



A **Stevanato** Group Brand

Gaetano Baccinelli Sales Manager
Optrel Inspection systems
A Stevanato Group Brand

INSPECTION OF SUSPENSIONS, MILKY AND VISCOUS PRODUCTS

Inspection Machines: available solutions

— Very high speed solution

*Continuous motion
(up to 660 pcs/min)*



- CVT

Optical tracking cameras for high accuracy and very high speed

— High speed solution

*Continuous motion
(up to 400 pcs/min)*



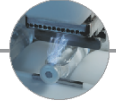
Exacta Plus

Tracking cameras for high accuracy in detection



Exacta Easy

Fixed cameras for high productivity and low maintenance



LKD

Leak test machine

— Medium speed solution

*Intermittent motion
(up to 200 pcs/min)*



MCA

Very flexible machines for inspection of a wide range of products

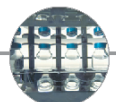


FD

Dedicated machine for Freeze-Dried products

— Semi-automatic solution

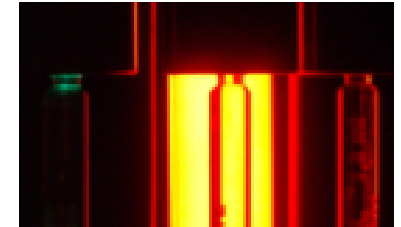
(up to 100 pcs/min)



PWL

Ideal for small volume inspection or critical products

Automatic inspection, controls Available for liquids

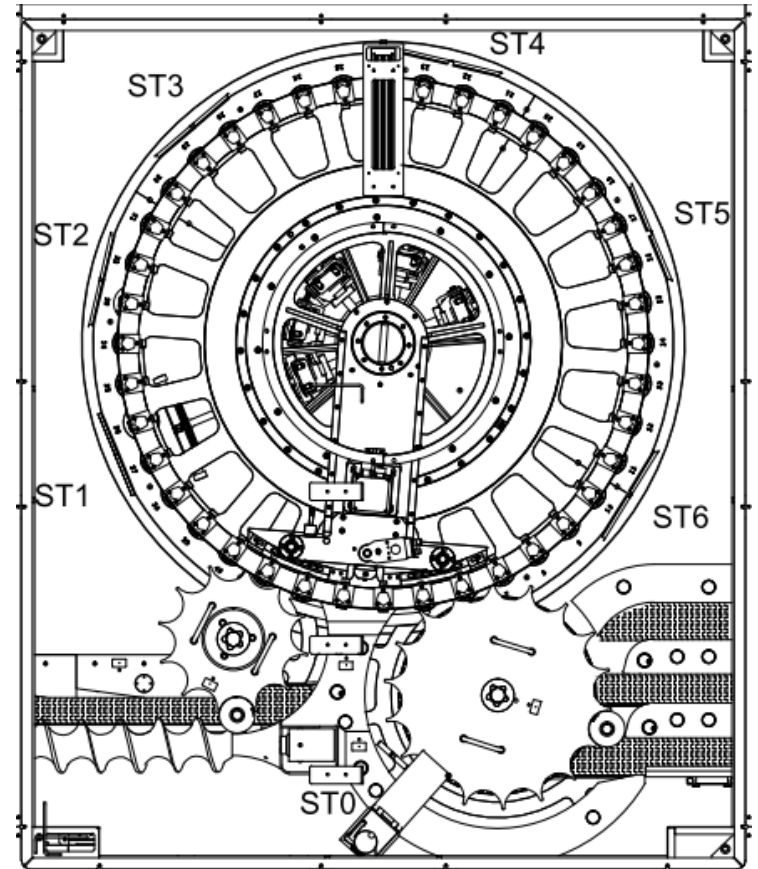


	AMPOULES	VIALS	CARTRIDGES	SYRINGES
Standard Inspections	<ul style="list-style-type: none"> particles inspection fill level tip inspection Leak test 	<ul style="list-style-type: none"> particles inspection fill level alu-seal crimping stopper presence 	<ul style="list-style-type: none"> particles inspection fill level alu-seal crimping stopper presence 	<ul style="list-style-type: none"> particles inspection fill level flange integrity needle shield presence plunger presence
Additional Inspections	<ul style="list-style-type: none"> tip ring color/OPC tip black spot printing integrity glass surface 	<ul style="list-style-type: none"> glass surface lateral side OCR and OCV Reading Leak test 	<ul style="list-style-type: none"> cartridges bottom edge glass surface plunger position and orientation plunger integrity and defects bead presence 	<ul style="list-style-type: none"> glass surface plunger position and orientation plunger integrity and defects needle shield defects

Automatic inspection, standard layout for liquid products

	Type	Position
ST0	Closure control	Exit
ST1	Crimping control	Turret
ST2	Body control lateral	Turret
ST3	Particle and fill level	Turret
ST4	Particle inspection	Turret
ST5	Particle inspection	Turret
ST6	Floating particles	Turret
ST7	Bottom inspection	Outfeed

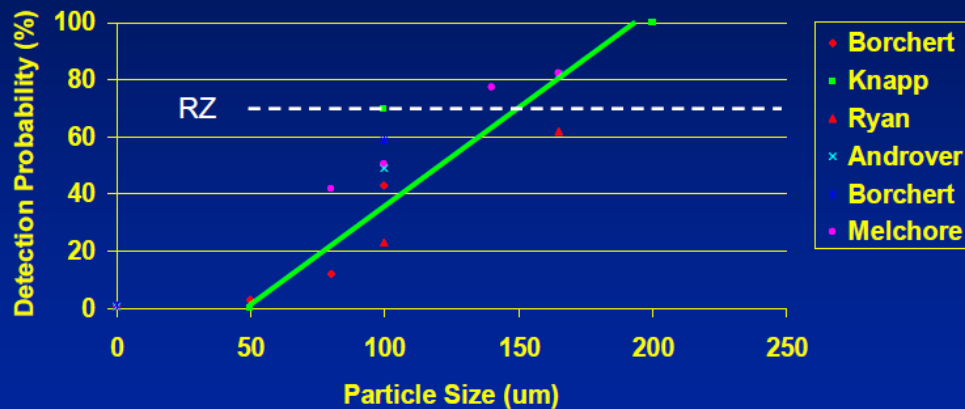
Difficult to combine all the different light setup and keep statistical redundancy with standard inspection technology



Particles inspection in regular liquid products

Particle Inspection in regular liquid products

Human Inspection Performance



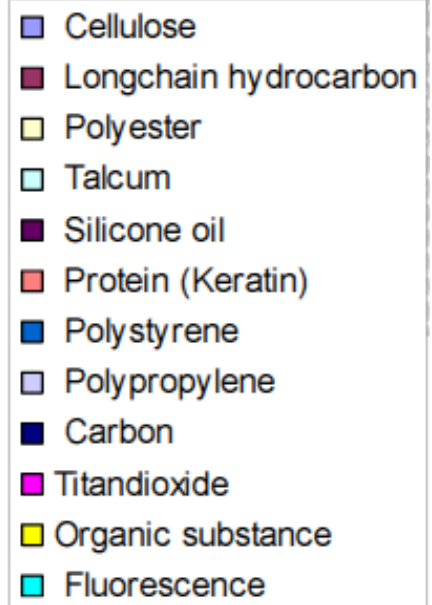
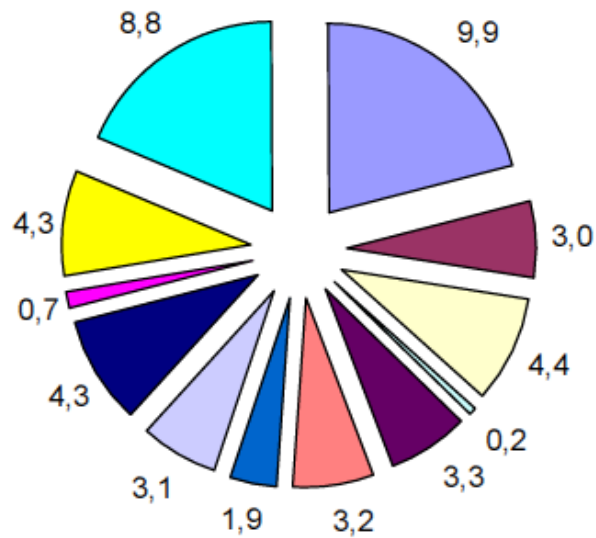
From Shabushnig, Melchore, Geiger, Chrai and Gerger, PDA Annual Meeting 1995

100% inspection (human or machine) is needed to detect small quantities of randomly sourced foreign material.

- 100% inspection (man or machine) is not 100% effective.
- Zero is not a practical limit.

Most common foreign matter found in drug production, beside glass particles

Substance	%	Nature	Source
Cellulose	9.9	fibers	clothes, towels, wipers, autoclave paper
Longchain hydrocarbon	3.0	rubber, PE	stopper, bottles
Polyester	4.4	fibers, particles	Cleanroom clothes and filters
Talcum	0.2	product	API
Silicon oil	3.3	particles, drop	Sealing, siliconisation
Protein (Keratin)	3.2	mostly flakes	Human skin dust, hair
Polystyrene	1.9		
Polypropylene	3.1		
Carbon	4.3		
Titandioxide	0.7		
Organic	4.3		
Fluorescence	8.8		

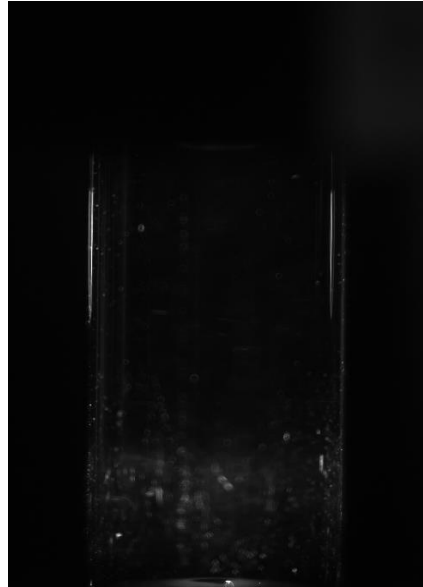


Different contaminants have different response to light



Absorbing

- Carbonization
- Impurities
- Rubber frag



Reflecting

- Glass fragments
- Crystallization
- Silicone oil
- Delamination



Polarizing

- Fibers
- Impurities
- Product aggregation



Suspension

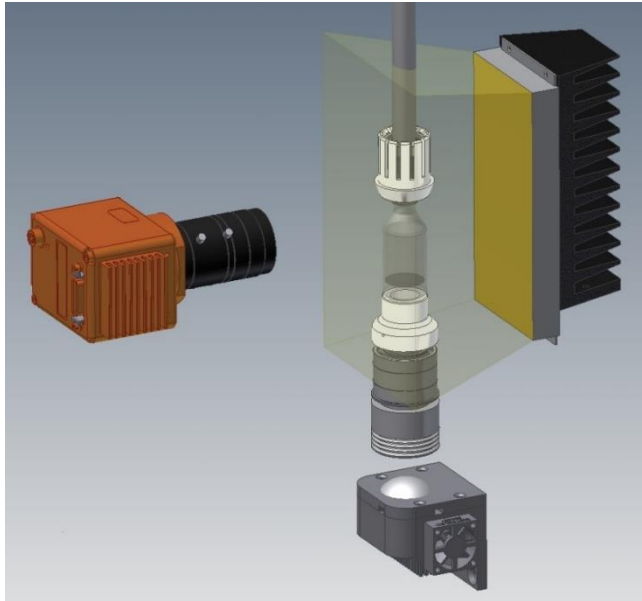
- Fibers
- Impurities
- Glass fragments

The machine combine the advantages of the various lighting methods in order to detect the largest range of different particles.

