
Non-Destructive Container Closure Integrity Testing

**Presented at the New England
Chapter of the PDA March 11, 2009**

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PTI Inspection Systems**

Outline

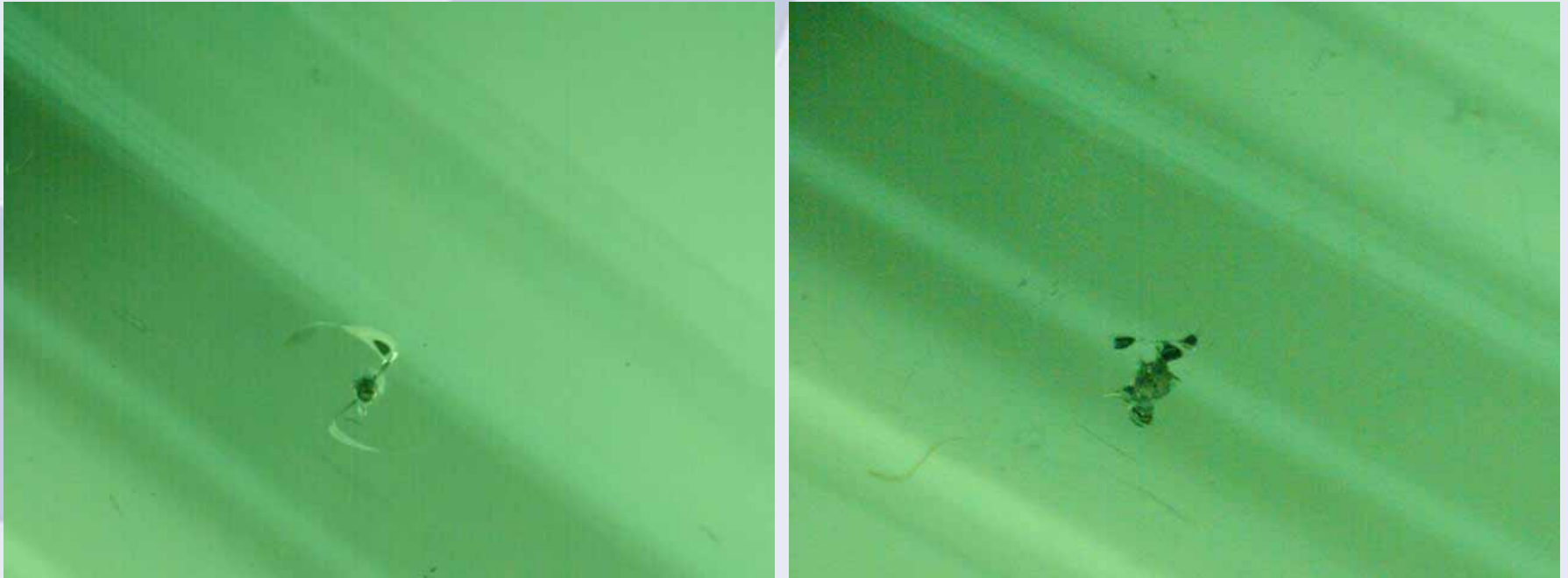
- **Prefilled Syringe Artificial Defects**
- **ASTM F2338-09 Round Robin Study**
- **Dye Ingress Comparison**
- **Airborne Ultrasonic Technology**
- **Test method for Tyvek Tray**

Prefilled Syringe

- 1 mL Glass Syringe, Staked Needle
- Holes laser drilled in barrel wall
 - Air flow through defect correlated to standard orifices
 - Grouped as either 5, 10 or 15 μm ($\pm 2 \mu\text{m}$)

Defects by Lenox Laser

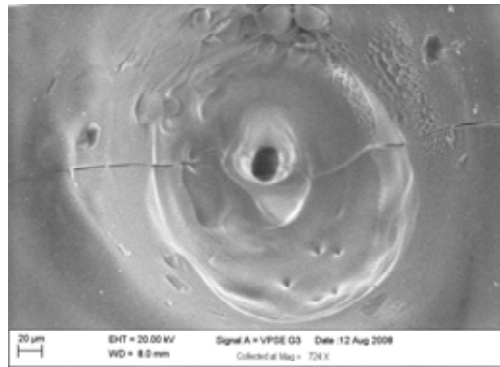
1 mL glass syringes, staked needle



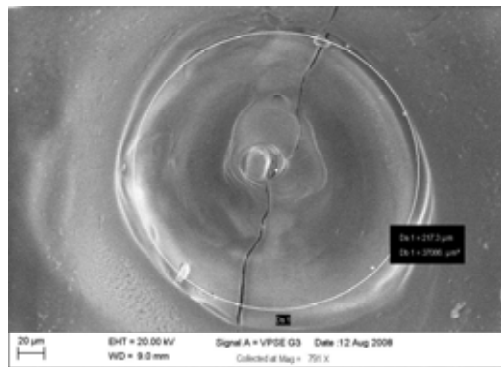
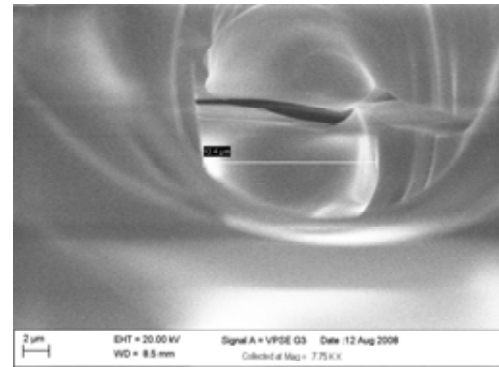
Nominal hole size 5 μm

Defects by Lenox Laser

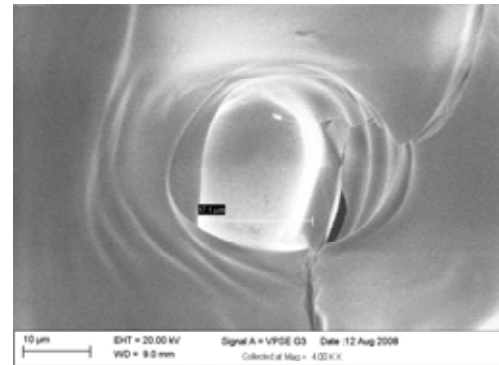
1 mL glass syringes, staked needle



106



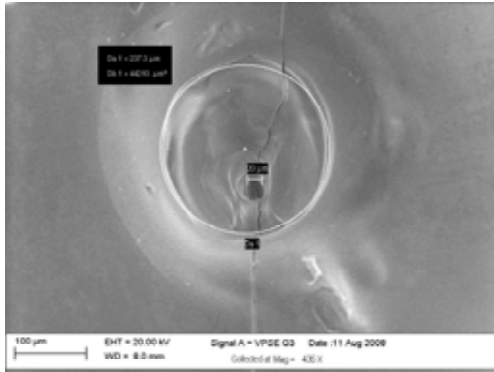
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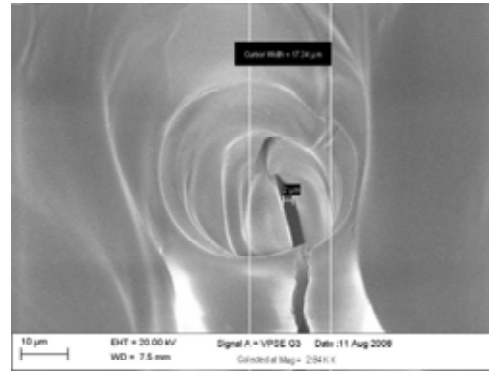
Nominal hole size 5 μm

