PDA® Parenteral Drug Association Training and Research Institute

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

- Case Studies:
  1) HVLD with Albumin Solution
  2) HVLD Vs. Vacuum Decay with Albumin Solution
  3)HVLD performance with High viscosity products
  4)New features

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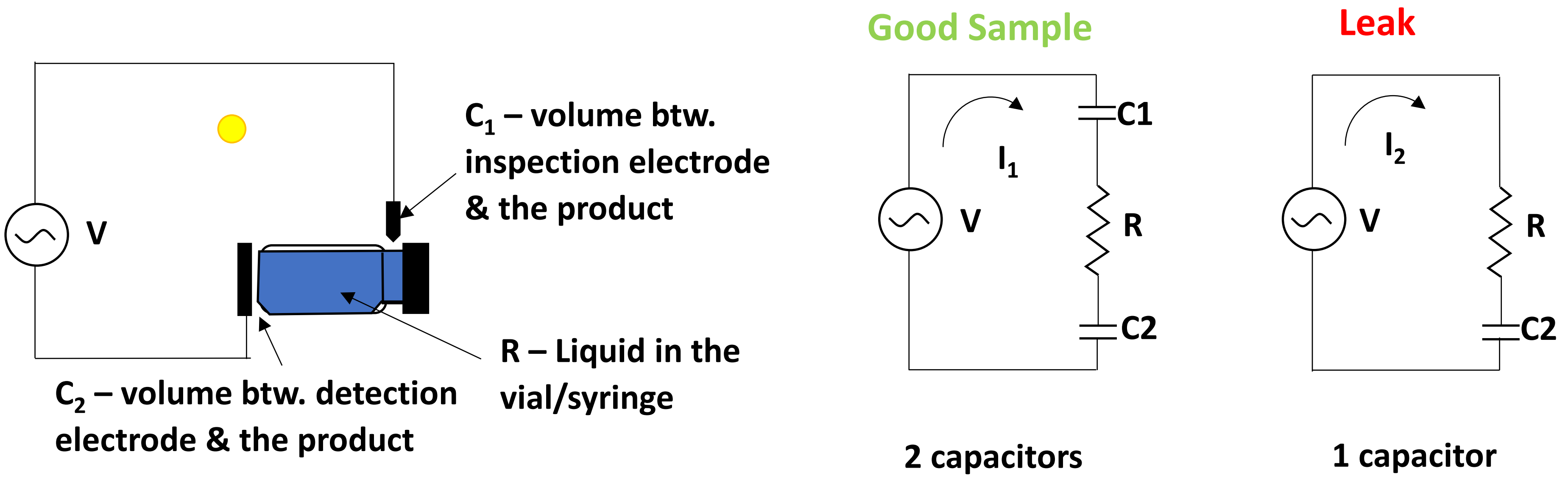
PDA, Vienna 2025

pti® science of quality

Functional Principle of HVLDmc Test



V – High Voltage Source

R – Electric Resistance of the product

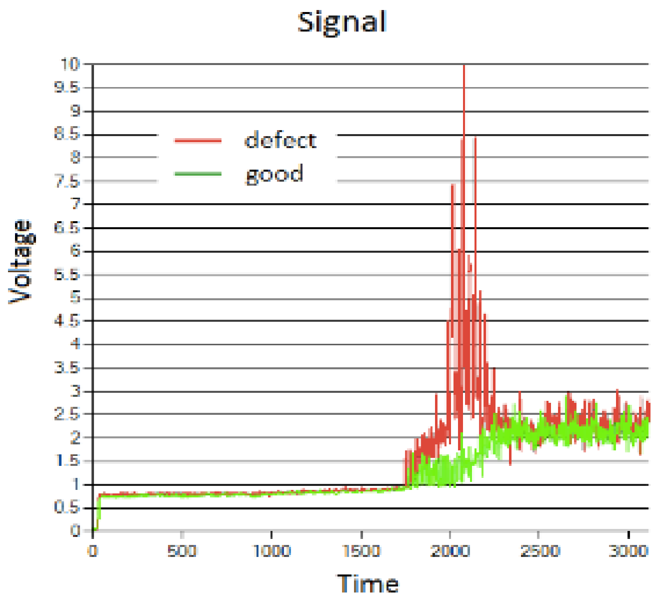
C_1 – Capacitor 1: Glass between the inspection electrode and product

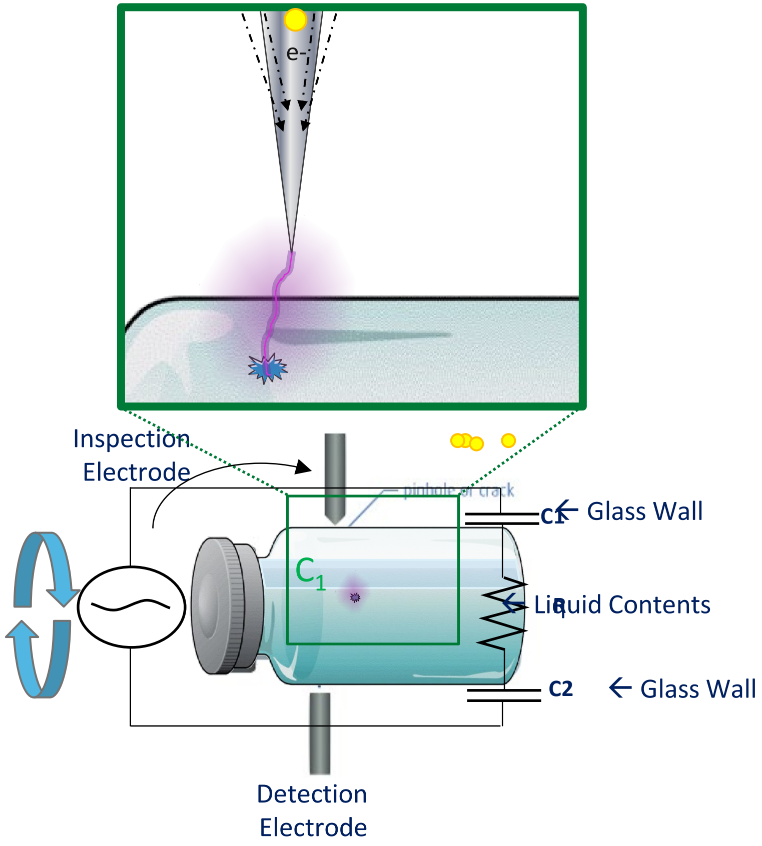
C_2 – Capacitor 2: Glass between the detection electrode and product

I_1 – current produced when product container is sealed

I_2 – current produced when product container is defective

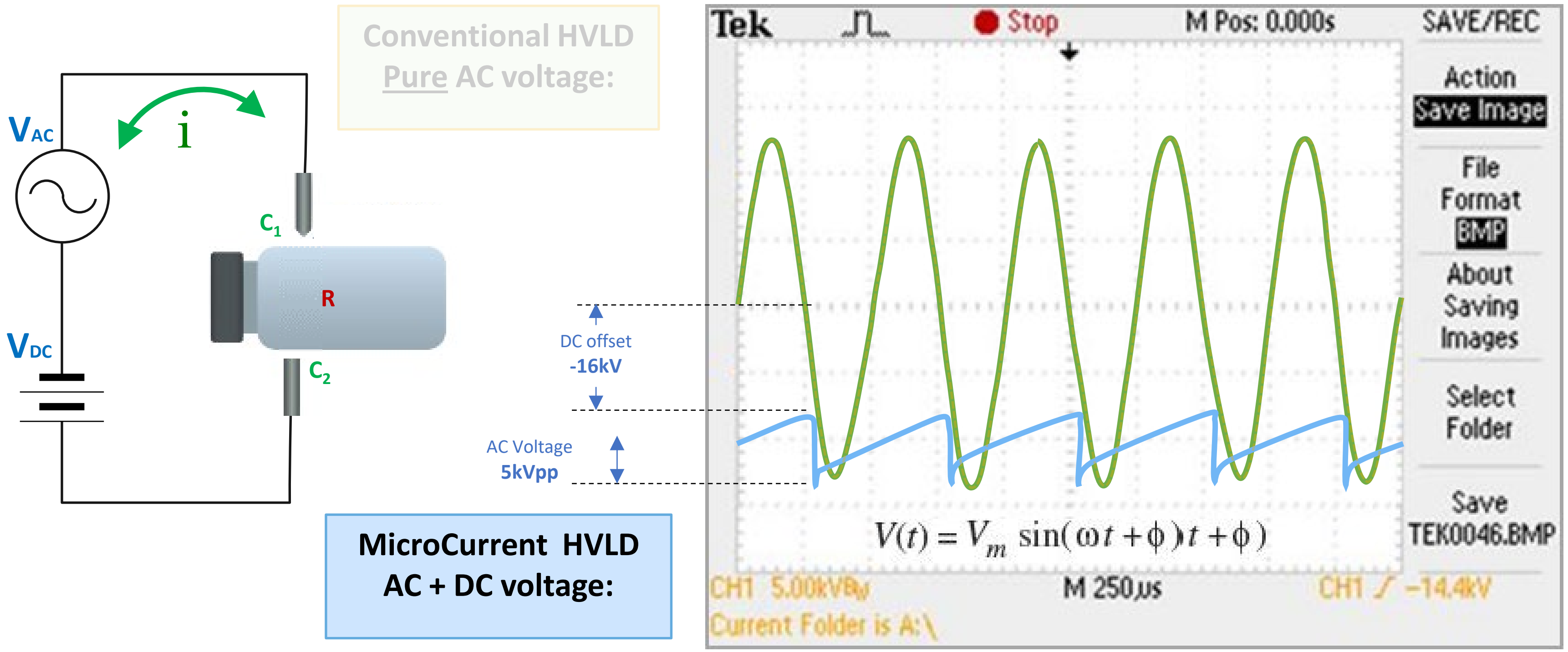
High Voltage Leak Detection (Microcurrent)