Particle inspection : particle in white background

Possible Source:

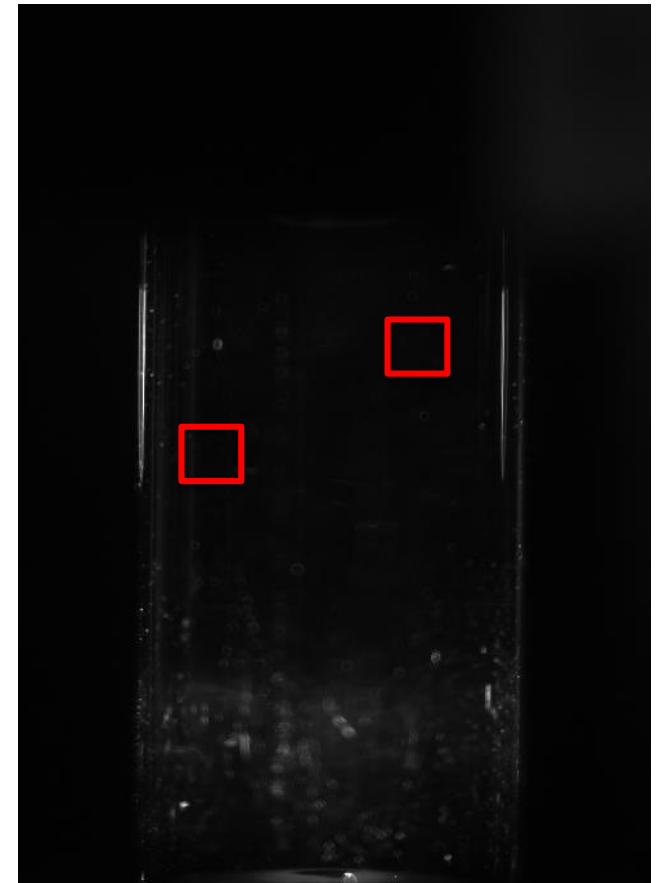
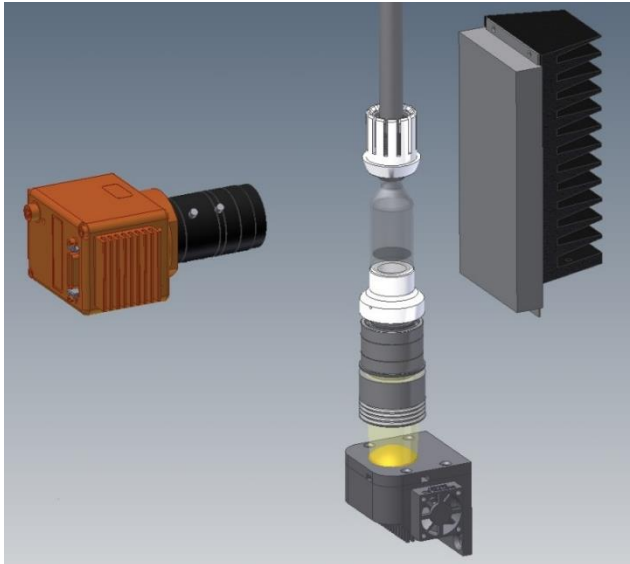
- Product carbonization for improper flame sealing of ampoules tip
- Impurities from API/WFI
- Rubber particles



Particle inspection : particle in black background

Reflecting particles:

- Glass fragments, filling needle not centered
- Product crystallization
- Silicone oil from stopper/plunger
- Glass Delamination



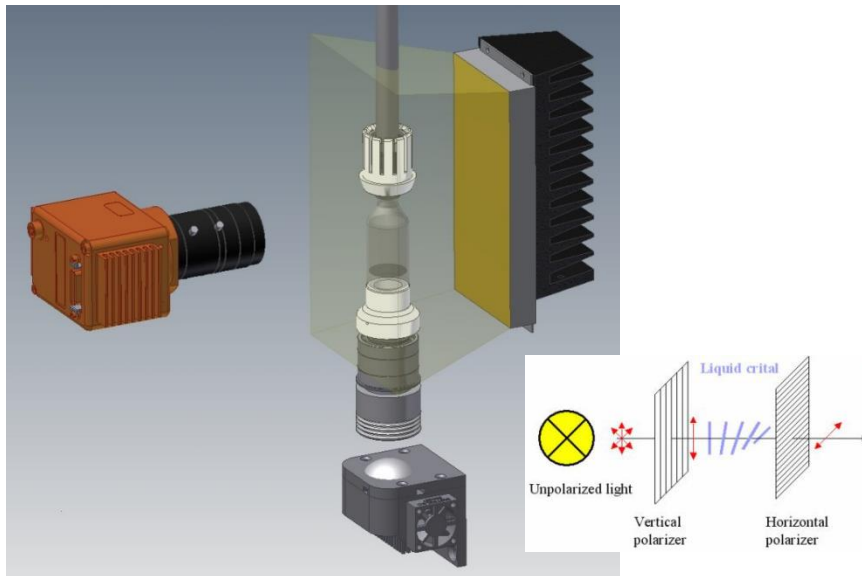
Particle inspection : fibers in polarized light

Inspection method:

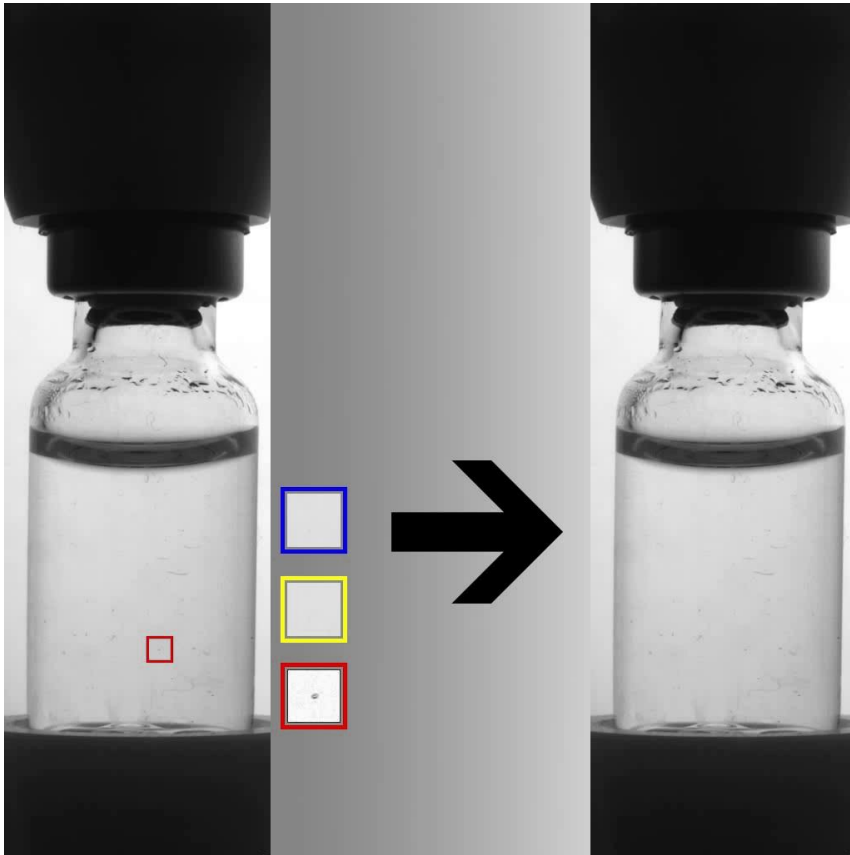
- Polarized light illumination

Possible Source:

- Fibers from filter/wipper
- Impurities from API/WFI
- Fibers from clothing

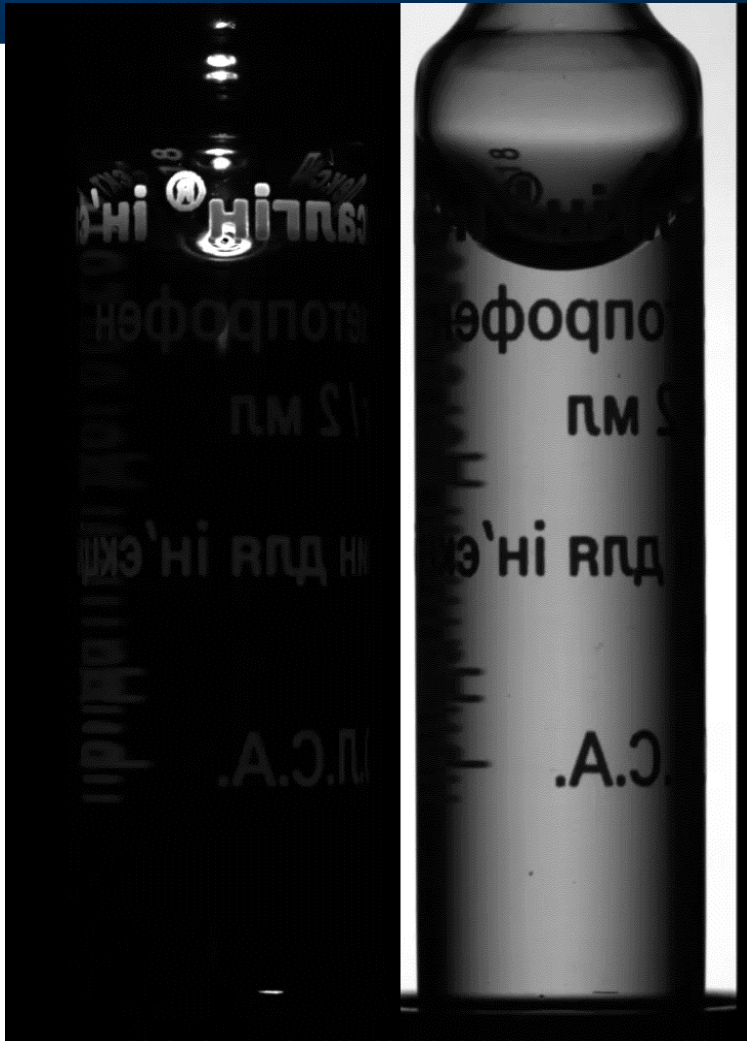


Particle inspection : trajectory algorithm, innovative solution



- Particle trajectory reconstruction using the Kalman filter
- Trajectory post analysis filtering
- Analysis of the meniscus
- Analysis of the container bottom

How to combine all these setup in a single camera station?