Defects by Lenox Laser

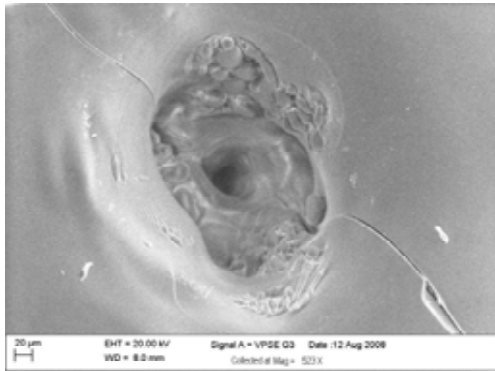
1 mL glass syringes, staked needle



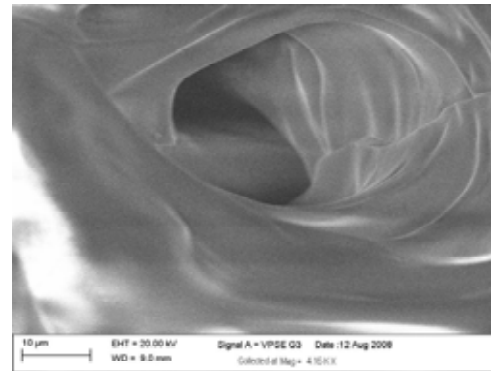
124



Nominal hole size
10 μm



136



Nominal hole size
15 μm

ASTM F2338-09

Standard Test Method for Non-destructive Detection of Leaks in Packages by Vacuum Decay Method

- **Pharmaceutical, food, medical device packages**
- **Recognized Consensus Standard by the US FDA, CDRH, March, 2006**
- **Precision and bias (P&B) studies for scope expansion**
 - Prefilled syringes – Air or Liquid Leaks

ASTM Vacuum Decay

Round Robin P&B Tests

– Packages

- 1mL BD glass syringes
- Positive controls: nominal holes 5, 10, 15 μm

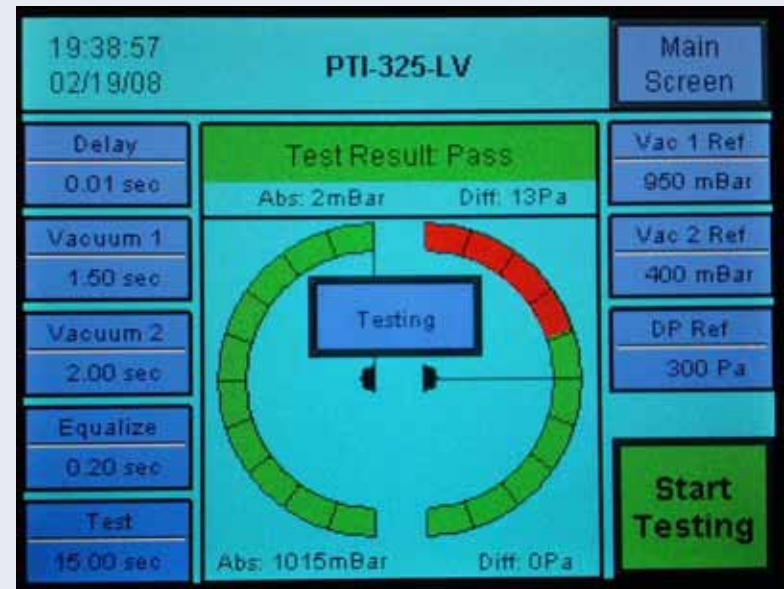
– Leak tests

- **Study 4** Air-filled syringes
- **Study 5** Water-filled syringes

– Logistics

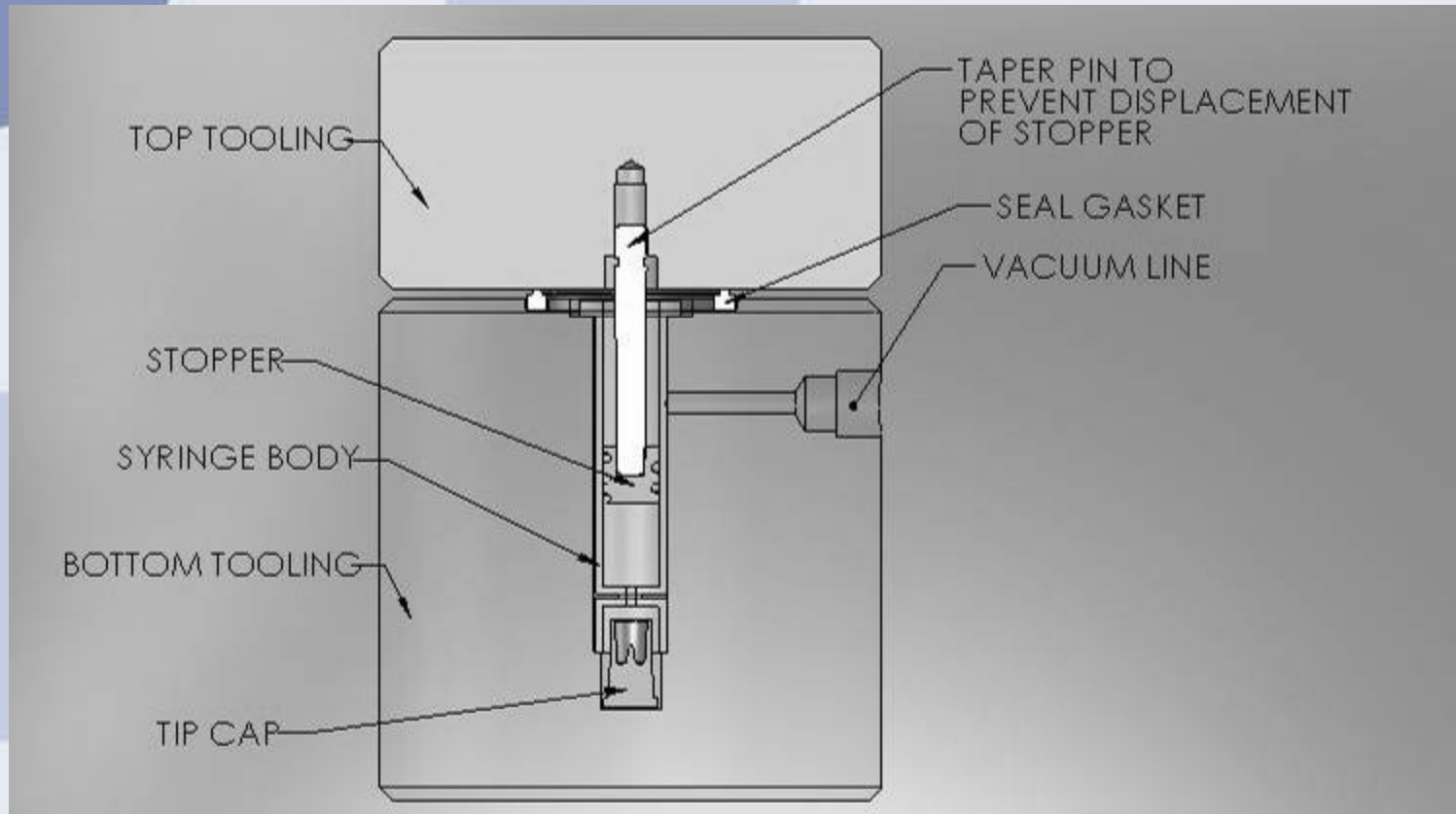
- 3 Test sites
- 3 Instruments PTI VeriPac 325-LV
- 3 Replicates of ea. study at ea. site (2 days per site)
- Samples randomized within ea. study

