small Scratch	0.00
19	0	0	0.00000	Small Scratch	0.00
20	0.016	1600	0.96000	Large crack	10.95

Sample 2



Sample 6



Sample 3



Sample 16

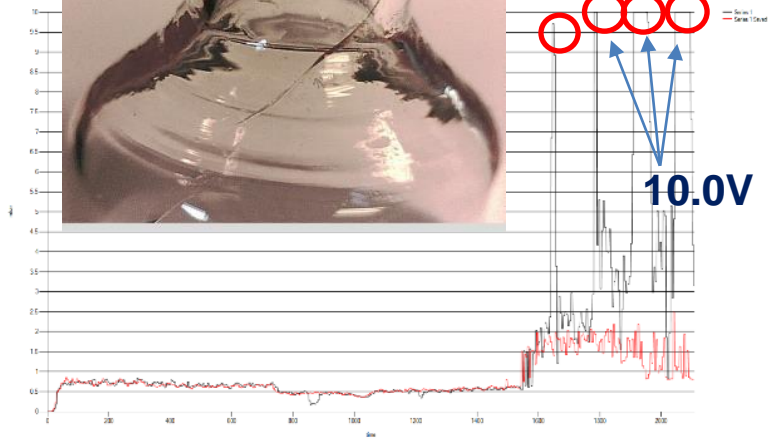


Defect Detection

- ❖ Controlled crack produced.
- ❖ Certified flow measurement with Helium mass spec.
- ❖ Peak signal response is recorded.
- ❖ Voltage signal response with each rotation.



Sample 1

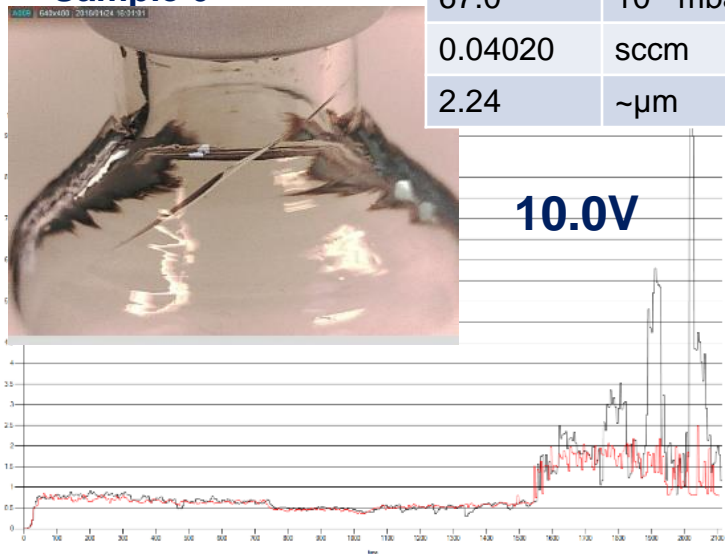


He Certified Leak Rate	
95.0	10 ⁻⁵ mbar·l/s
0.05700	sccm
2.67	~µm

Traditional Target Leak Sizes

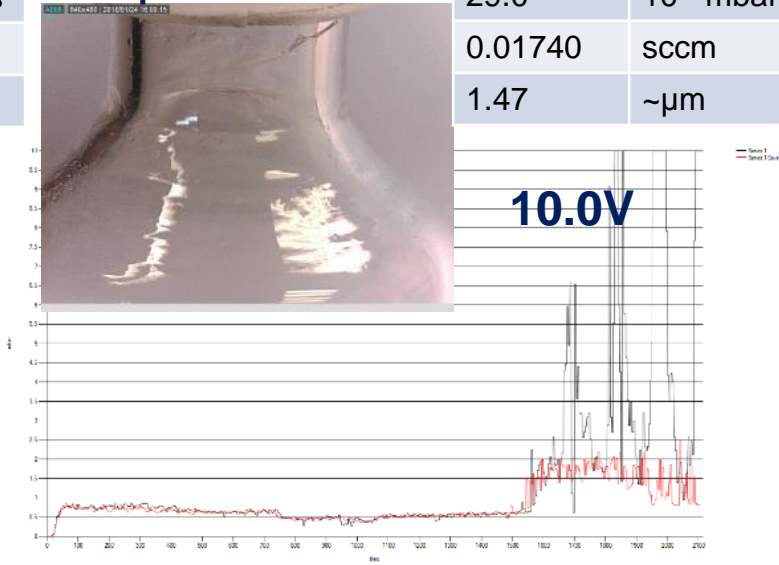
Sample 6

He Certified Leak Rate	
67.0	10^{-5} mbar·l/s
0.04020	sccm
2.24	$\sim\mu\text{m}$



Sample 3

He Certified Leak Rate	
29.0	10^{-5} mbar·l/s
0.01740	sccm
1.47	$\sim\mu\text{m}$