High resolution high speed cameras acquire from **40 to 120 images**, half with one illumination setup half with another to detect all kind of contaminants

USP32 - Problematic Products and Containers

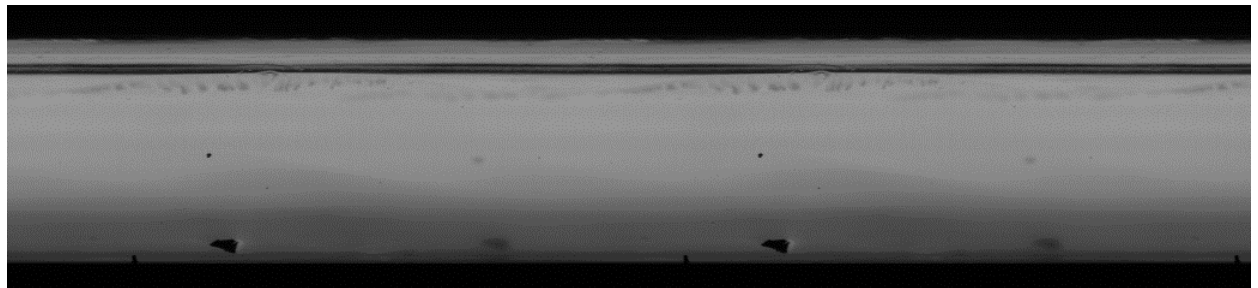
Solid	Suspensions	Opaque Containers viscose
		

United States Pharmacopeia (USP 32 – NF 27)
General Chapters <1> Injections – Foreign and Particulate Matter
“Where the nature of the contents or the container-closure system **permits only limited capability** for the inspection of the total contents, the 100% inspection of a lot **shall be supplemented with the inspection of constituted** (e.g., dried) or withdrawn (e.g., dark amber container) contents of a sample of containers from the lot.”

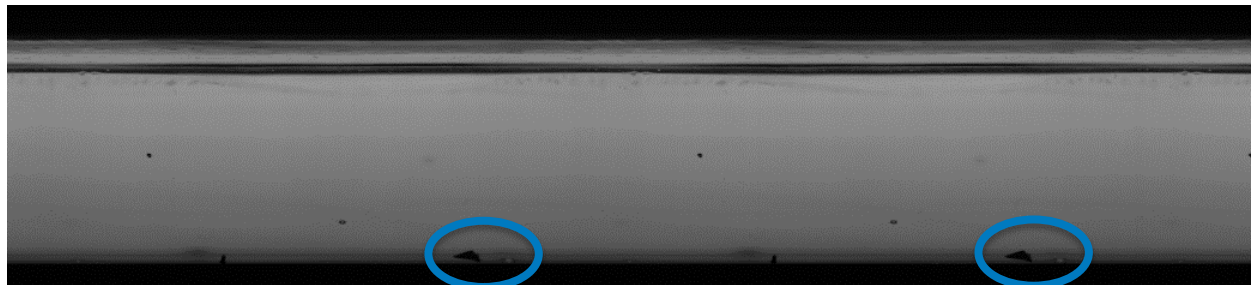
High viscous liquid automatic inspection : Correlation system

Inspection of **viscous liquid** is **not effective** using the standard **Spin&Stop™** Inspection. For these category of products the **Spin&Inspect™** approach is more effective because it is not based on the particle movement. To cancel the potential false reject coming from the dirty on the container it is important to analyse the information coming from several camera stations like in the example

ST1 first analysis



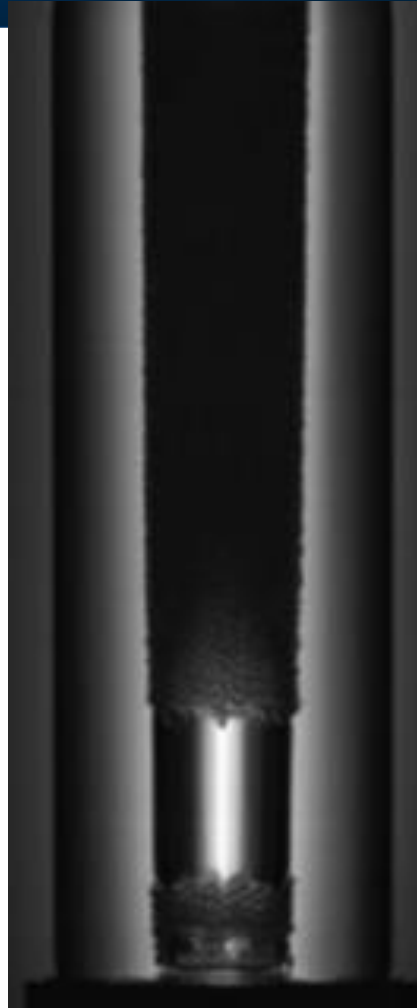
ST2 second analysis



Advanced analysis for foamy products



Foamy product



High speed
spinning

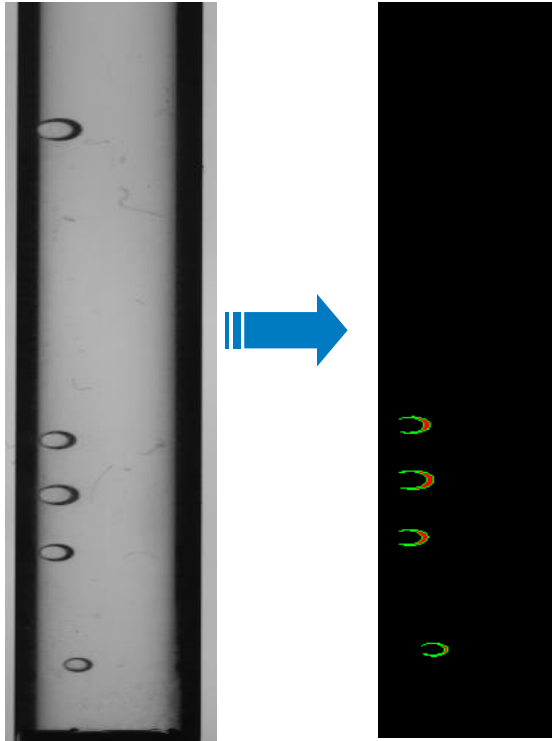


No air bubbles
interference

Air bubbles into viscous products, cause of false rejection

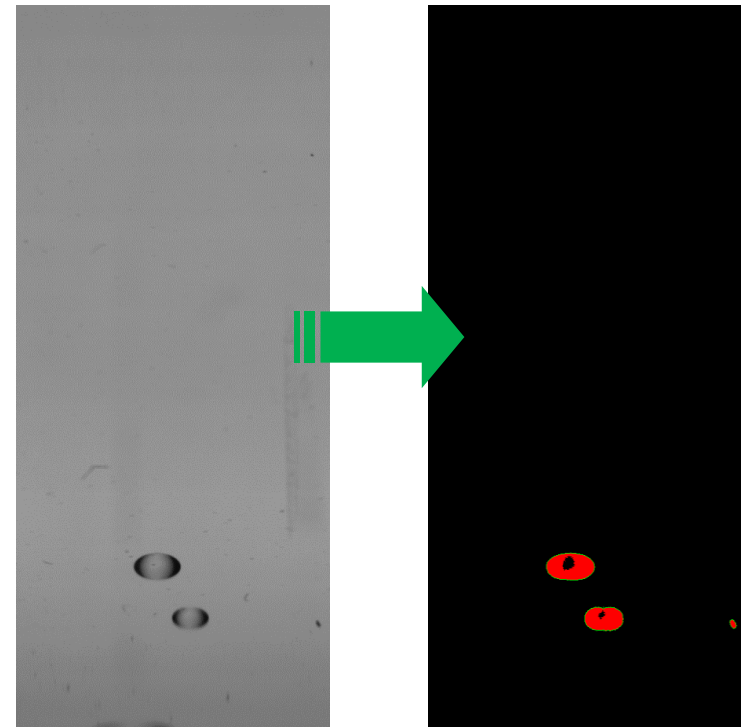
Linear scan camera: smart solution

Area Camera



**Hard to recognize,
false reject**

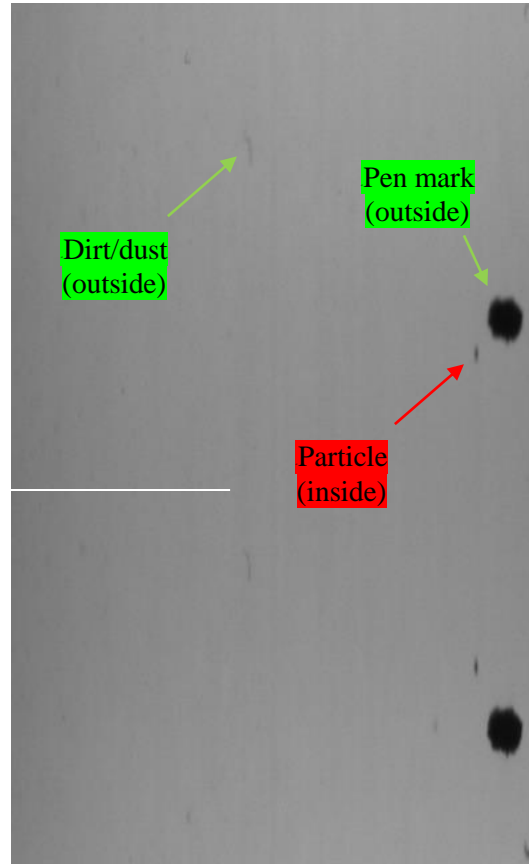
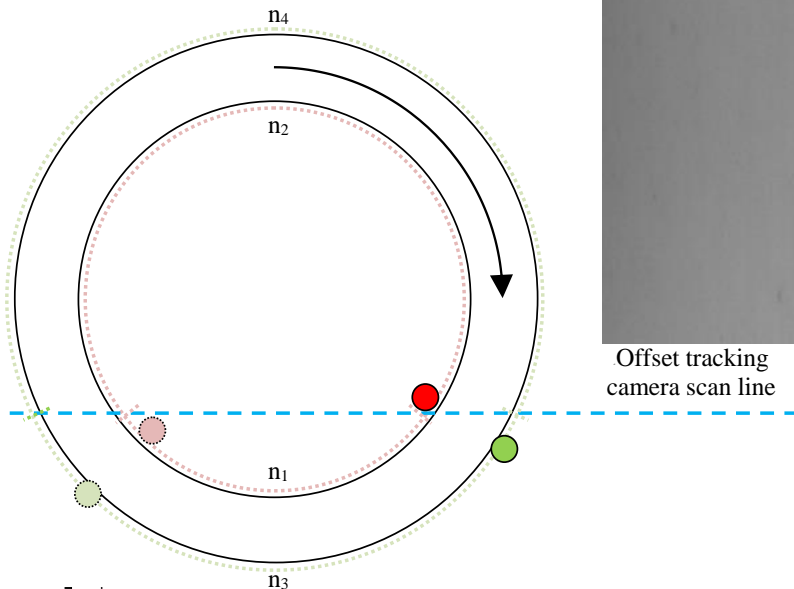
Linear Camera