PTI VeriPac 325/LV



Control Touch Screen

Single Package Test Fixture Concept

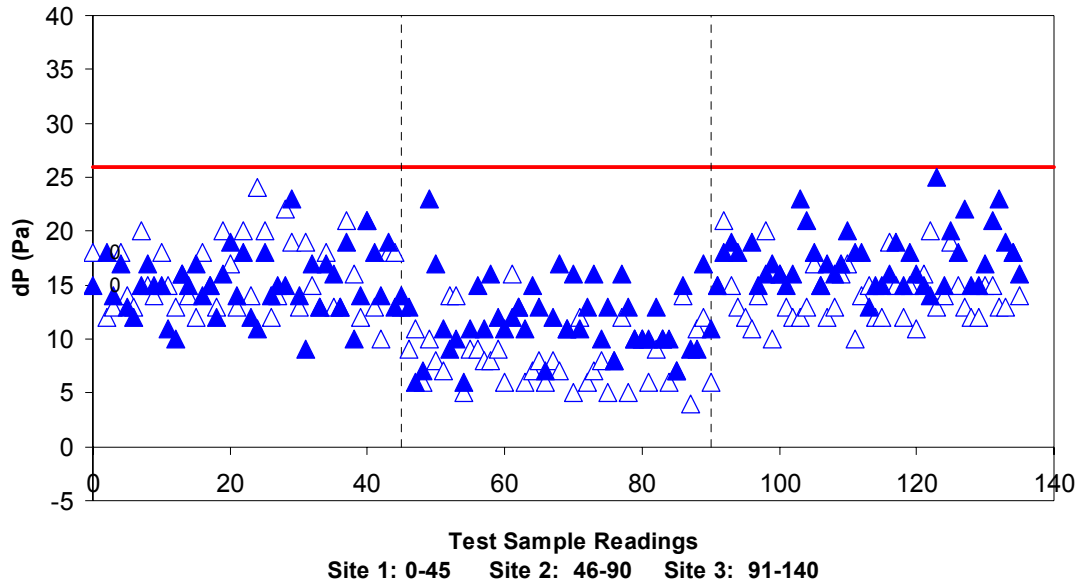


Vacuum Decay Test Method Parameters

- Total Test Time ~ 18 sec
- Differential Pressure Pass/Fail Limit (dP Ref)
NMT 25 Pa

Negative Control Samples

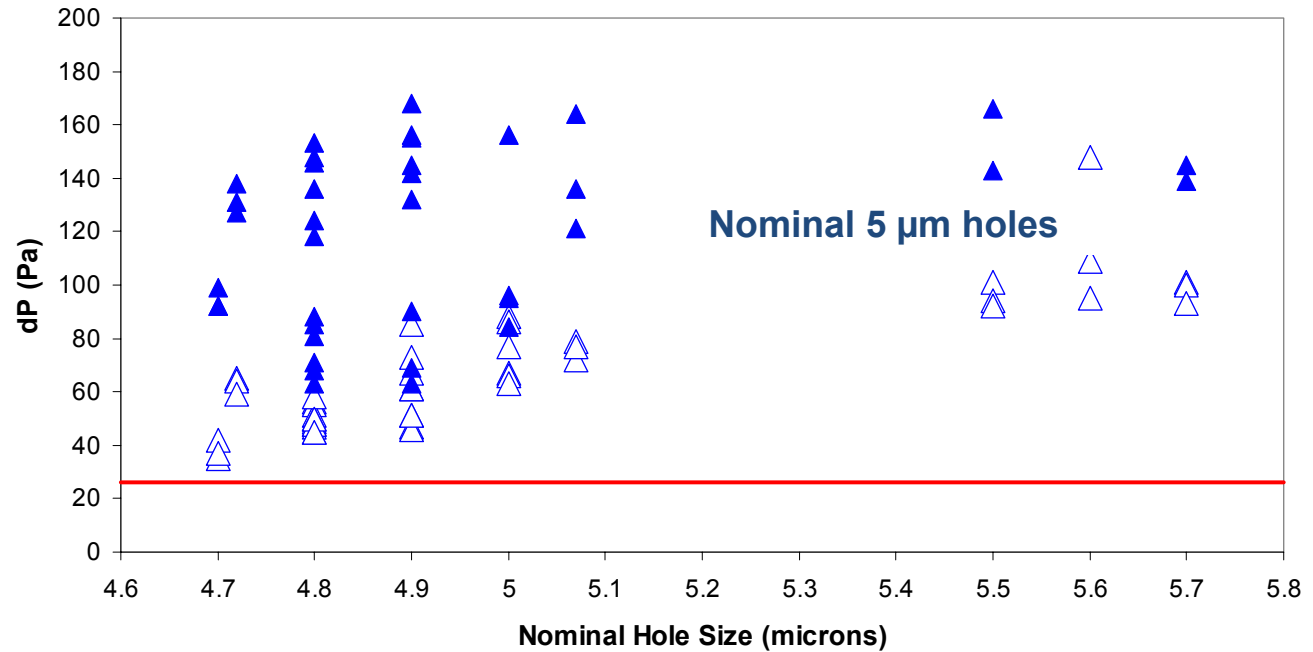
Vacuum Decay Leak Tests - Negative Control Syringes



- △ Study 4, Water-filled Syringes for Gas Leak Tests
- ▲ Study 5, Water-filled Syringes for Liquid Leak Tests
- dP Ref Pass/Fail Limit

Air-Filled vs. Water Filled Syringes

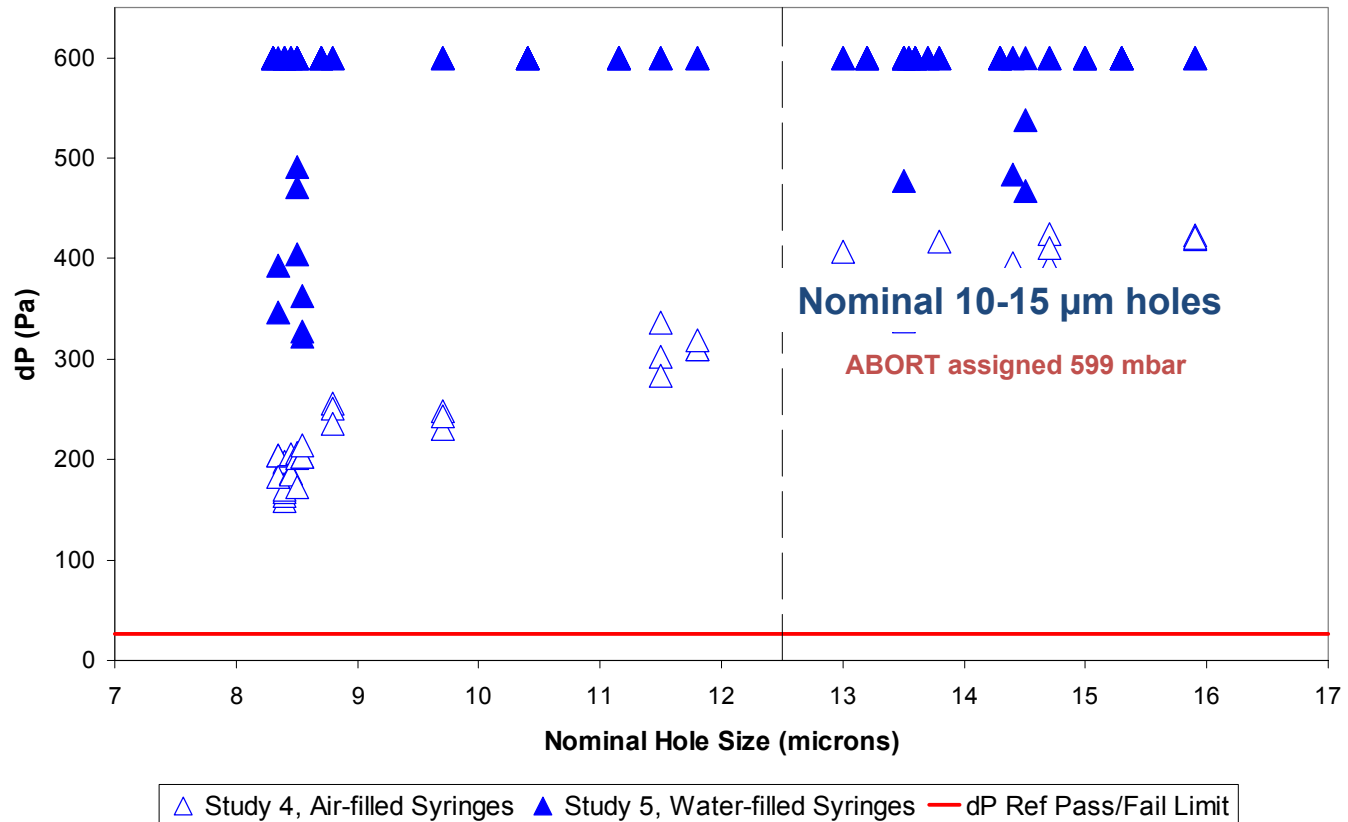
Vacuum Decay Liquid Leak Test, Air-filled vs Water-filled Syringes