MicroCurrent HVLDmc

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.



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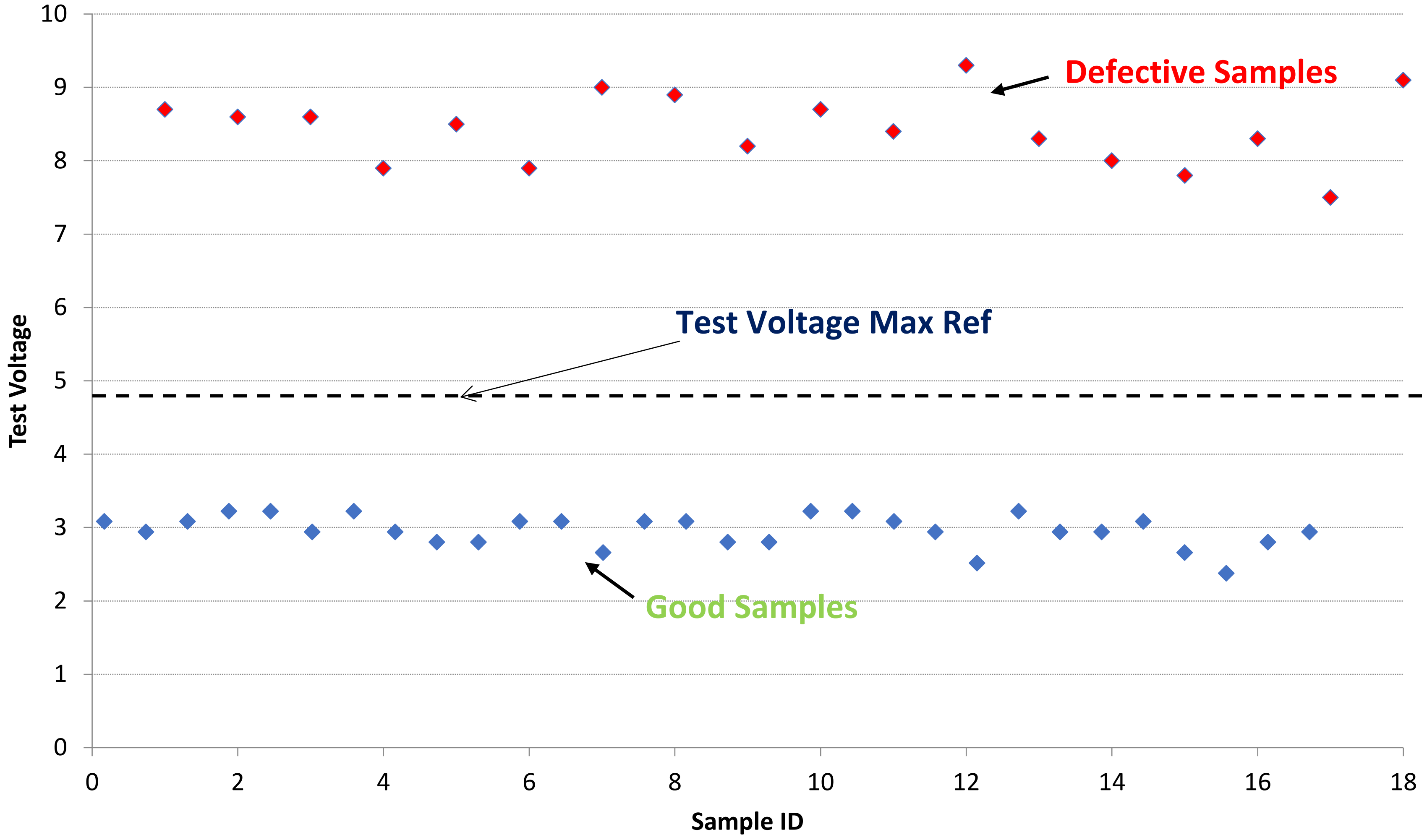
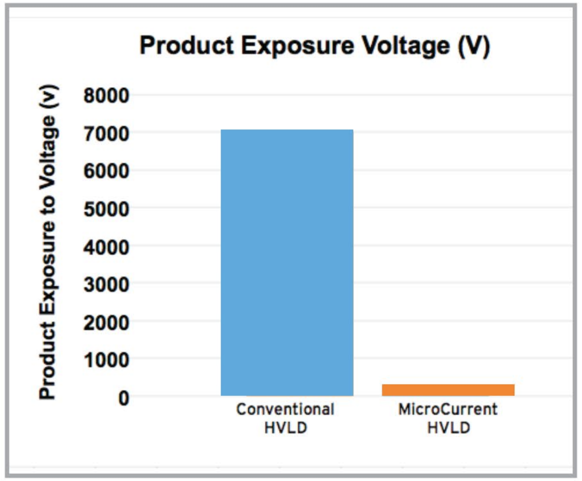
Voltage results for Negative and Positive Controls

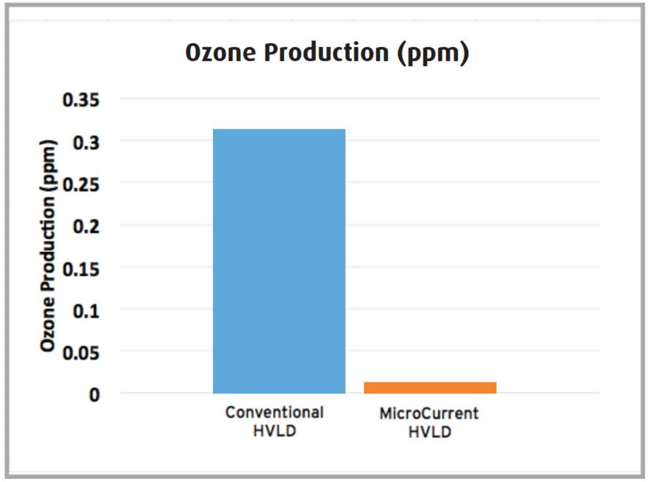


MicroCurrent HVLD - Benefits

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 HVLDmc

Technical aspects

- With MicroCurrent HVLDmc 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

Benefits

- MicroCurrent HVLDmc can measure **low conductivity products** - < 1 micro Siemens
- MicroCurrent HVLDmc can inspect products **containing alcohol**
- MicroCurrent HVLDmc is capable of inspecting **small Packages with low fill levels**
- MicroCurrent HVLDmc **does not adversely affect proteins**
- MicroCurrent HVLDmc **can detect defects under the crimping**
- MicroCurrent HVLDmc can detect **clogged cracks***

Case Studies

HVLD^{mc} with Albumin Solution (1,2,3 and 66 days)