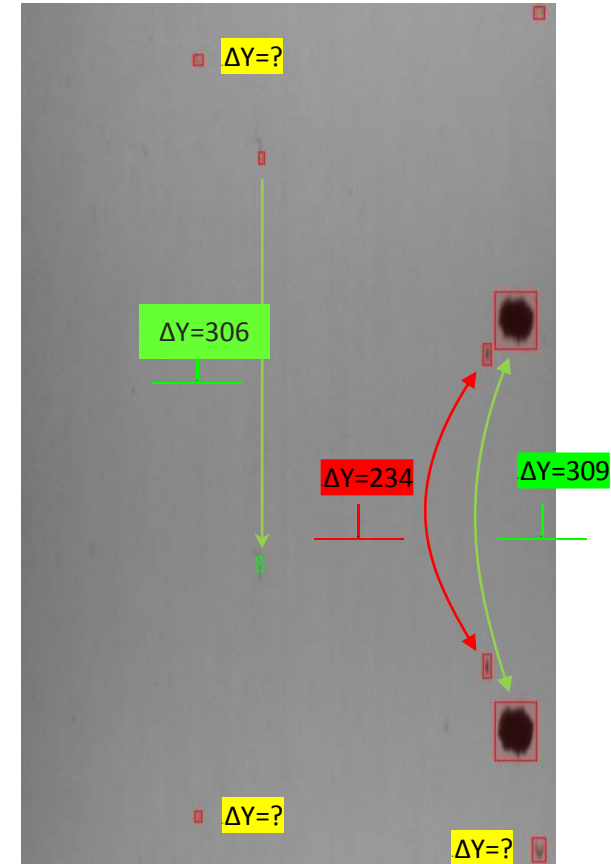
**Easy to recognize,
reliable control**

Dirty on the Outside: cause of false rejection

Offset Linear Camera
distinguishes between
internal and external
position on a full round

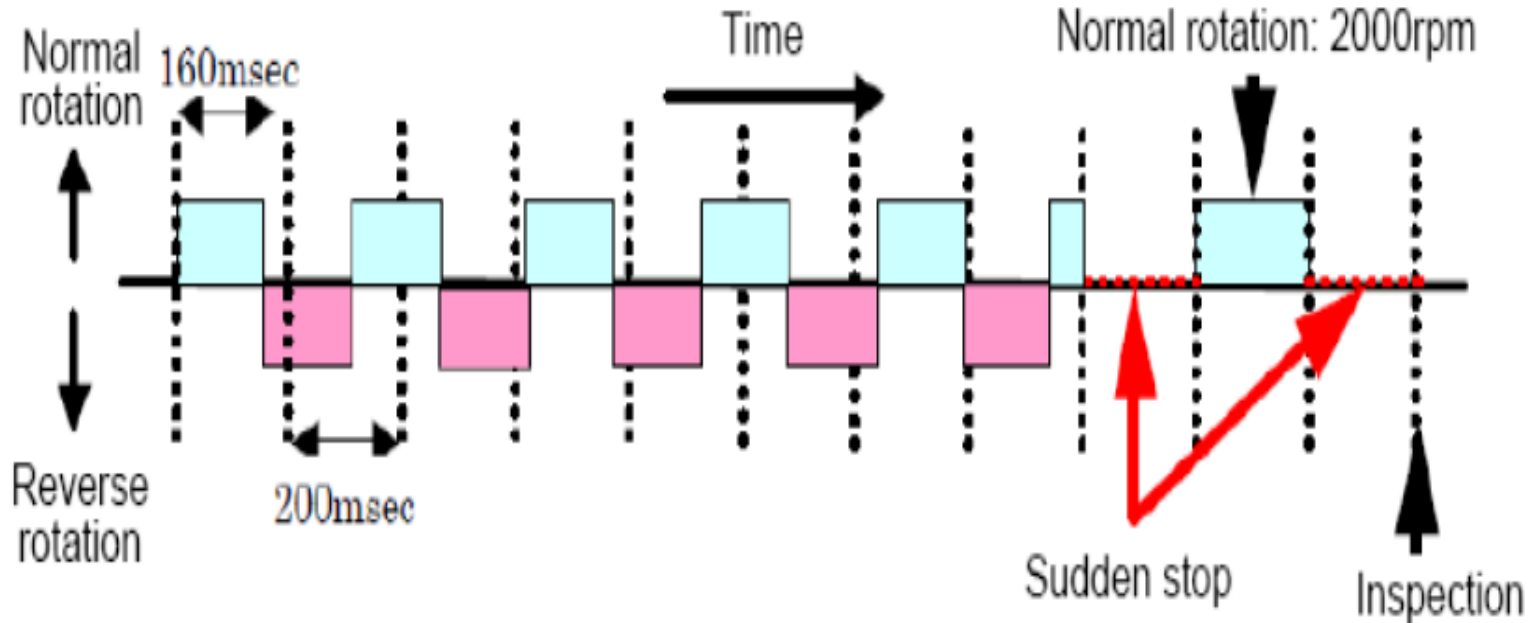


Offset tracking
camera scan line



Particles in suspensions and Milky products

Suspension Products: high speed spinning



Product preparation is fundamental for suspension

High Speed Spinning System: product homogenization



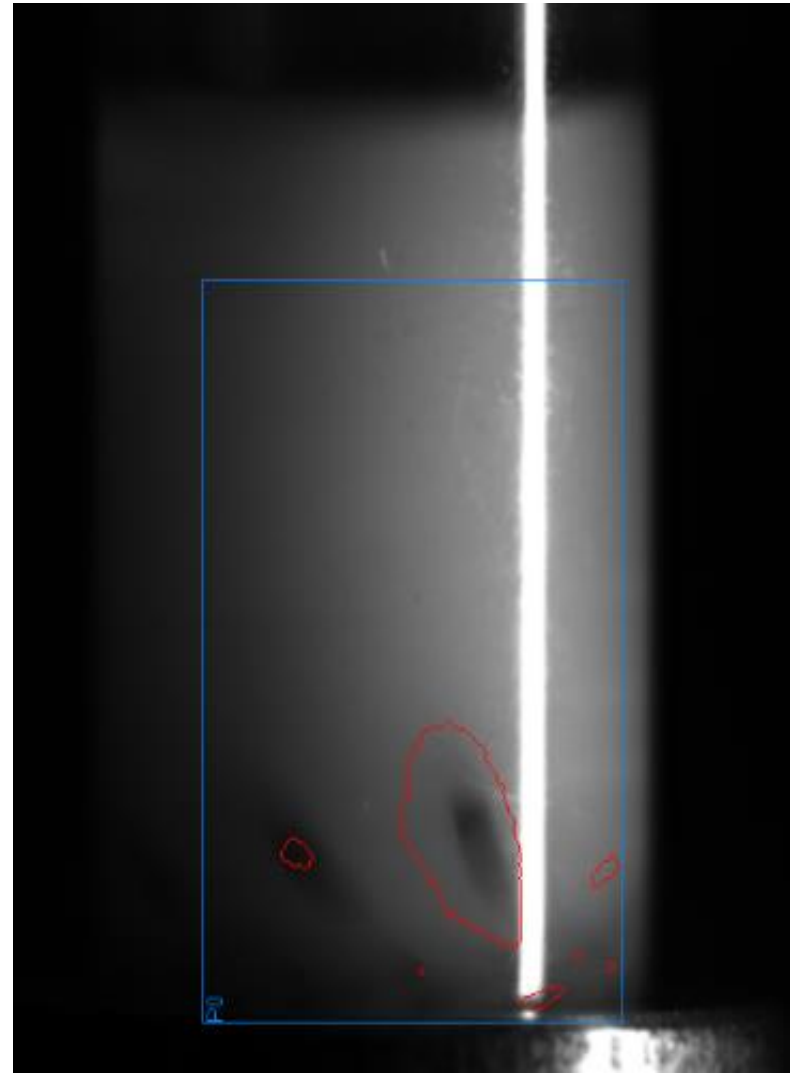
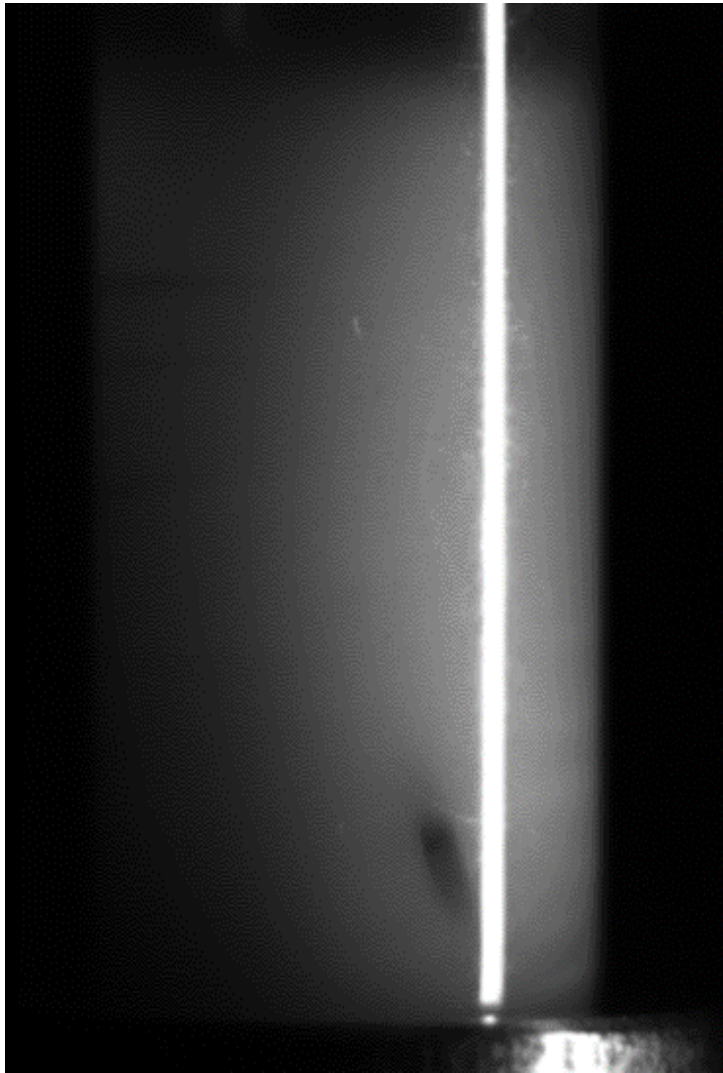
High Speed up to 6000rpm