△ Study 4, Air-filled Syringes ▲ Study 5, Water-filled Syringes — dP Ref Pass/Fail Limit

Air-Filled vs. Water Filled Syringes

Vacuum Decay Liquid Leak Test, Air-filled vs Water-filled Syringes



Vacuum Decay Conclusions

ASTM Round Robin P&B Studies

- **PTI VeriPac 325/LV Test Method Sensitivity**
 - $\geq 5.0 \mu\text{m}$ hole detected
- **Pass/Fail Criteria**
 - Quantitative readings (Pa)
 - No baseline drift
 - No calculations or algorithms required
 - Same settings across instruments and test sites

Dye Ingress Comparison

Test Requirements	USP 31 <381> Ph.Eur. 3.2.9	ISO 8362-5 Annex C	Modified Method
Dye	0.1% aq. Methylene Blue	0.1% aq. Methylene Blue	0.1% aq. Methylene Blue
Vacuum	-27 KPa	-25 KPa	-37 KPa
Time at Vacuum	10 min	30 min	30 min
Time at Atmospheric Pressure	30 min	30 min	30 min

Inspector Capability Tests

Test Syringes		Syringes Correctly ID'd		
Dye Conc. (ppm)	No. Syringes	Inspector 1	Inspector 2	Inspector 3
0	3	3	3	3
0.1	3	0	0	1
0.2	3	0	0	3
0.3	3	1	0	3
0.4*	3	3	3	3

* LOD for Test Site

Inspector Capability Tests

Test Syringes		Syringes Correctly ID'd		
Dye Conc. (ppm)	No. Syringes	Inspector 7	Inspector 8	Inspector 10
0	3	2	3	3
0.1	3	0	0	0
0.2	3	1	2	0
0.3	3	2	2	1
0.4	3	2	3	3
0.5*	3	3	3	3



* LOD for Test Site

Inspection Systems

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Test Samples	Air-filled Syringe Vacuum Decay dP (Pa) Pass or Fail	USP/Ph.Eur. Dye Test YES (Dye visible) or NO (Not visible)		
		Inspector 1	Inspector 2	Inspector 3
Negative Controls	11	No	No	No
	10	No	No	No
	12	No	No	No
	9	No	No	No
	9	No	No	No
5 µm	25 (4.7 µm)	No	No	Yes
	71	No	Yes	Yes
	80	No	Yes	Yes
	43	No	No	No
	42	No	No	Yes
10 µm	217	Yes	Yes	Yes
	177	Yes	Yes	Yes
	264	Yes	Yes	Yes
	231	No	No	Yes
	161	No	No	No
15 µm	ABORT	No	No	Yes
	344	Yes	Yes	Yes
	342	Yes	Yes	Yes
	350	Yes	Yes	Yes
	281	Yes	Yes	Yes

USP/PhEur Dye Ingress Test Samples

Negative
Controls

5 μm

15 μm



10 μm

Test Samples	Air-filled Syringe Vacuum Decay dP (Pa) Pass or Fail	ISO Dye Test YES (Dye visible) or NO (Not visible)		
		Inspector 1	Inspector 2	Inspector 3
Negative Controls	7	No	No	No
	6	No	No	No
	7	No	No	No
	6	No	No	No
	7	No	No	No
5 µm	22 (4.7 µm)	No	No	No
	66	No	No	Yes
	79	No	Yes	Yes
	44	No	No	Yes
	42	No	No	No
10 µm	205	Yes	Yes	Yes
	175	Yes	Yes	Yes
	260	Yes	Yes	Yes
	221	No	No	Yes
	154	No	No	No
15 µm	388	Yes	Yes	Yes
	346	Yes	Yes	Yes
	335	Yes	Yes	Yes
	337	Yes	Yes	Yes
	301	Yes	Yes	Yes

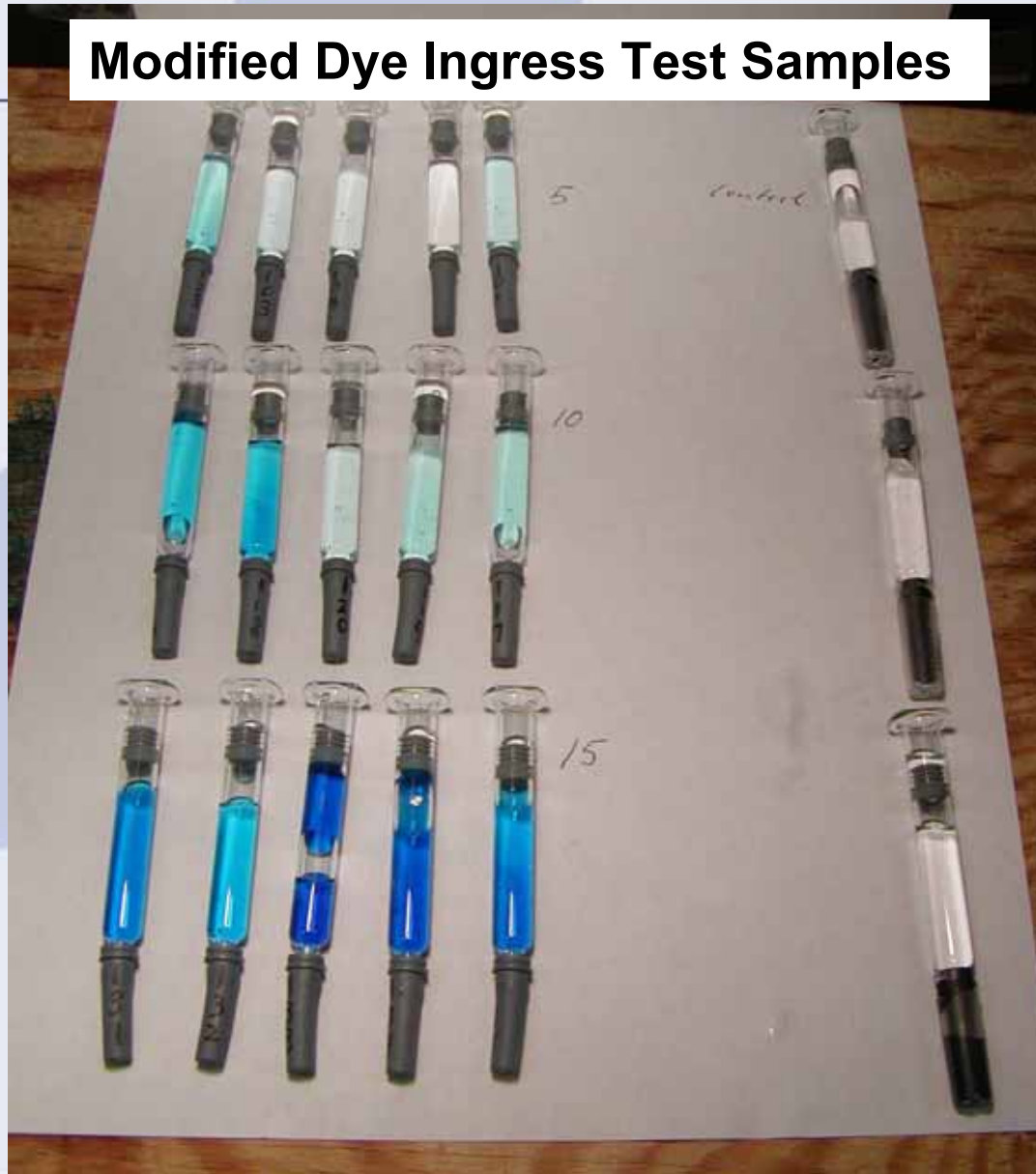
Test Samples	Air-filled Syringe Vacuum Decay dP (Pa) Pass or Fail	MODIFIED Dye Test YES (Dye visible) or NO (Not visible)		
		Inspector 7	Inspector 8	Inspector 10
Negative Controls	9	No	Yes	No
	9	No	Yes	No
	10	No	No	Yes
	9	No	Yes	Yes
	17	Yes	No	No
5 μm	57	Yes	Yes	Yes
	96	Yes	Yes	Yes
	43	Yes	Yes	Yes
	41	Yes	Yes	Yes
	51	Yes	Yes	Yes
10 μm	ABORT	Yes	Yes	Yes
	191	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes
	188	Yes	Yes	Yes
15 μm	ABORT	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes
	ABORT	Yes	Yes	Yes