² ²
He
Helium
4.002602

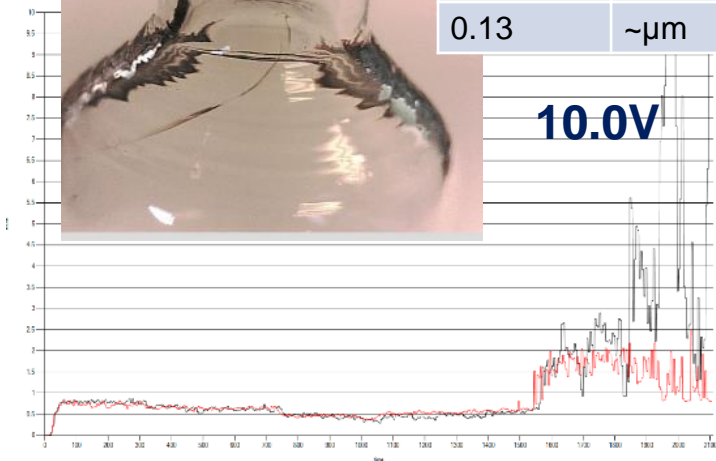
Leak Rates

Sample 2



He Certified Leak Rate	
0.21	10 ⁻⁵ mbar-l/s
0.00013	sccm
0.13	~μm

10.0V

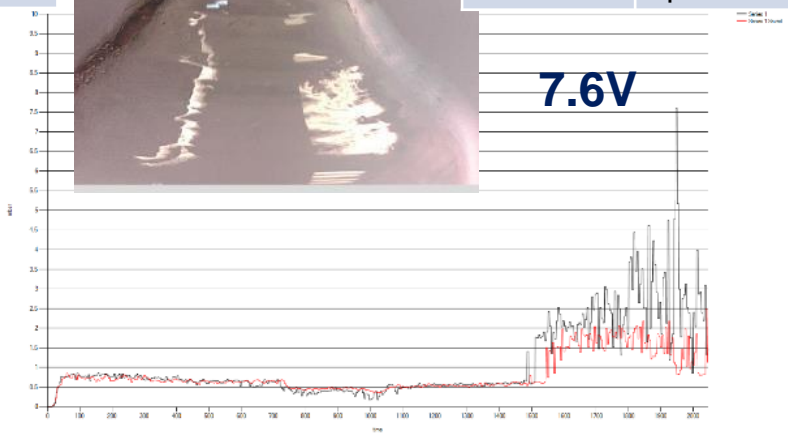


Sample 3



He Certified Leak Rate	
1.40	10 ⁻⁵ mbar-l/s
0.00084	sccm
0.32	~μm

7.6V



Summary

- **Vacuum decay is a sensitive and reliable test method for gas applications**
- **Reliability and capability of Vacuum decay is adversely affected by large molecule products such as Albumin, producing a low to zero detection capability for protein base solutions**
- **MicroCurrent High Voltage Leak Detection (HVLD^{mc}) is capable of detecting micro cracks down to the MALL, including for low conductivity liquids**
- **HVLD^{mc} is not time critical (time zero vs. day 66).**
- **MicroCurrent HVLD^{mc} generally effective for wide range of product conductivities.**
- **Naturally occurring defects below the 1 μ m level can be readily detected using HVLD^{mc}**
- **Nonvisible cracks below the crimping are detectable**