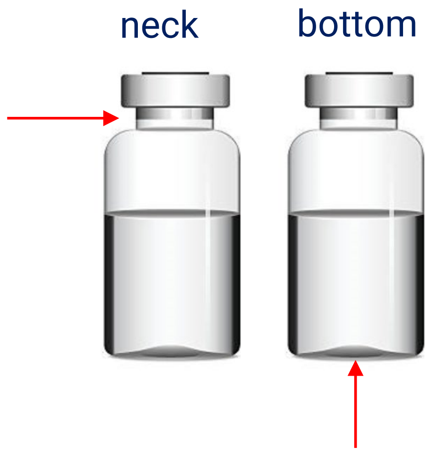
HVLD^{mc} vs. Vacuum Decay with Albumin Solution

HVLD performance with High viscosity products

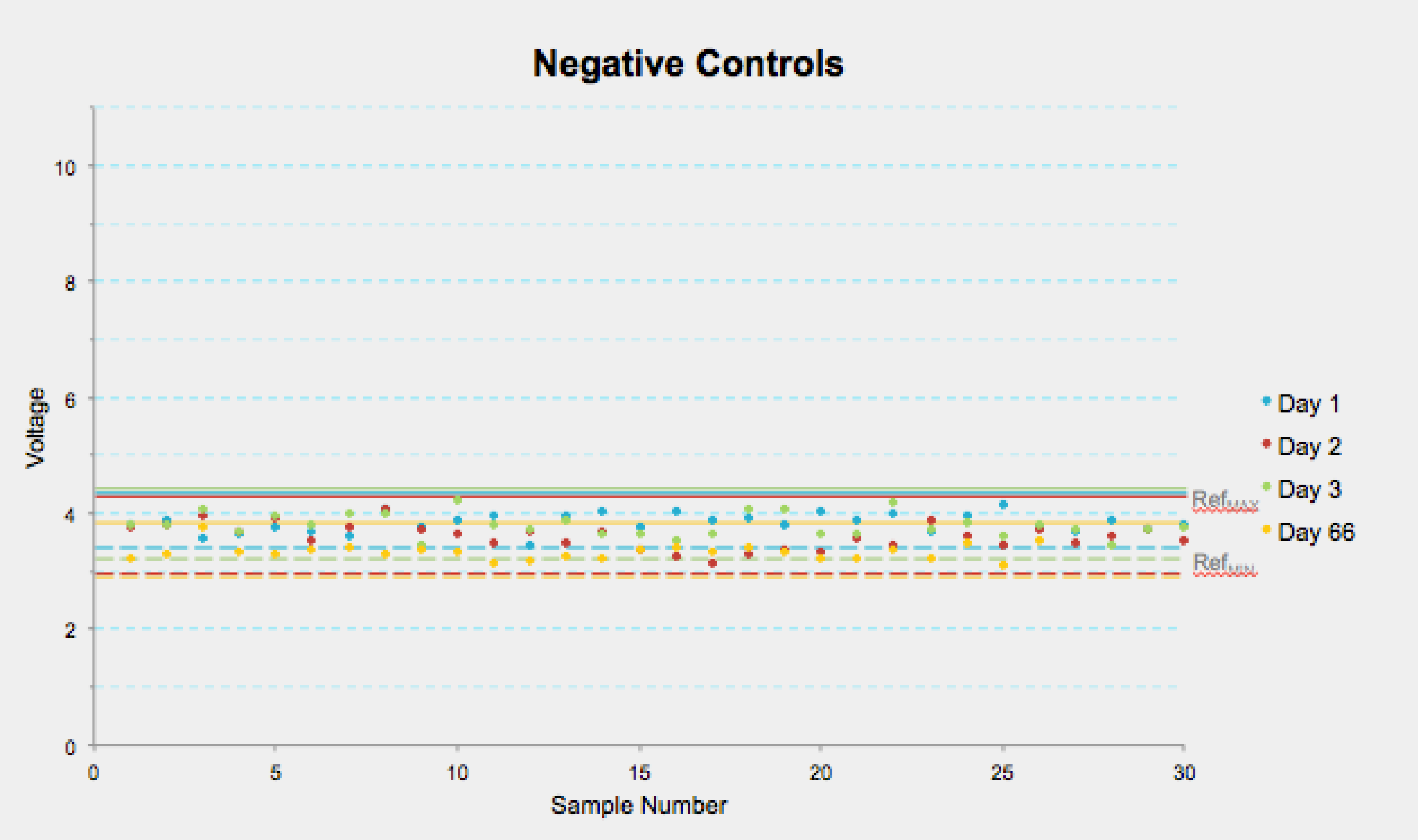
New features

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)



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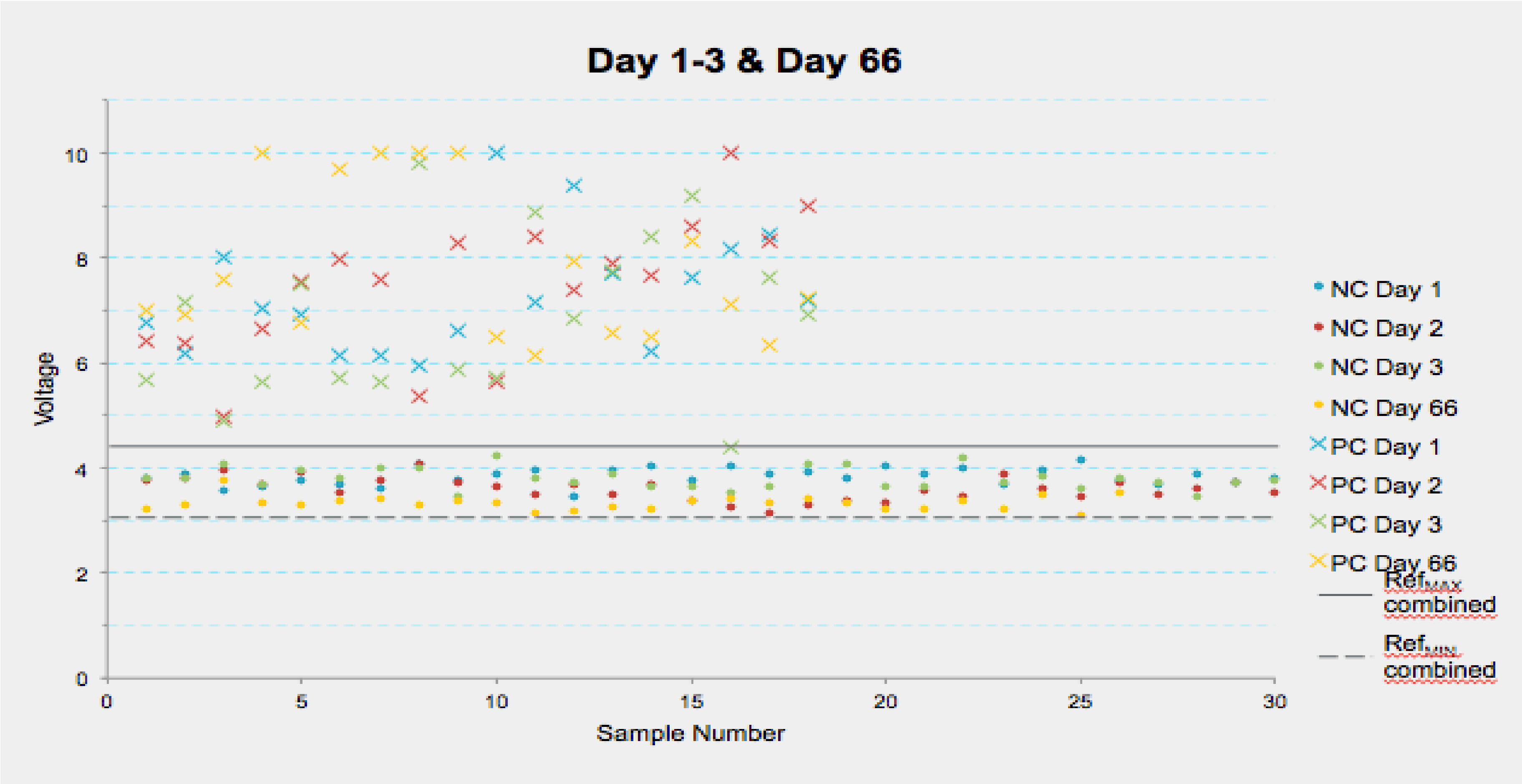
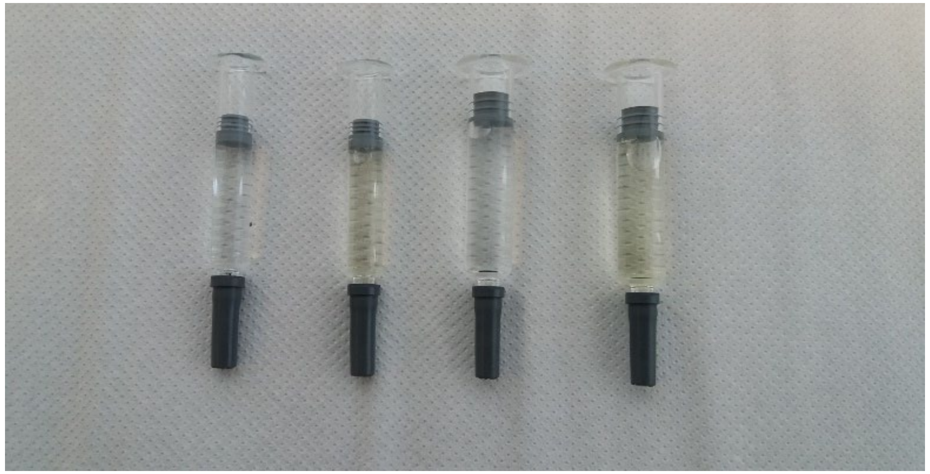
Case Study 1: HVLD with Albumin Solution (1,2,3 and 66 days)