Modified Dye Ingress Test Samples

5 μm

10 μm

15 μm



**Negative
Controls**

Dye Ingress Conclusions

USP/Ph.Eur. and ISO methods

- **PTI 325/LV Vacuum Decay Method is**
 - **More sensitive**
 - **More reliable**
 - **Provides quantitative pressure readings (Pa)**
 - **Not subject to human interpretation**

...than USP/Ph.Eur. or ISO closure self-seal dye ingress methods

- **Dye tests can be made more sensitive, but false positive risks remain**

Packaging Technologies & Inspection

Medical Device Packaging Non-Destructive, Non-Invasive Inspection Methodologies

Package Quality

Why Failures Occur

- **Lack of sufficient inspection**
- **Lack of process monitoring/process control**
- **Use of unreliable manual/visual techniques**
- **Use of methods that produce subjective results**
- **Lack of proper process validation**

Inspection Methods

Choose the right method!

- **Assess specific needs to verify package integrity**
- **Ensure package maintains integrity until product is used**
- **Determine how, when and why packages fail**
- **Evaluate inspection method and results**
- **Determine how results correlate to packaging process**
- **Quality control / process control**

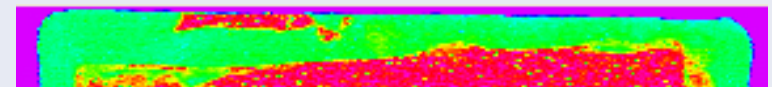
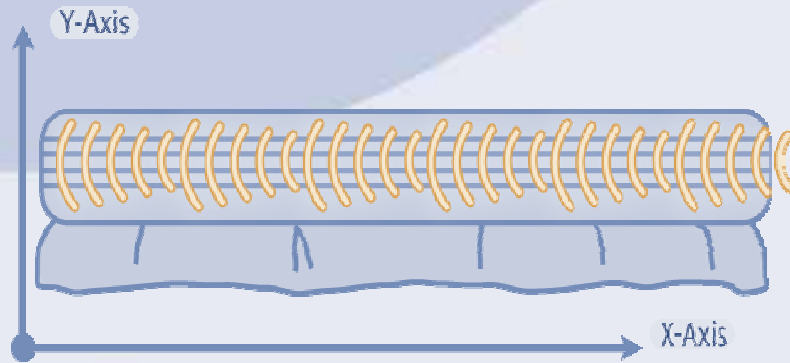
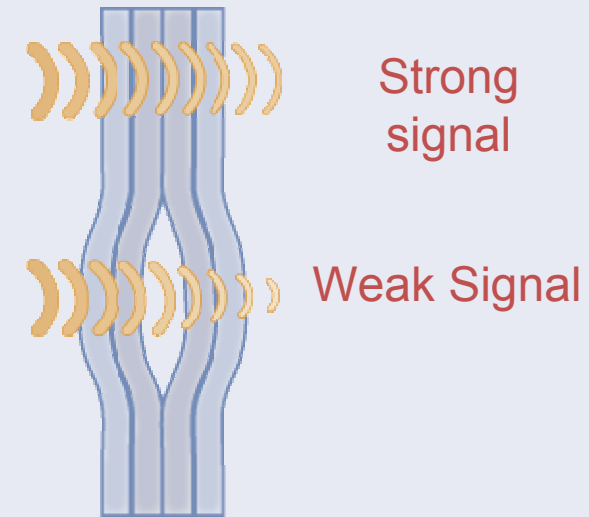
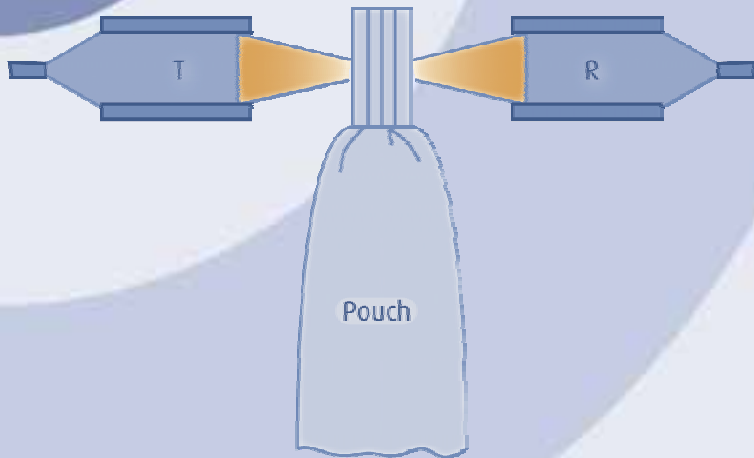
Seal Quality Inspection with Seal-Scan™

based on

Airborne Ultrasonic Technology

Seal-Scan™ Technology

Ultrasonic signal is transmitted along the X-axis through seal and signal is recorded



Signal measurement is quantitative and correlates to color gauge, creating high resolution image of seal structure and quality.