emulsion inspection: Particle inspection

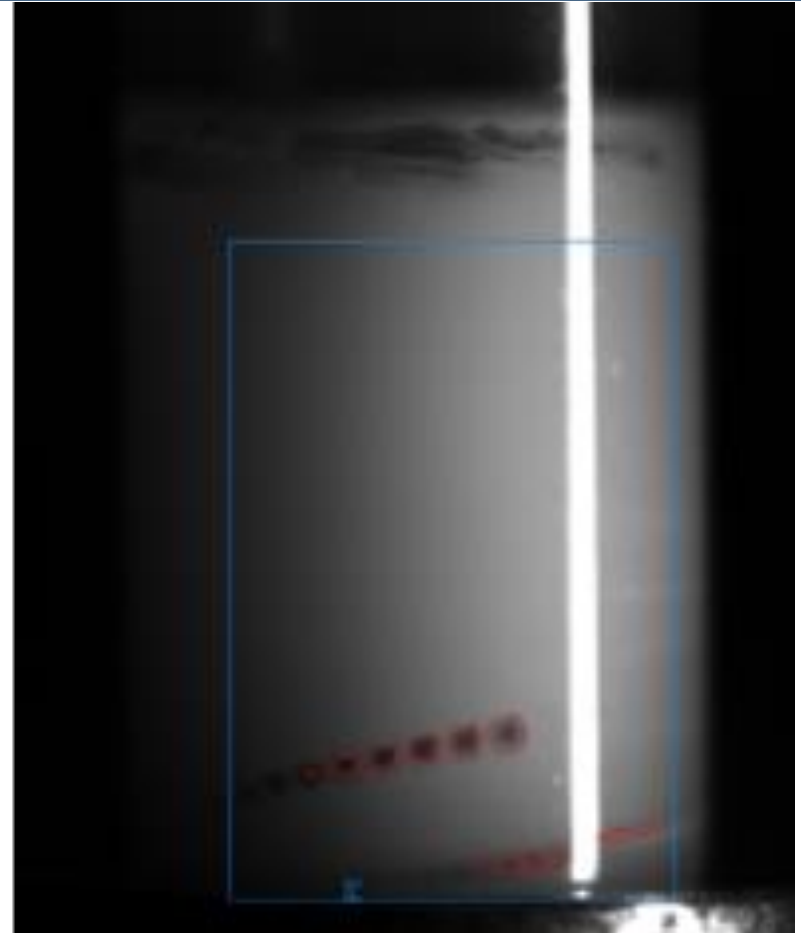


Special light combined with high speed rotation (pat.)

example of particles Inspection



More example of particles Inspection



More example of particles Inspection

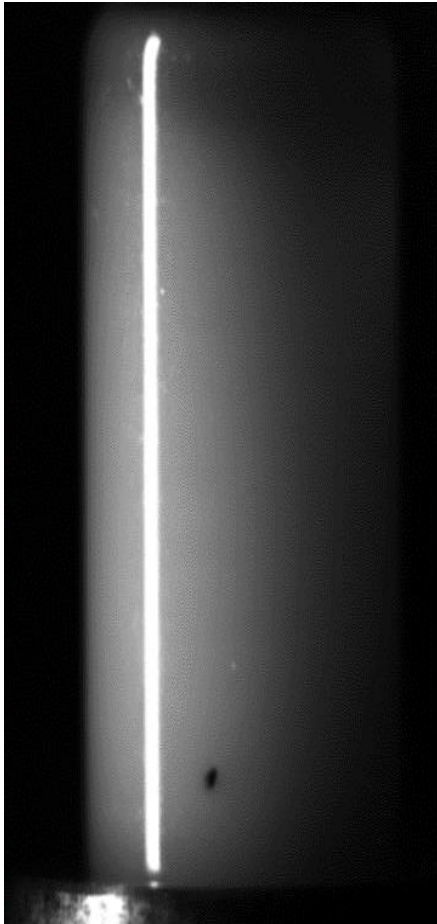


Figure 4 Sample #09, black particle

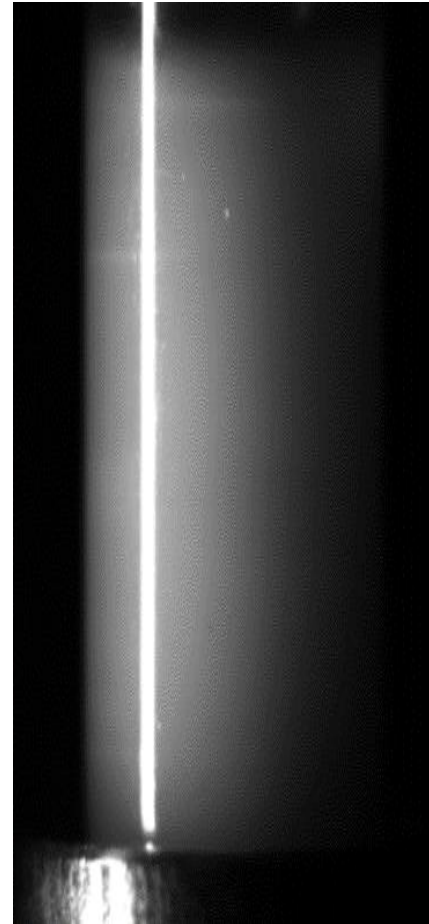
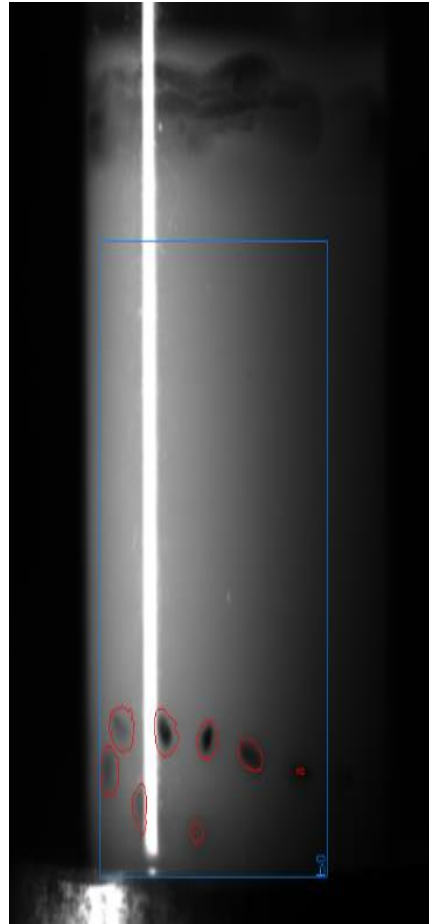
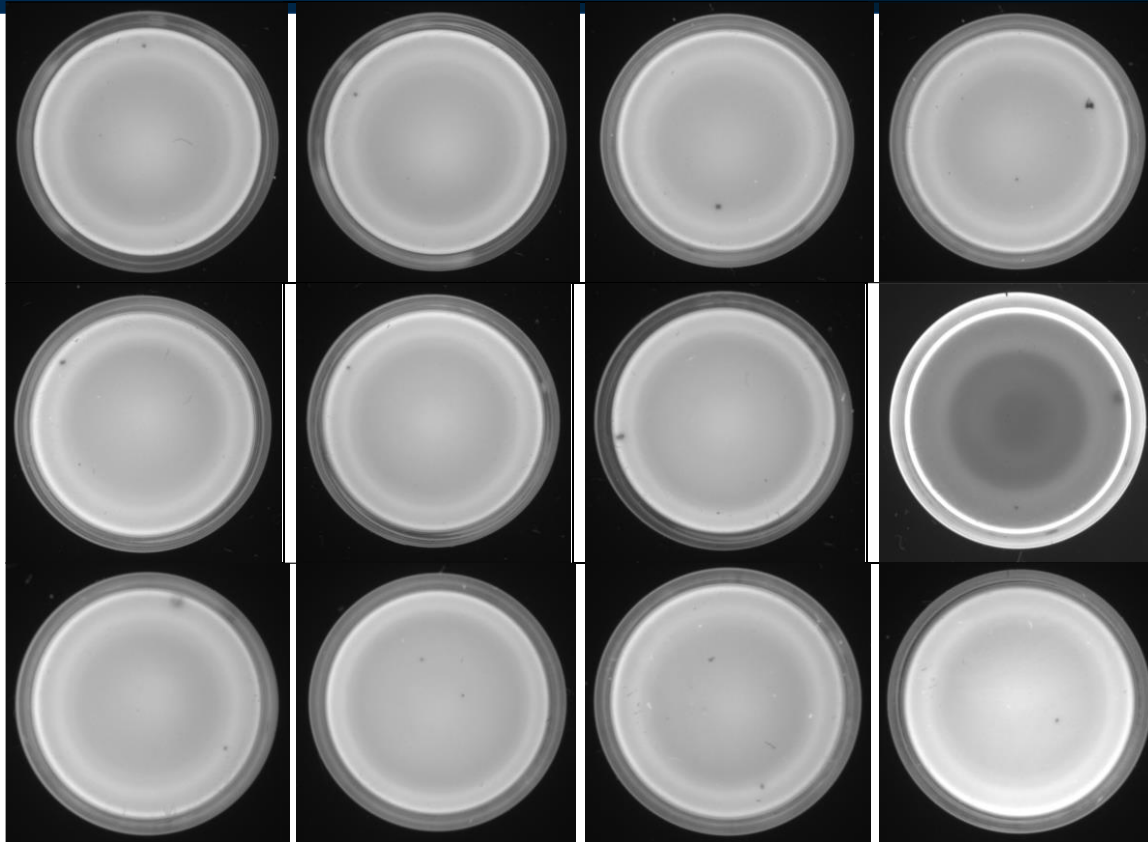


Figure 6 Sample #29, white fibre

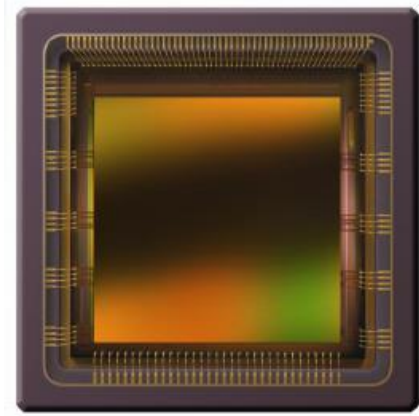


Bottom inspection



Bottom inspection at infeed complement particle inspection

How to reach those performances?