Case Study 2: Vacuum vs. HVLDmc 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}



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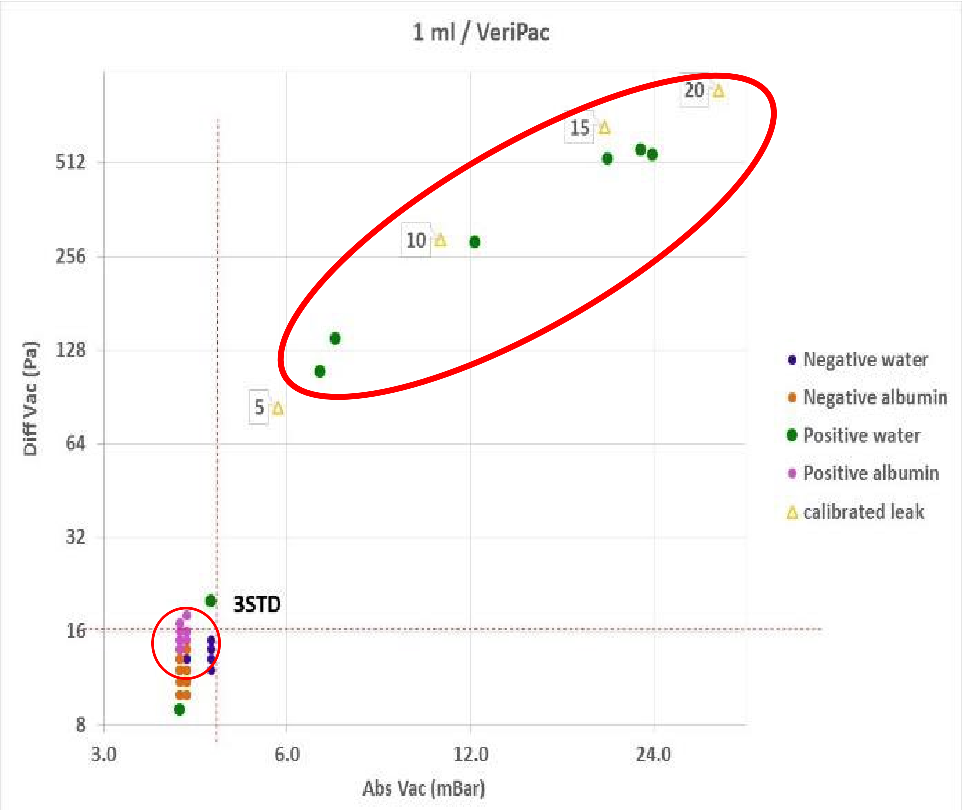
Case Study 2: Vacuum vs. HVLDmc for PFS

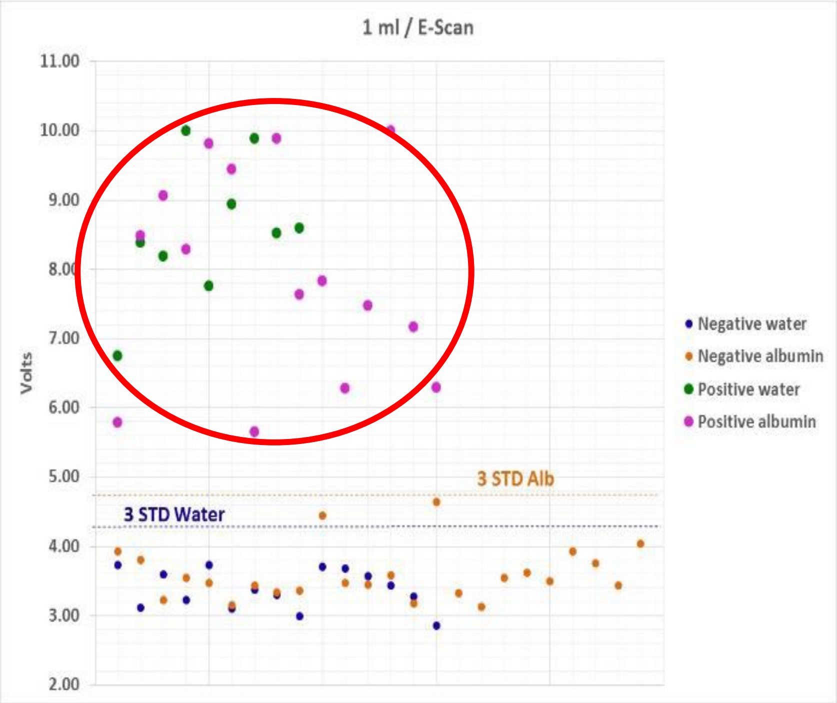
Vacuum Decay

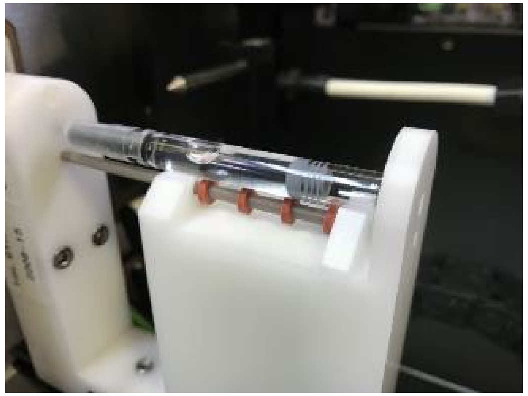


- Vacuum Decay @ <5.0mbar
- Albumin & Water Samples
- Laser Drilled Defects 5, 10, and 20µm.

Case Study 2: Vacuum vs. HVLDmc for PFS

HVLDmc

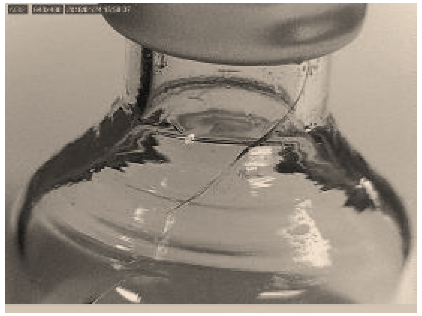
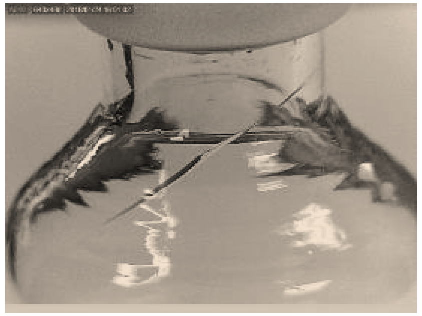
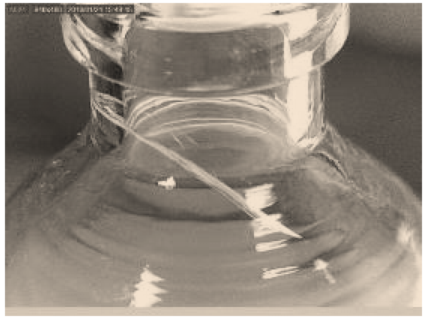