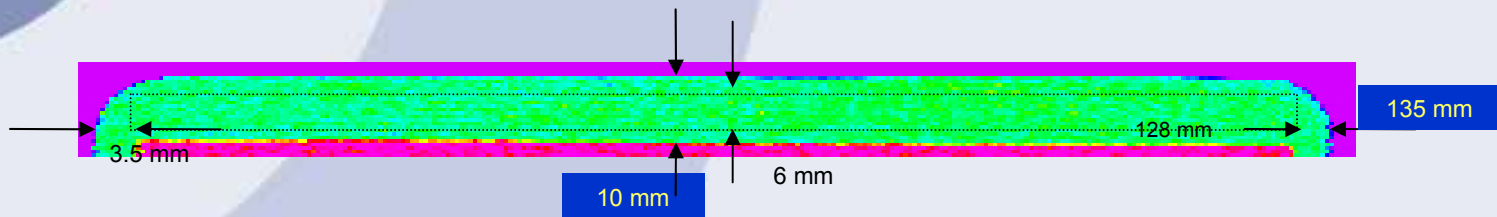
Seal-Scan™ 525

Off-line Heat Seal Analytical



C-Scan Analytical Tools

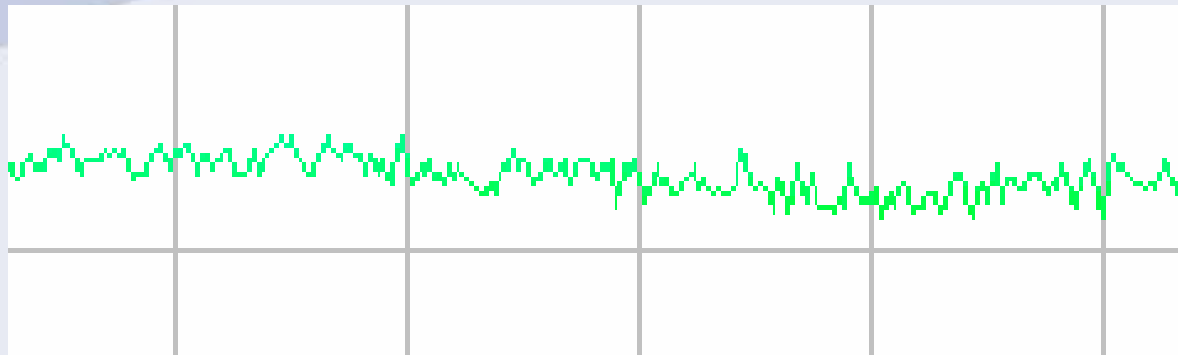
How to analyze a heatseal



C-Scan window statistics within the rectangular box

Position, mm	Length, mm	Width, mm	Pixels	Avg	Min	Max	Std
3.5	128.0	6.0	3072	13.5	-23.3	36.1	7.8

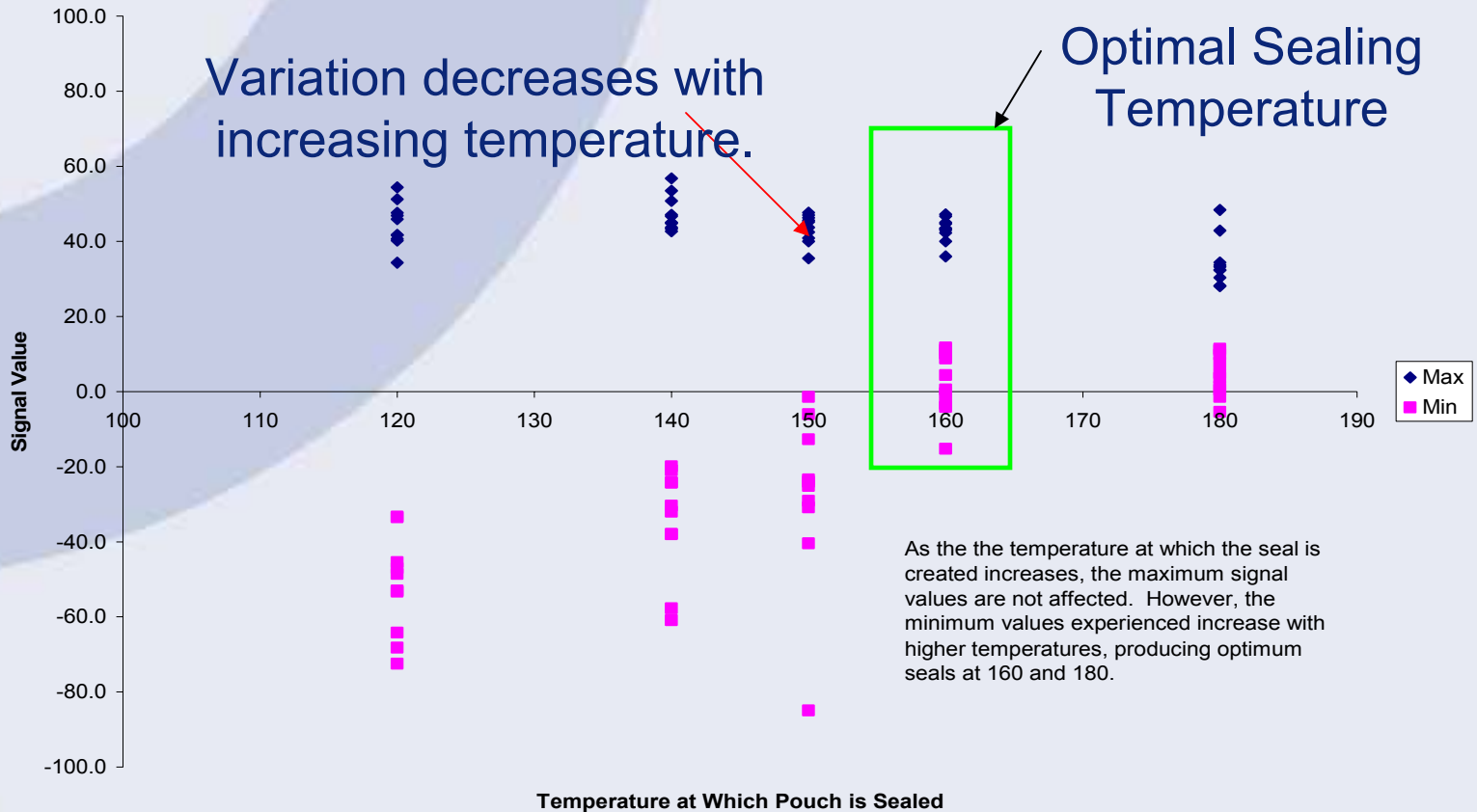
Modified L-Scan



Optimizing the Sealing Process

Seal-Scan™ serves as an analytical tool to determine optimal sealing conditions; e.g. temperature, dwell time, etc.

Maximum and Minimum Signal Values at Different Temperature



Material Analysis

HDPE exhibits better sealing uniformity and quality at higher temperatures.

TYVEK® exhibited weaker bonding at higher temperatures.



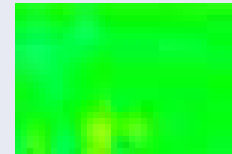
105 C HDPE



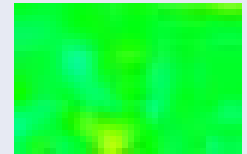
105 C HDPE



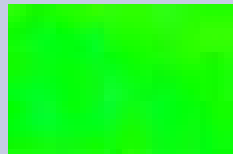
105 C HDPE



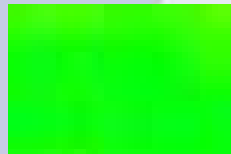
105 C HDPE



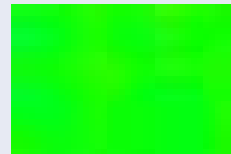
105 C HDPE



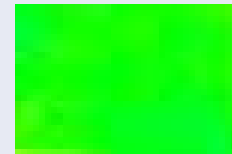
128 C HDPE



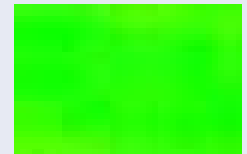
128 C HDPE



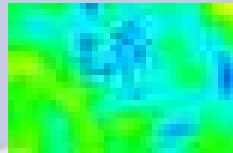
128 C HDPE



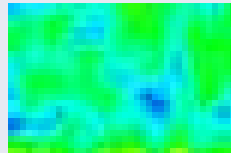
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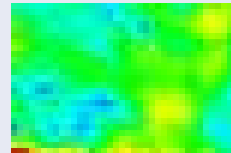
128 C HDPE



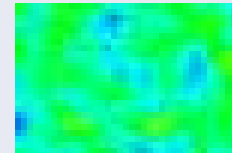
108 C TYVEK



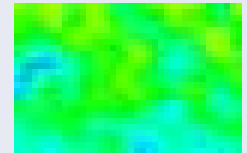
108 C TYVEK



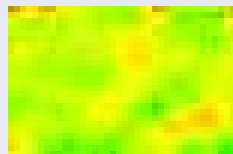
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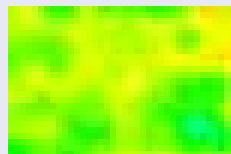
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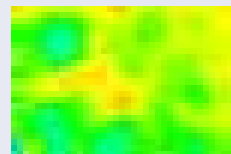
108 C TYVEK