New Generation Advanced Vision System Facts:

- 64 high resolution images per container per each particle station (2000x2000pxls)
- 256 images per container for particle inspection
- 1GB of particle inspection data per container to process in real-time

Cosmetic Inspection

PVSI: Example of FlipOff/AluSeal inspection

ST0 - CAM0 - FLIPOFF INSPECTION

(H0) Bottle FlipOff Inspection (VID=0) (GRY=58)

Head Time =12
Discharge Class =0

BlobArea =0
Hue =47
Gray =112
Area =32549

(G1) Bottle Inspection (VID=0) (GRY=59)

Head Time =22
Discharge Class =0

Crimp Max.Bend =6
Crimp Def.Area =57
AluSeal Blob Area =0
FlipOff Blob Area =0
FlipOff Width =272
AluSeal Width =250
AluSeal Height = 99 (L), 100 (R)
Bottle Height =182

(G2) Bottle Inspection (VID=0) (GRY=58)

Head Time =18
Discharge Class =0

Crimp Max.Bend =6
Crimp Def.Area =72
AluSeal Blob Area =0
FlipOff Blob Area =0
FlipOff Width =261
AluSeal Width =237
AluSeal Height = 99 (L), 94 (R)
Bottle Height =183

(G3) Bottle Inspection (VID=0) (GRY=61)

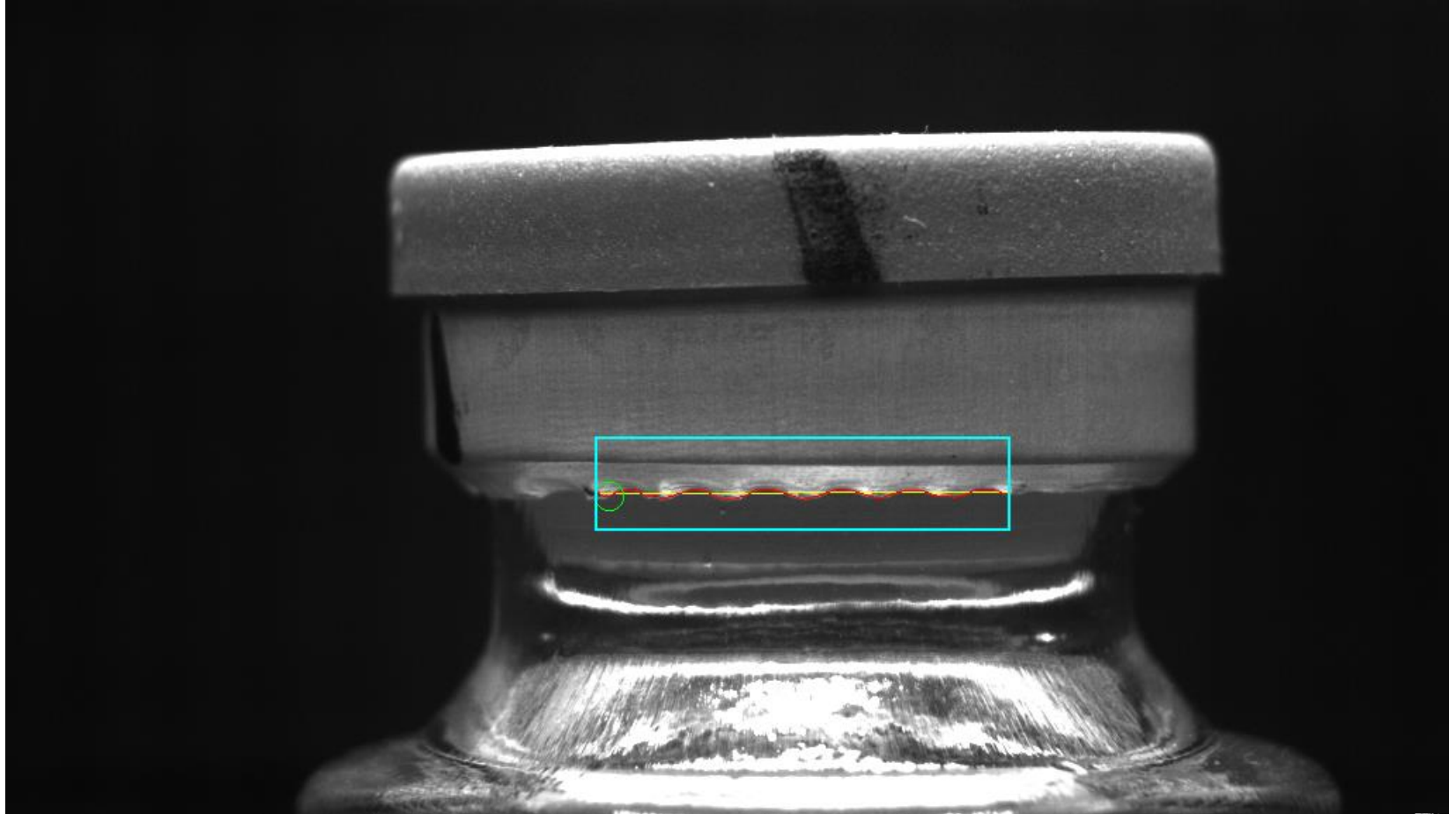
Head Time =18
Discharge Class =0

Crimp Max.Bend =6
Crimp Def.Area =133
AluSeal Blob Area =0
FlipOff Blob Area =0
FlipOff Width =267
AluSeal Width =245
AluSeal Height = 102 (L), 100 (R)
Bottle Height =180

Camera: configurate: 12, trovate: 12 Stop Vial50ml (ver 001)

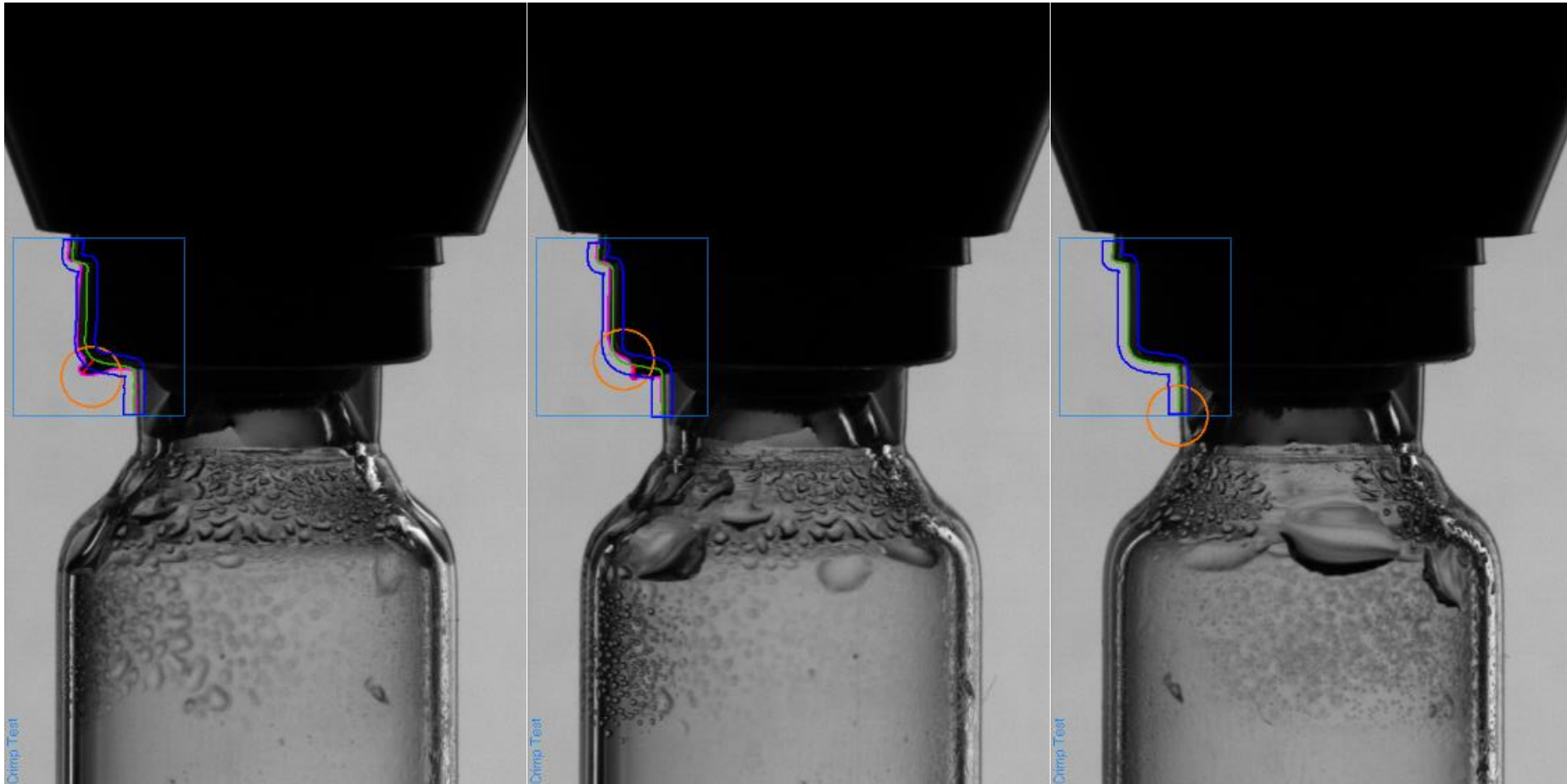
✓ 15:57:29.948	15:57:29.948	WRNGEN_0	ALM WRN00000 ESCLUSIONE RIPARI
✓ 10:22:03.059	10:22:03.059	ALARMGENERAL_72	ALM ALM00072