Conclusion

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
	mbar·l/s	10^{-5} mbar·l/sec	sccm		um
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

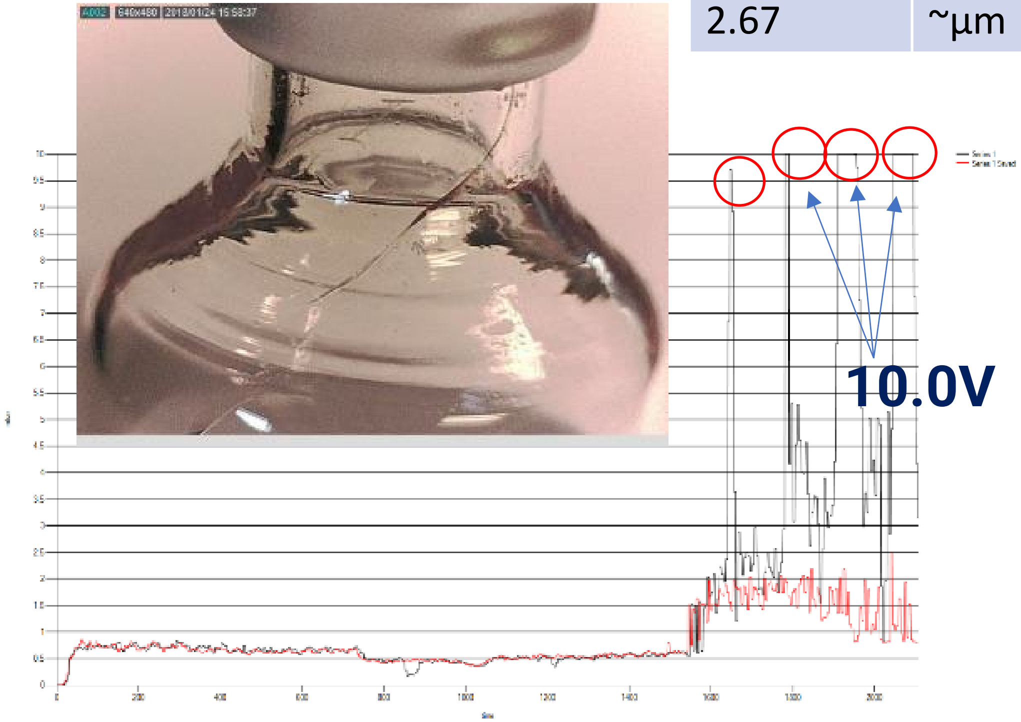
Sample 16

Defect Detection

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

He Certified Leak Rate	
95.0	10^{-5} mbar·l/s
0.05700	sccm
2.67	~µm

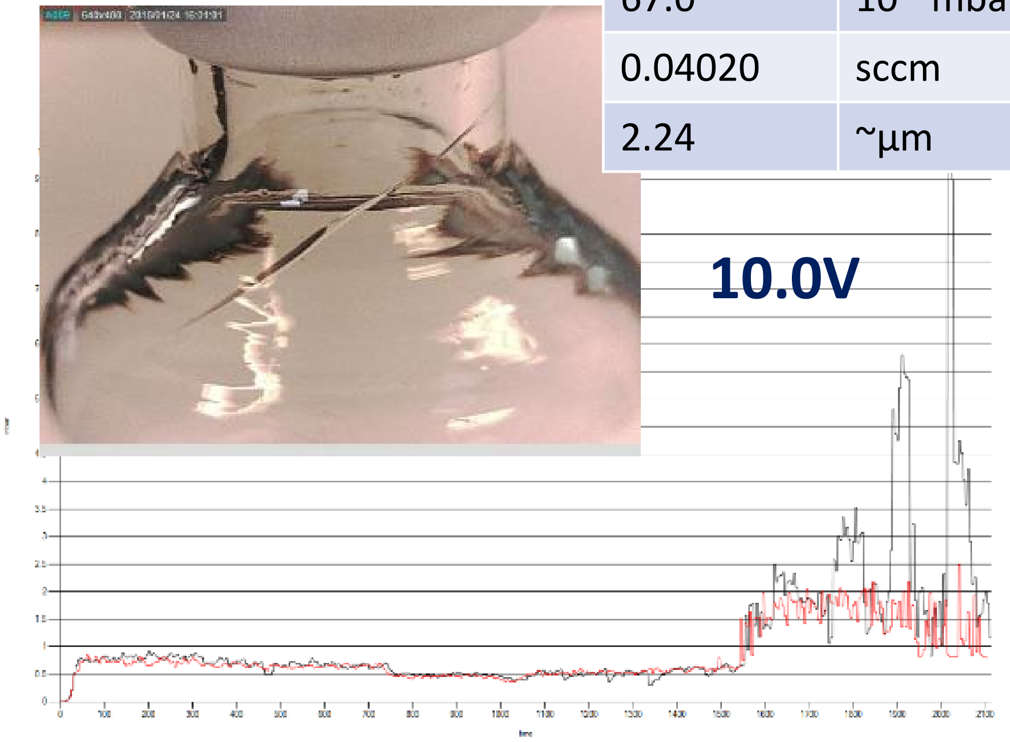
Sample 1



Traditional Target Leak Sizes

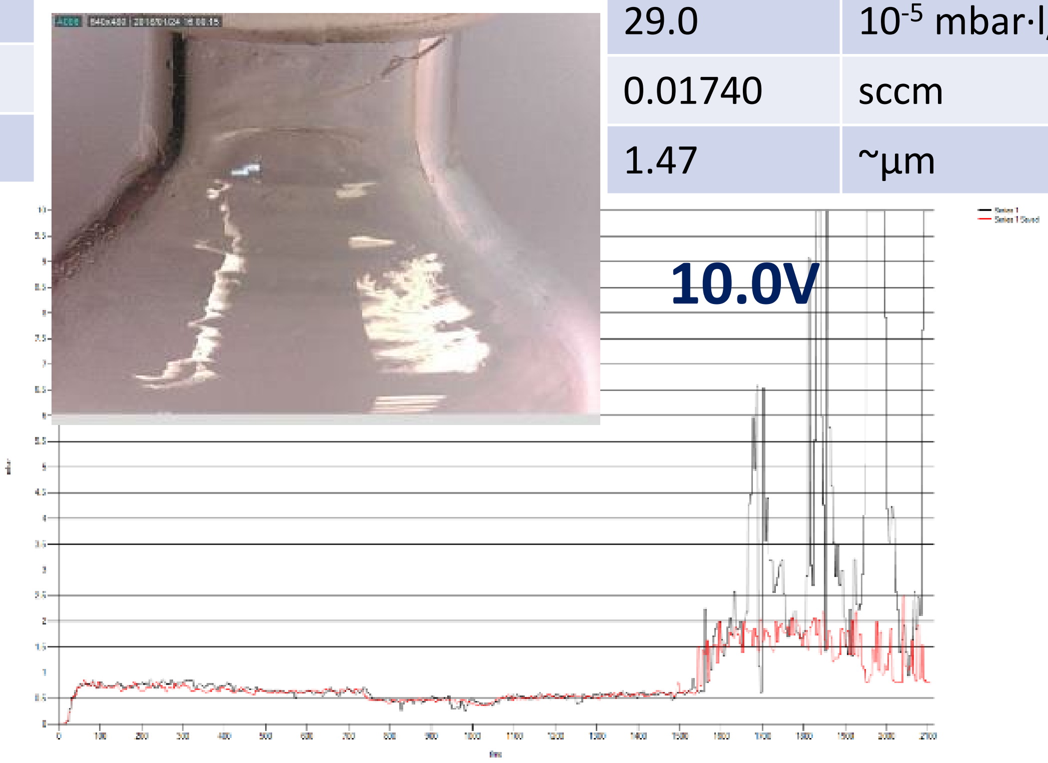
Sample 6

He Certified Leak Rate	
67.0	10^{-5} mbar·l/s
0.04020	sccm
2.24	~µm



Sample 3