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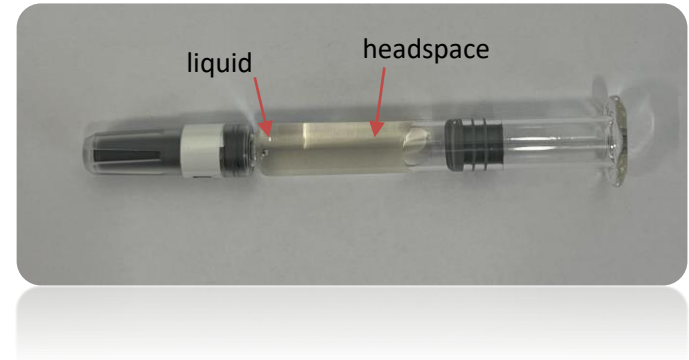
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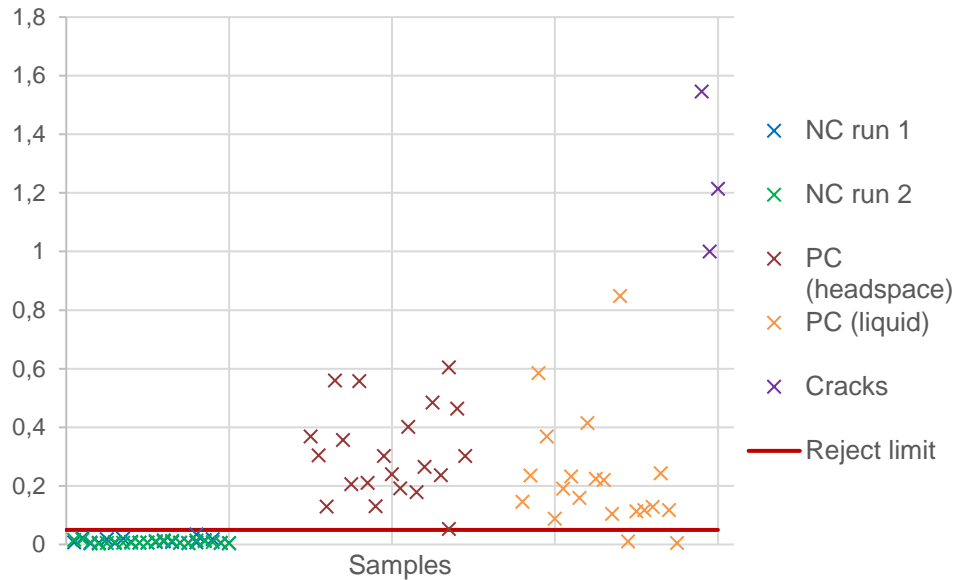
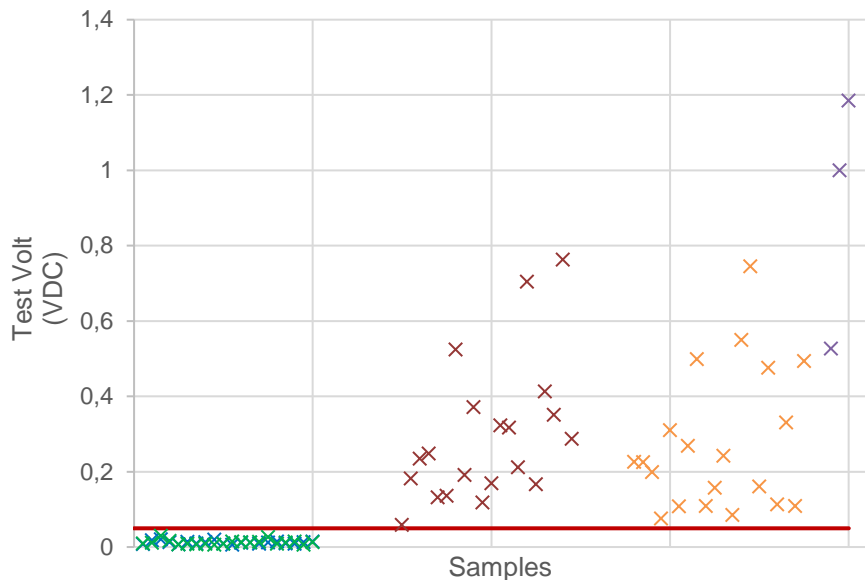


Establishing repeatability

- Study performed on E-Scan® 615 HVLD^{MC} Instrument
- 1mL syringe, ca. 0.71mL fill volume
- Same tests performed 4 weeks in a row
- Viscous Product- NDA
- Results:
 - Week 1 & 2 : All samples detected as expected
 - Week 3 & 4 : Two PC samples not detected → clogging

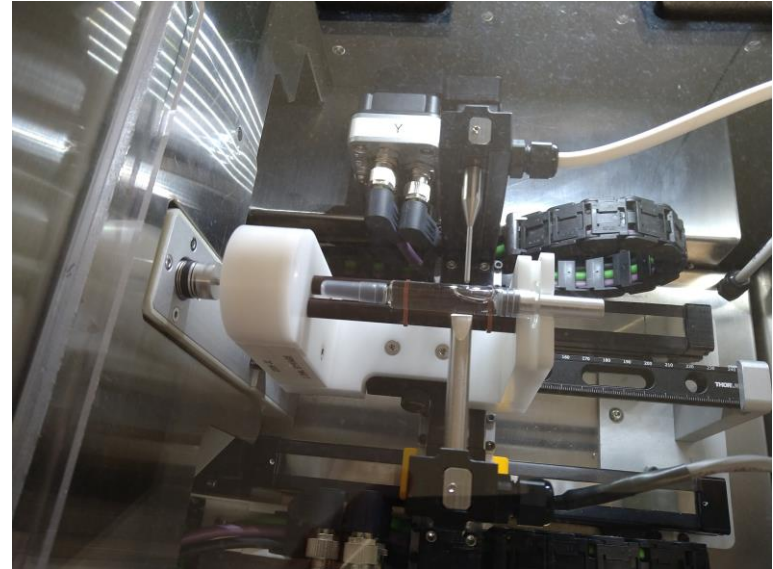


Week 1 vs Week 4



Testing the plunger of a 3mL cartridge

- Defects done using capillaries (between the glass and the plunger) or laser drilled holes in the stopper
- Additional metallic pin touching the stopper
→ when electrode touches the metallic pin, defects can be detected
- Tests performed over multiple days (6 days)



3mL cartridge (plunger defects)