Example of Crimping control



Precise crimping Control in 1° Resolution Step

Crimping Profile learning by training

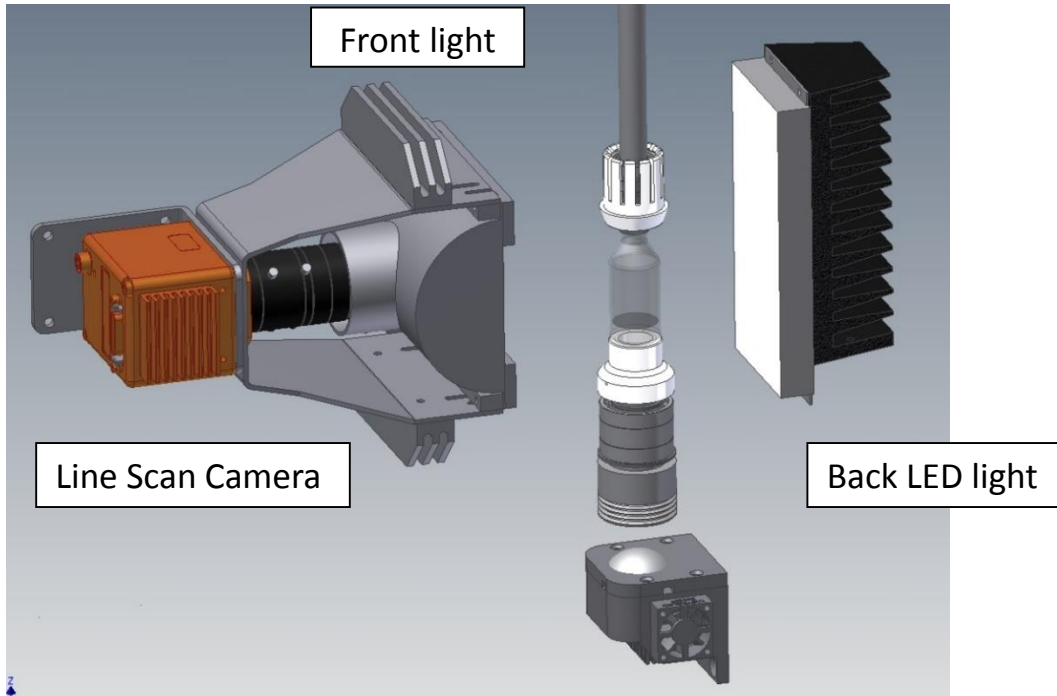


Not conform

Not conform

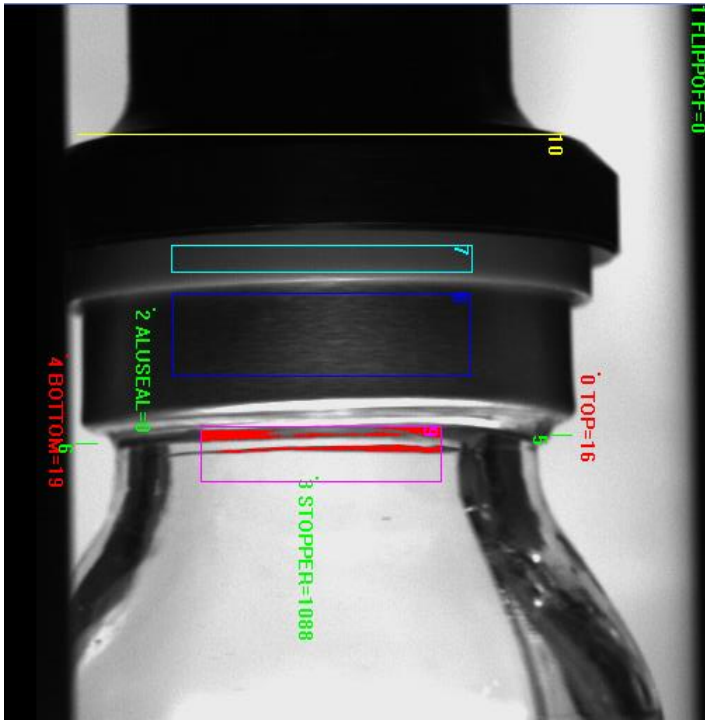
Conform

Linear Scan Camera for Cosmetic Inspection

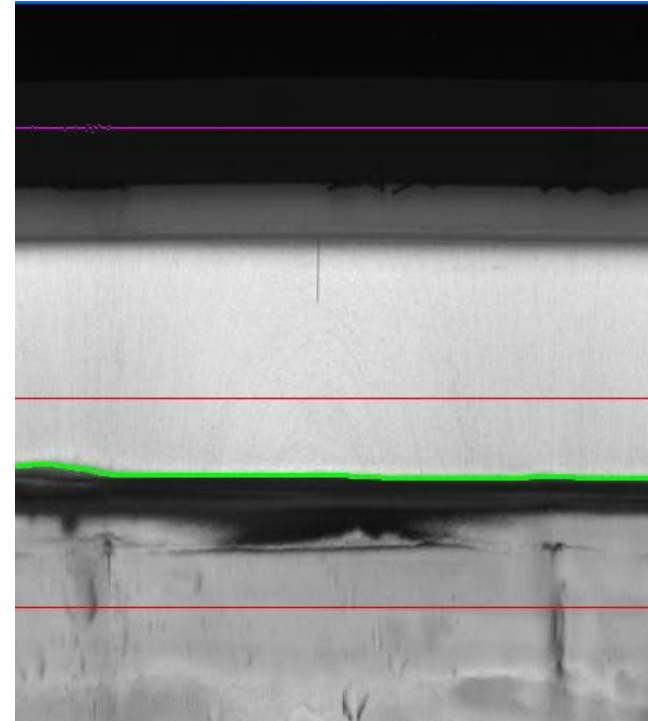


- Special linear scan camera ranging from 512 pixel up to 2048 pixel that guarantee high inspection resolution.
- Special light sources developed by Stevanato Engineering.
- The container is rotated in front of the camera in order to scan the whole surface of the vial.

Liner scan camera for cap inspection



The competitors way

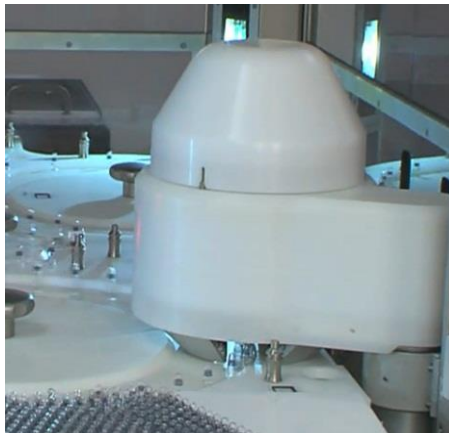
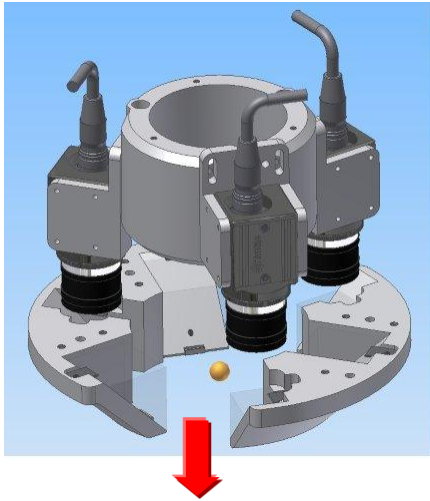


Linescan cover 360° without gaps

- **Linescan technique is more stable and accurate**
- **FPGA preprocessing is best matched to line scanning**

Ampoules Tip inspection

Three views image acquisition



Interactive definition of the tip shape

TipControl settings

Load Image: Load from file, Select PYSI Bank: COB2-0, Apply Bayer Filter:

Tip Model Load/Save: Load model, Save model to .DXF

Tolerance: L: [Slider], H: 15, Max: Angle Curv.: 4.00

Operation: Get edge profile, Check Fit, Fast edge:

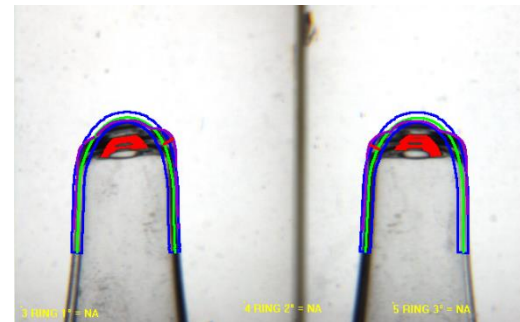
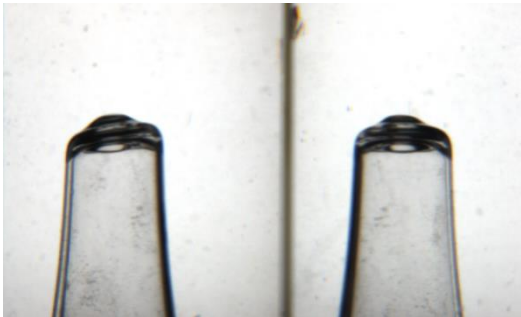
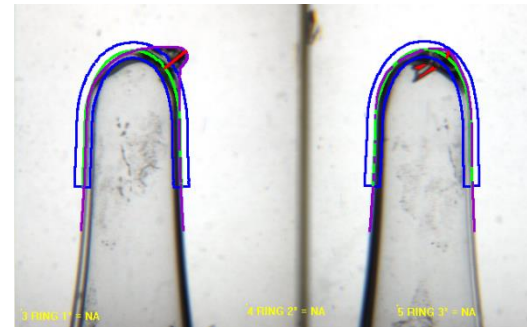
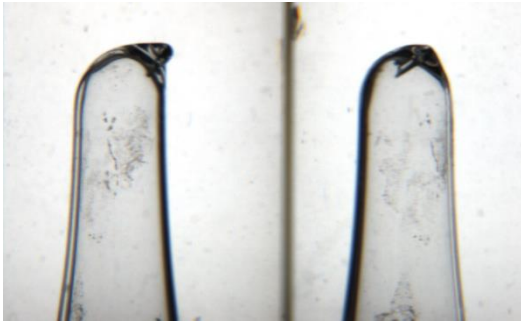
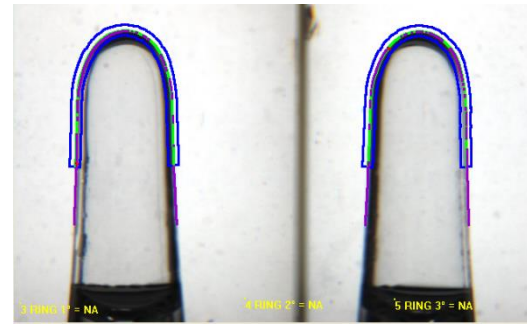
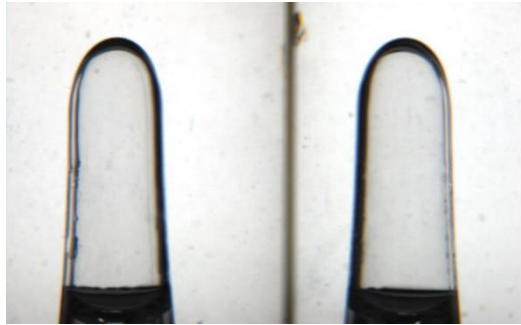
Tip profile data		Edge Fit		Angle Fit	
Type	Value	Type	Value	Mean error	Max error
Edges	1	Match points	142		2.65
Edge points	495	Fit Score	81.4%		
Angle	-0.60°	Max Gap	4.56		
Tin Height	417.0	Mean Gap	2.40		2.70