He Certified Leak Rate	
29.0	10^{-5} mbar·l/s
0.01740	sccm
1.47	~µm

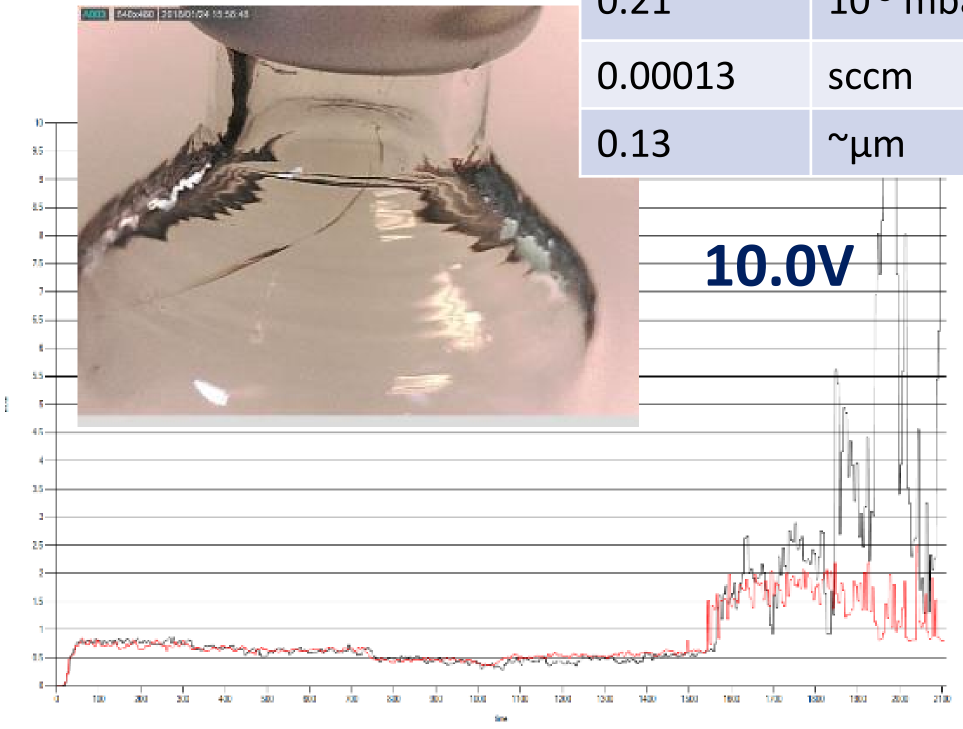


2 He Helium 4.002602

Leak Rates

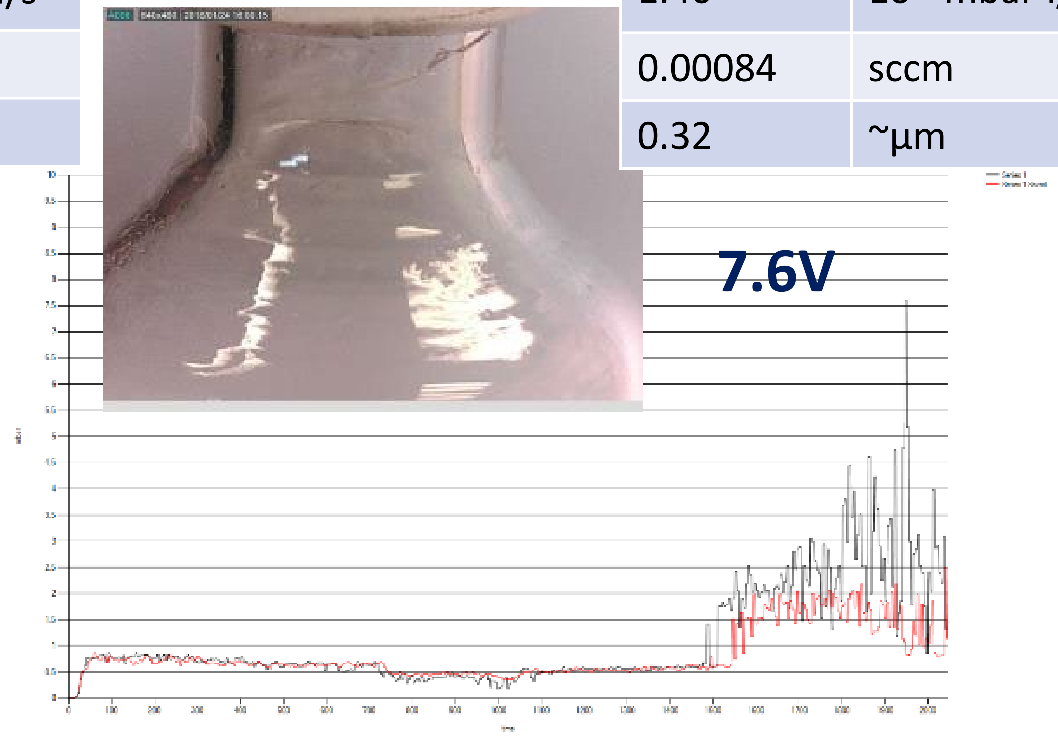
Sample 2

He Certified Leak Rate	
0.21	10^{-5} mbar·l/s
0.00013	sccm
0.13	~µm



Sample 3

He Certified Leak Rate	
1.40	10^{-5} mbar·l/s
0.00084	sccm
0.32	~µm

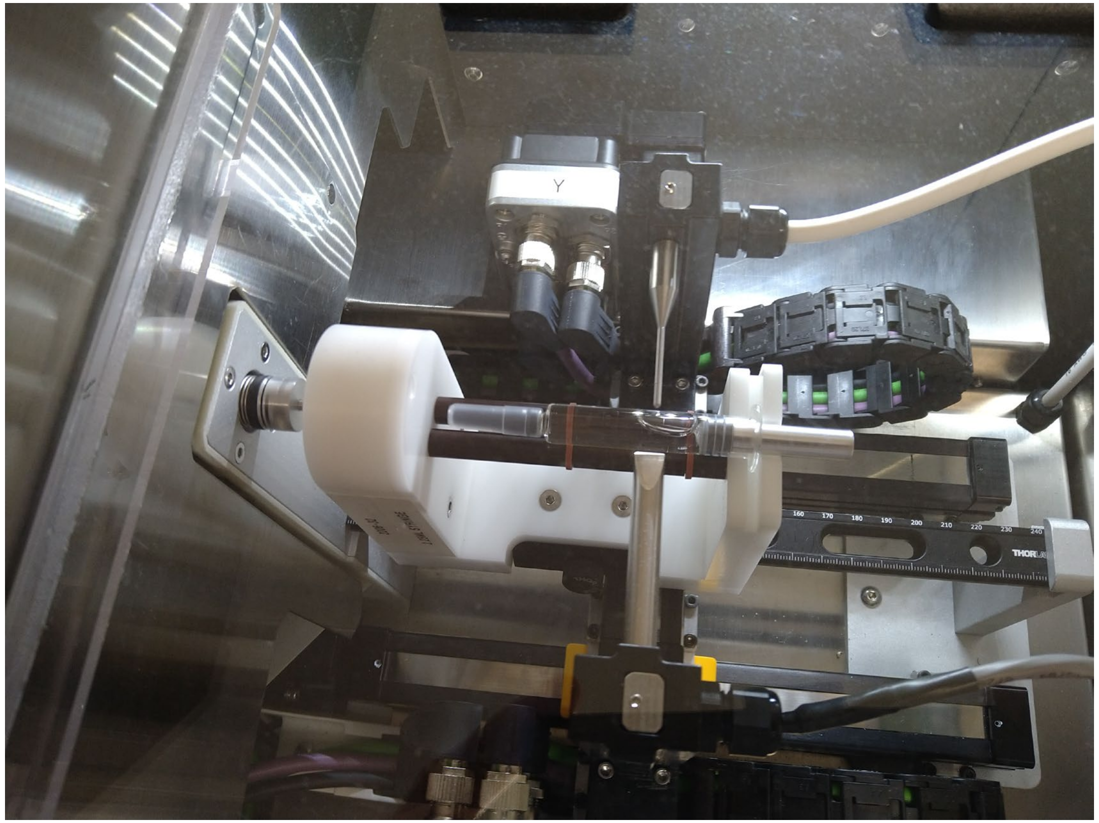


Testing the plunger of a 3mL cartidge

- 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

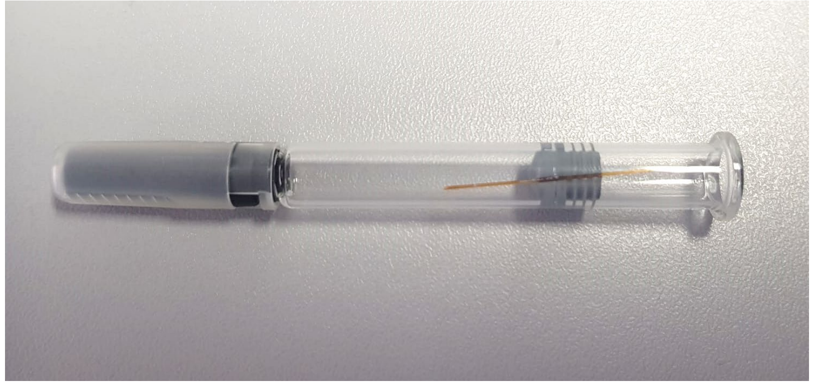
- Tests performed over multiple days (6 days)