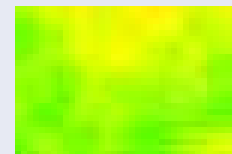
134 C TYVEK



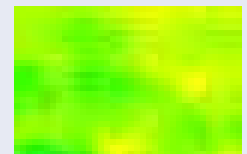
134 C TYVEK



134 C TYVEK



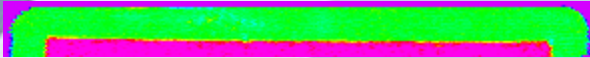
134 C TYVEK



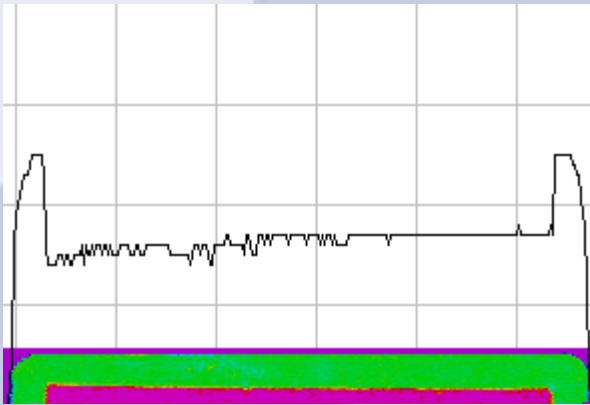
134 C TYVEK

Good Seal Profile (Film-Pouch)

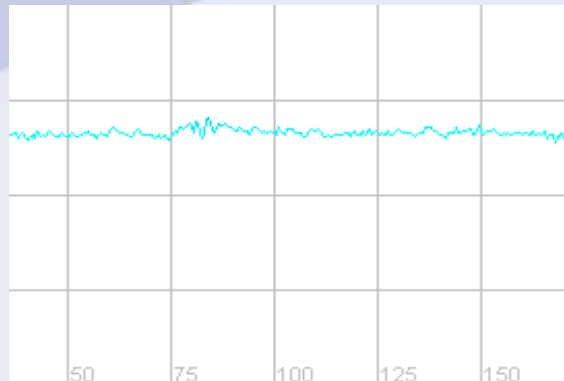
C-Scan



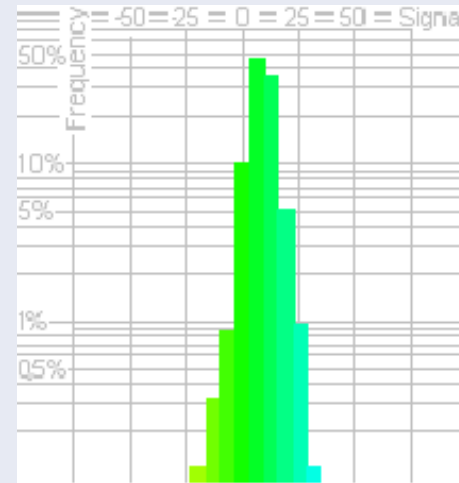
Seal width profile



L-Scan



Seal Quality Histogram



Seal Width Data, mm

Avg	Min	StD
8.2	7.0	0.7

L-Scan Statistics, % Signal Value

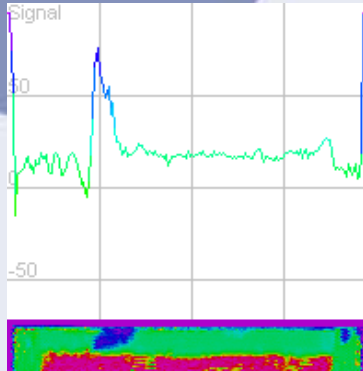
Avg	Min	Max	StD
33.1	27.7	41.2	1.9

Test results to be compared against Pass-Fail reference values.

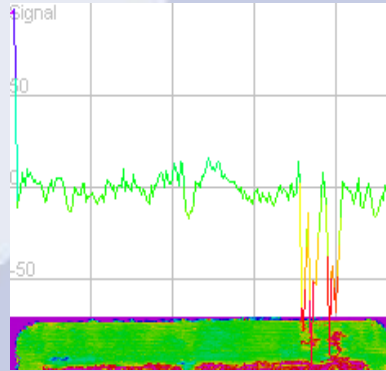
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Seal-Scan™ Defect Gallery