Inspection of the plunger

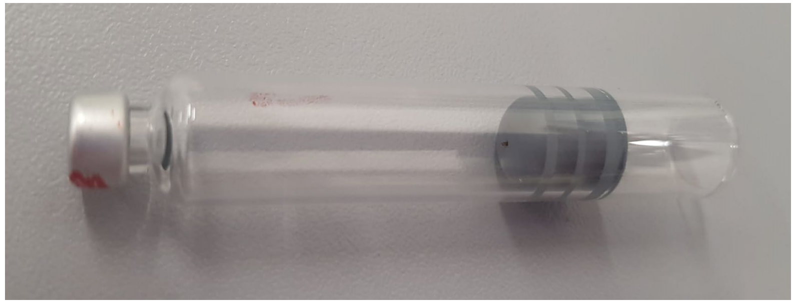
Creation of plunger defects

1. Capillary between glass and plunger



2. Laserdrilled hole at plunger level

3. Capillary through middle of the plunger



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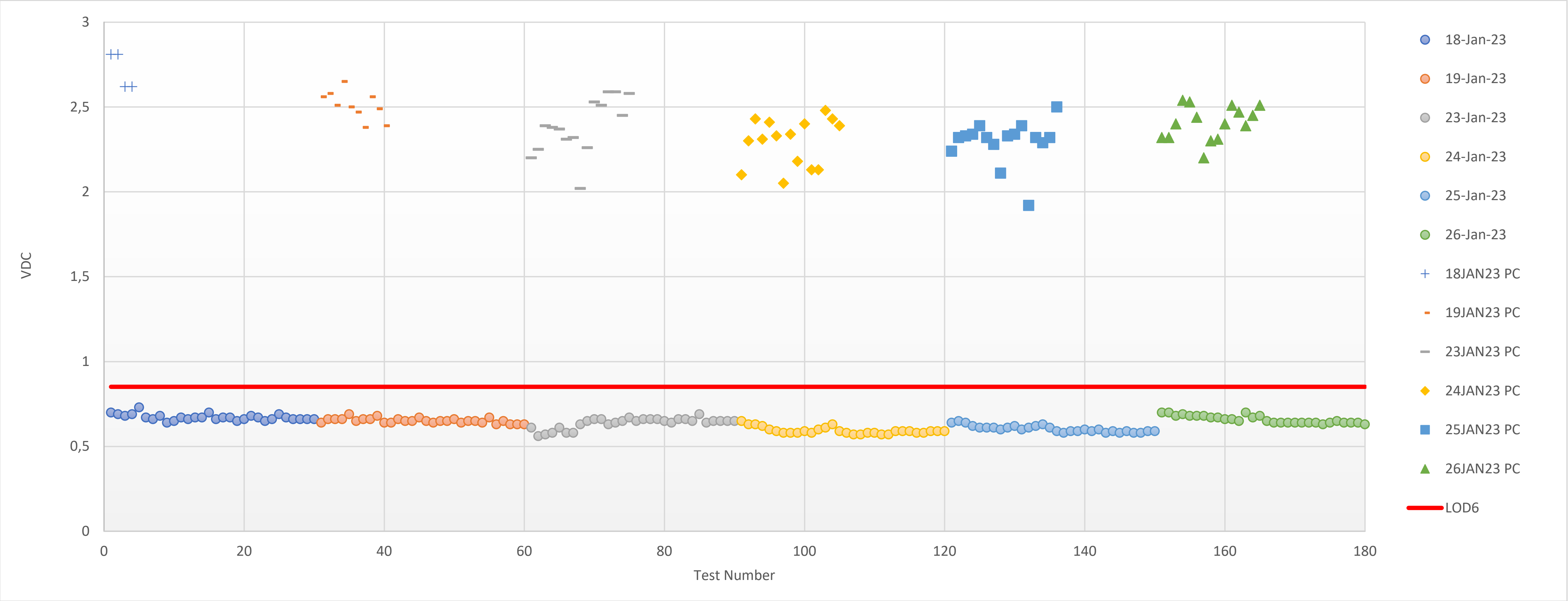
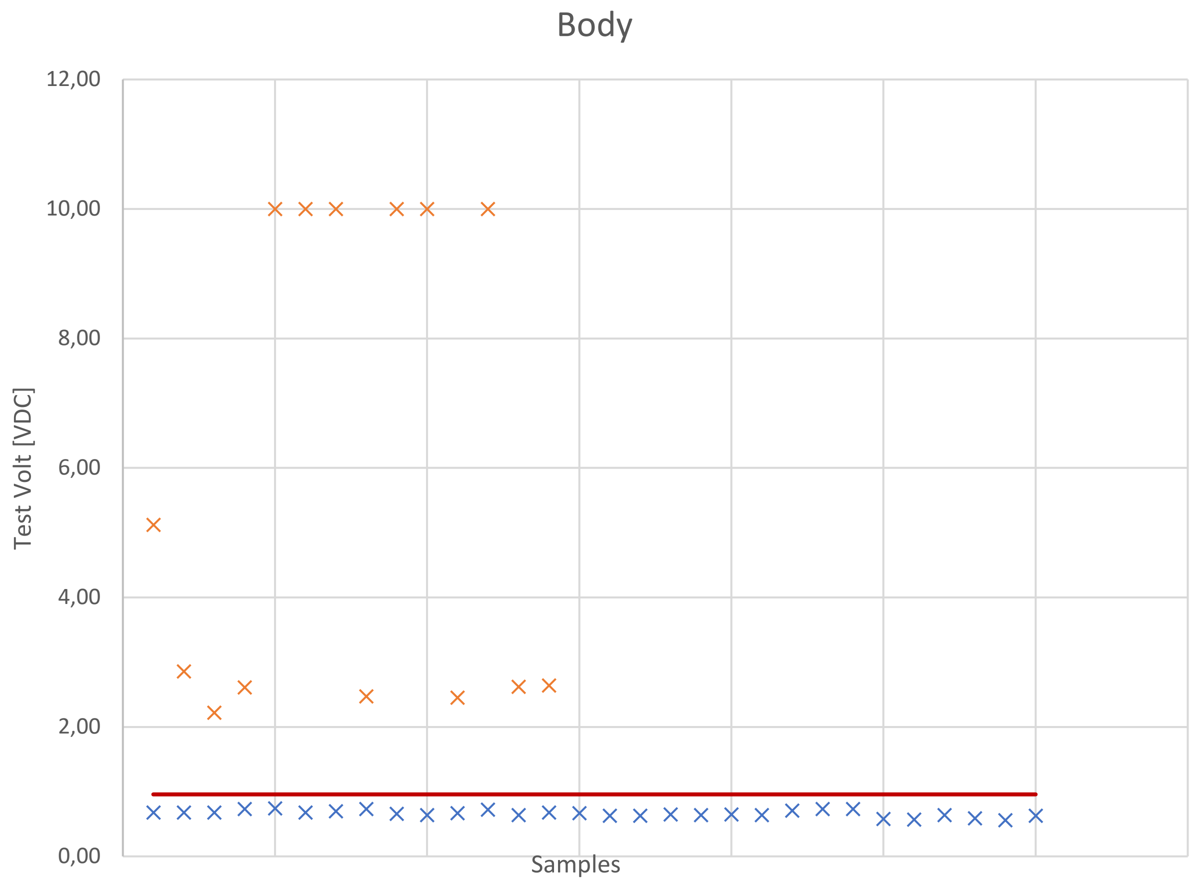
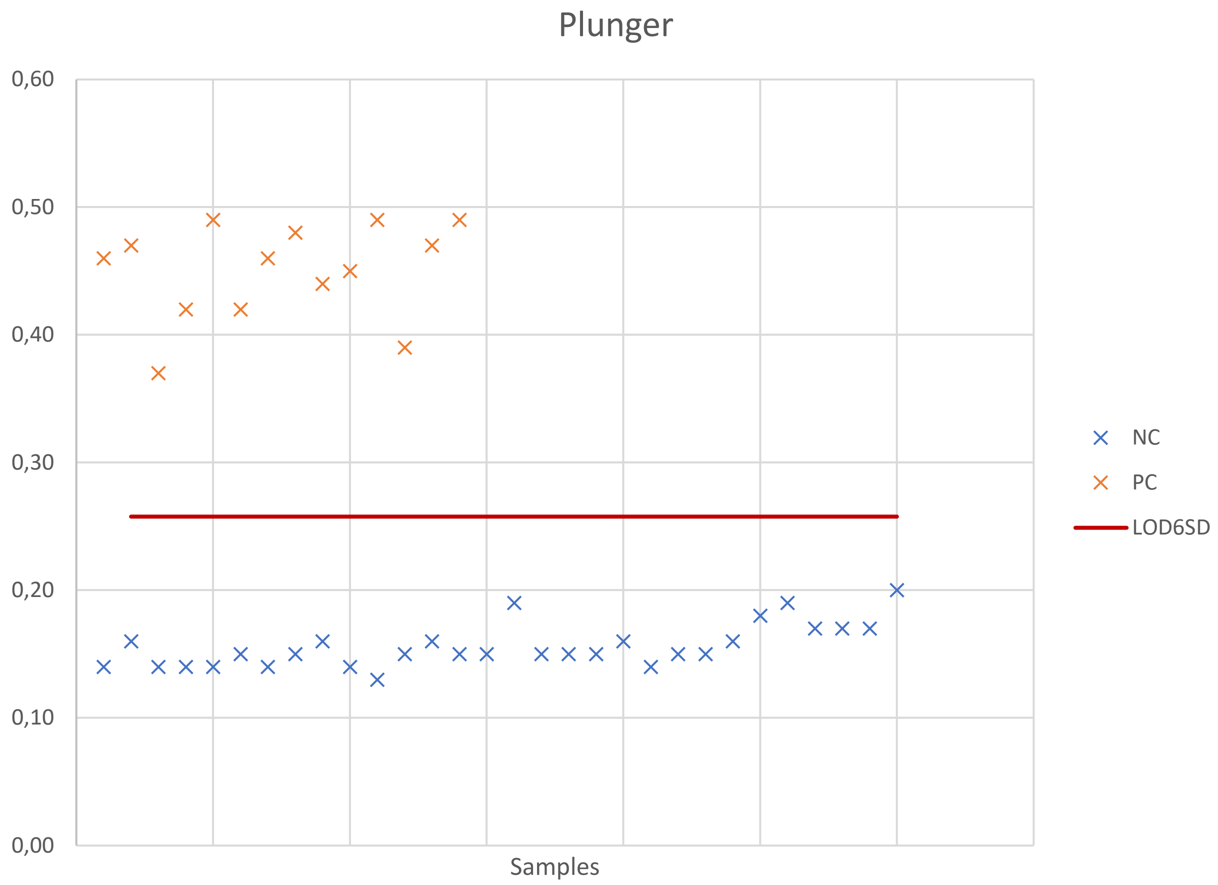
3mL cartridge (plunger defects)



Body and plunger inspection





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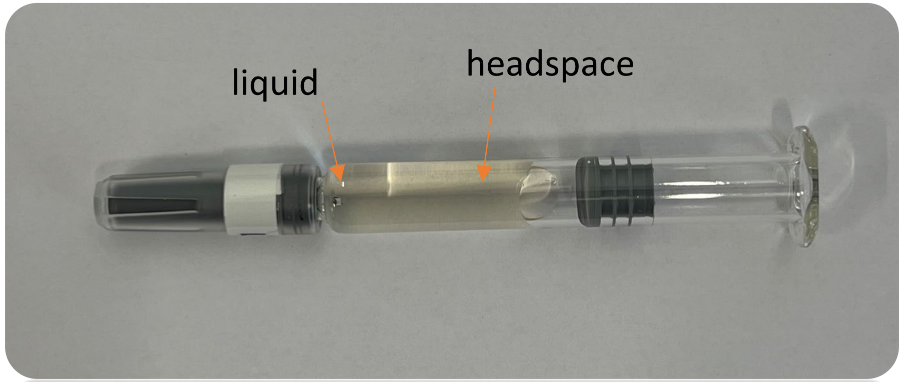
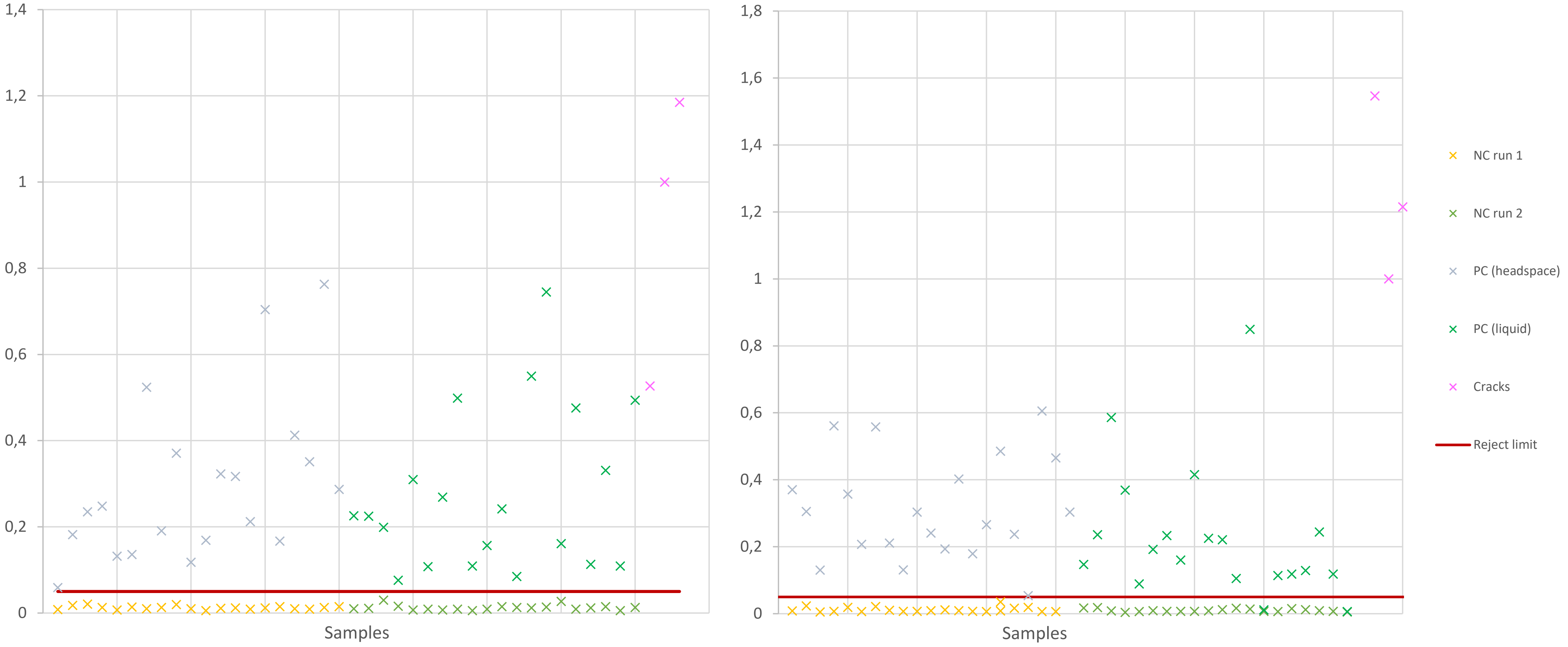
Establishing repeatability

- 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



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 and plunger stopper defects.
- $HVLD^{mc}$ 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 1µm level can be readily detected using $HVLD^{mc}$
- Nonvisible cracks below the crimping are detectable

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