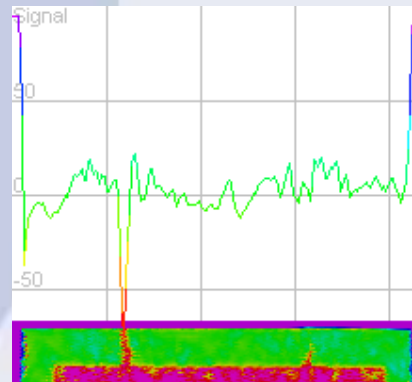
Abrasion



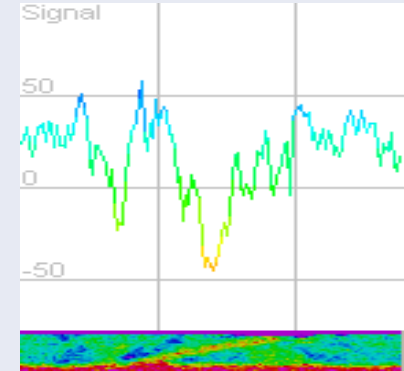
Blister



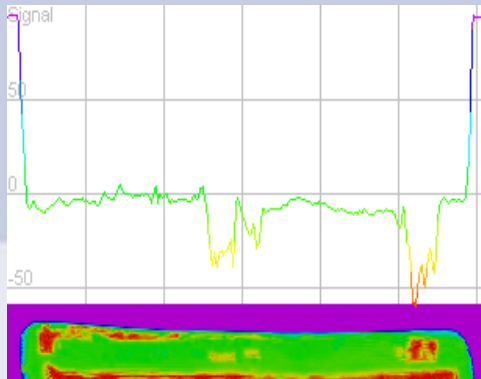
Channel



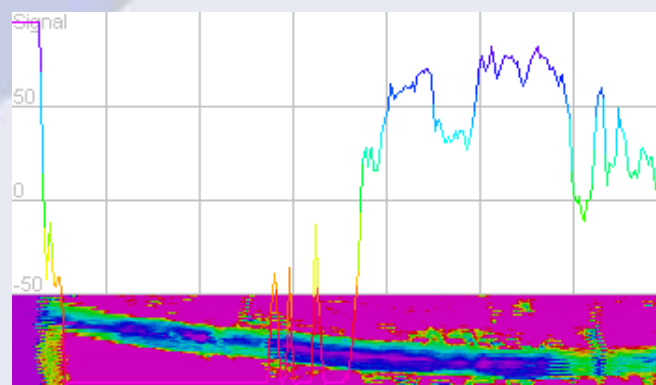
**Compressed
Overheated Seal**



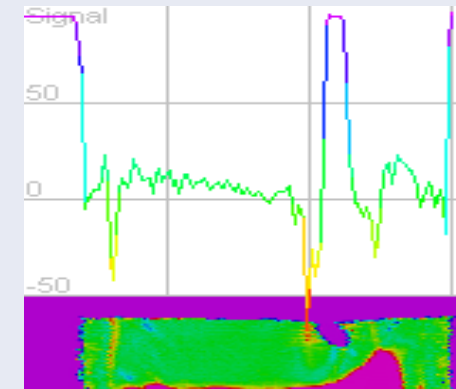
Contamination



Crooked Seal



Cut

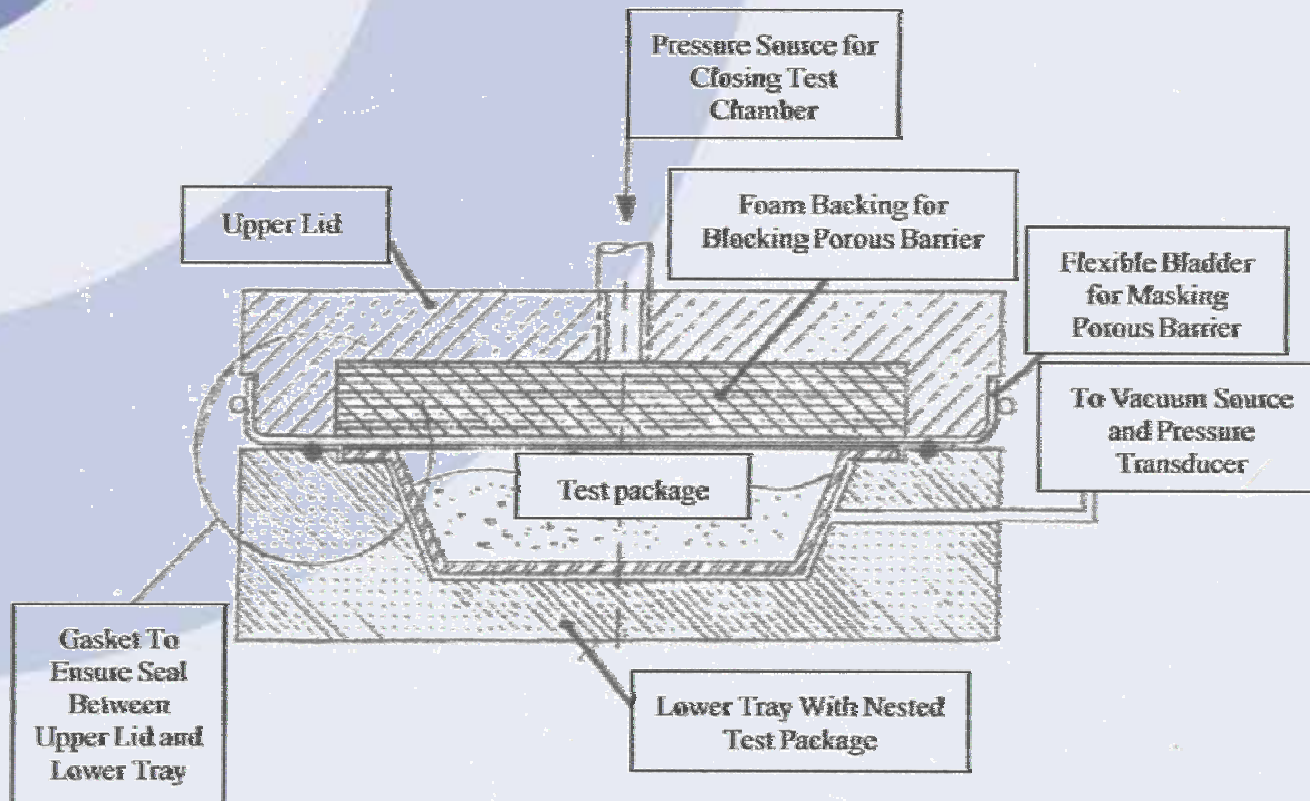


Applications of Seal-Scan™ Ultrasound Inspection

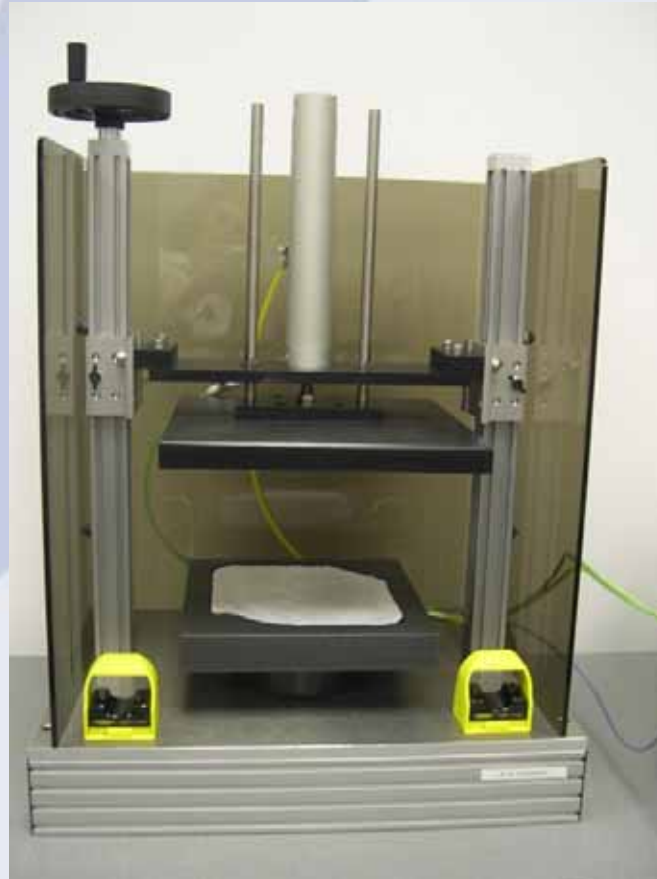
- On-line defect detection
- Analyzes seal quality of pouches
- Characterizes bonded materials
- Works with all materials: film, alu, paper, Tyvek® or composite
- Process control
- On-line Inspection
- Quality control
- R&D for package/seal parameters optimization

ASTM F2338-09

Test method development for Tyvek®



Test Set-Up for Tyvek® Tray



Product		1	10/11/2003					Product Code	Tyveck Tray	
P225		TStroke	2.00	Notes:				Tester S/N	020-5381	
		TEqual	0.10					1) The left part of the table for automatic data recording only		
		TTest	3.00					2) Optional numeric data for information only		
Vac.	400.0							Software Rev.		
	Vacuum, mb	dP/dt, mbar/s	TFill, s					Chamber S/N	000-1001	
Ref	349.9	25.1	0.50					Stage	1	
Min	356.4	14.3	0.09					Operator	HW	
Avg	364.4	16.0	0.10					Test location	PTI	
Max	369.8	18.6	0.10					Test conditions	Lab	
				3) The right part of the table to be filled by operator				Main Air supply, b	90 PSI	
10	pass			10	no leak					
5	fail	FALSE		5	leak					
15	total			15	total					
Test #	Vacuum, mb	dP/dt, Pa/s	Time	Pass/Fail	V.Ref, mb	dP/dt Ref, Pa/s	TFill Ref, s	Leak, ccm	Sample ID	Comments
1	369.8	14.3	3:56 PM	P	349.9	25.1	0.50			good
2	368.8	15.0	3:56 PM	P	349.9	25.1	0.50			good
3	365.2	15.9	3:57 PM	P	349.9	25.1	0.50			good
4	356.4	18.6	3:57 PM	P	349.9	25.1	0.50			good
5	361.3	16.6	3:57 PM	P	349.9	25.1	0.50			good
6	363.9	16.3	3:58 PM	P	349.9	25.1	0.50			good
7	363.6	16.6	3:58 PM	P	349.9	25.1	0.50			good
8	365.5	15.3	3:59 PM	P	349.9	25.1	0.50			good
9	363.3	16.6	3:59 PM	P	349.9	25.1	0.50			good
10	366.2	15.3	3:59 PM	P	349.9	25.1	0.50			good
11	349.1	39.1	3:59 PM	F	349.9	25.1	0.50			.005" channel leak
12	351.6	29.9	4:00 PM	F	349.9	25.1	0.50			.003" channel leak
13	328.3	48.7	4:00 PM	F	349.9	25.1	0.50			.005" leak in tray
14	280.3	96.4	4:01 PM	F	349.9	25.1	0.50			blown seal
15	315.9	62.5	4:01 PM	F	349.9	25.1	0.50			dot pattern

Thank you!