Angle graphs | Distance graph | Model profile

Model vs Tip angle profile

Angle Fit Error

Example of Tip inspection



Dynamic Analysis of black spot in presence of inside drops

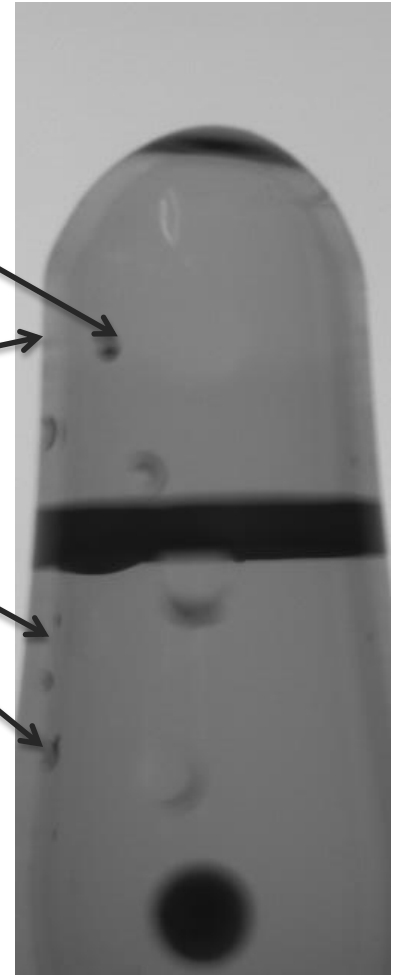
Black spot

Drop

Liquid drops behave differently from cosmetic defects.

Following the change of appearance it is possible to determine the nature of the contamination

False reject < 1% even in presence of liquid drops



Containers closure integrity, Leak detection

Container Closure Integrity: Cosmetic Visual Inspection

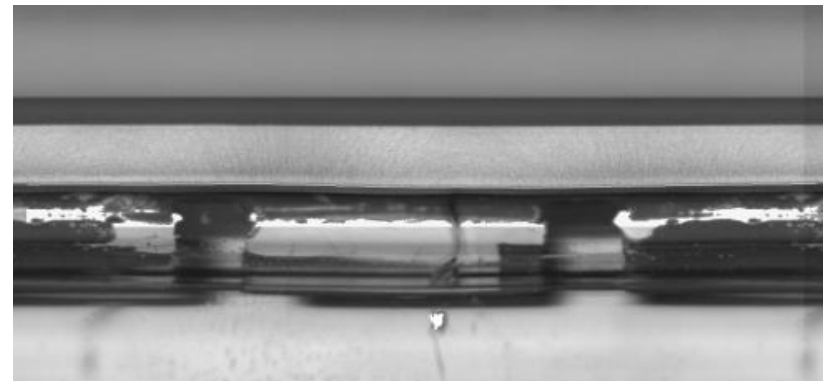
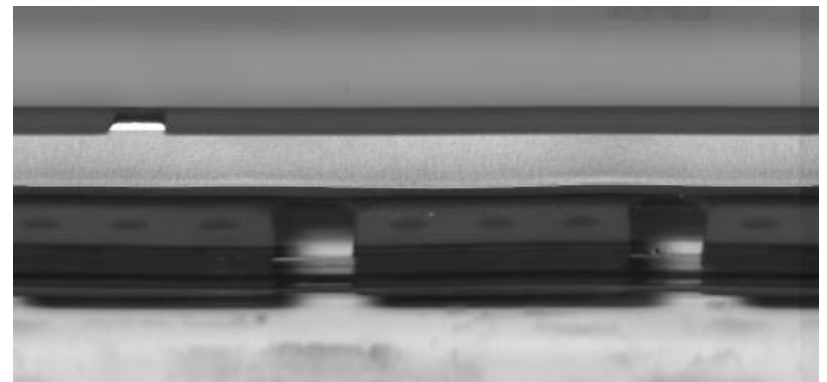
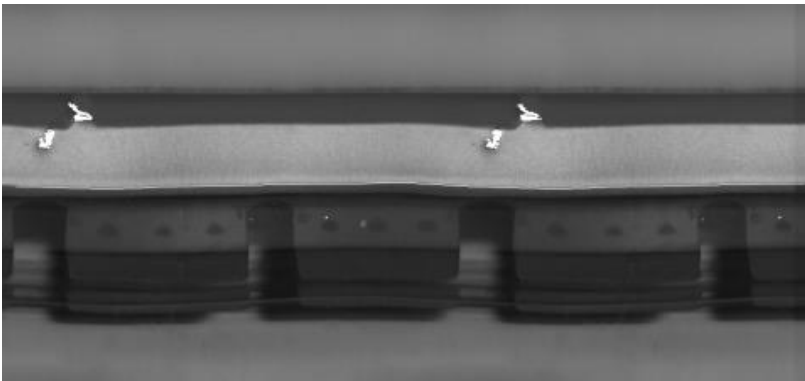
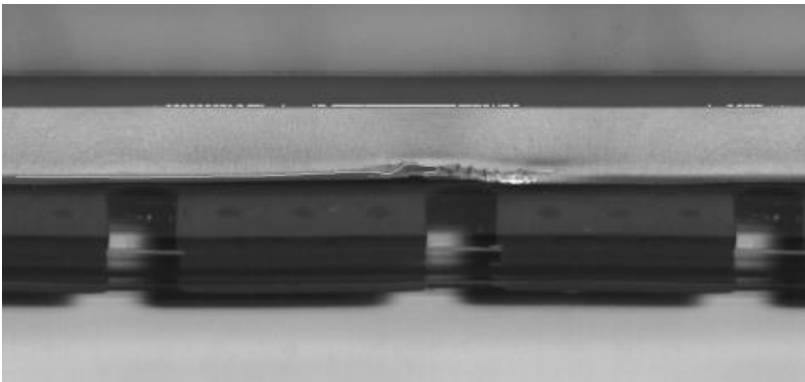
Possible Source:

- Improper crimping station setup
- Variability on closure components

Resolution:

- Detect crimping defect smaller than 50 μ m

Not enough for Integrity Assurance
Risk of microbial Contamination if >1 μ m



Container Closure Integrity: Dye Ingress Leak Detection

Dye Method	USP31<381> Ph.Eur. 3.2.9	ISO 8362-5 Annex C
Dye	0.1% aq. Methylene Blue	
Vacuum	-27KPa	-25KPa
Time at Vacuum	10 min	30 min
Time at ambient	30 min	30min
Detection	Visual inspection	

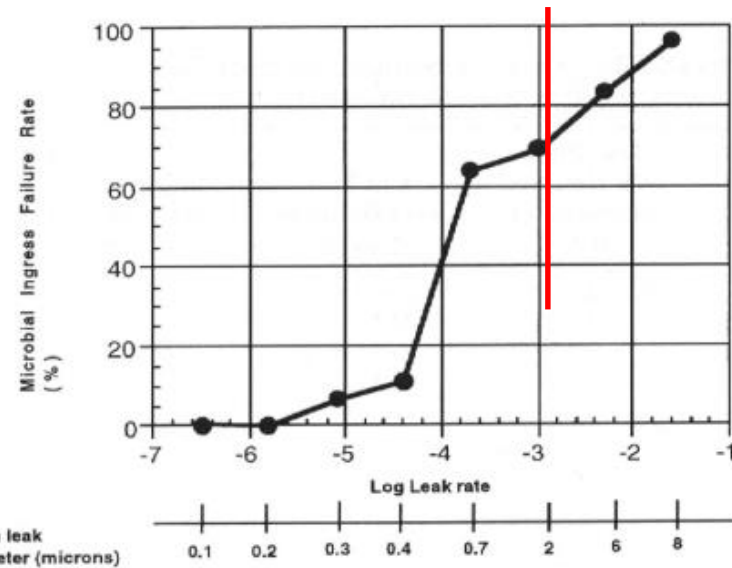


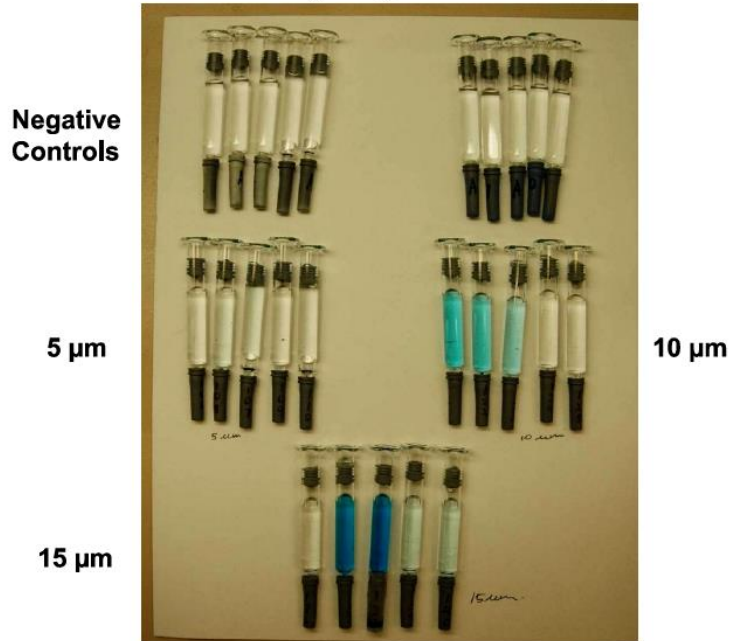
Figure 2—The correlation of microbial failure rate (%) and the mean logarithm of the absolute leak rate and nominal leak diameter for modified SVPs. The absolute leak rate (standard cubic centimeters per second) was determined by mass spectrometry-based helium leak rate detection. Microbial failure was measured by microbial ingress after 24 hour immersion in a bath (37°C) containing 10^8 to 10^{10} *P. diminuta* and *E. coli* organisms/mL and a 13 day, 35°C incubation.

Kirsch, et al, *PDA J Pharm Sci & Technol* 51, 5, 1997 p. 200

Risk of microbial Contamination if >1um

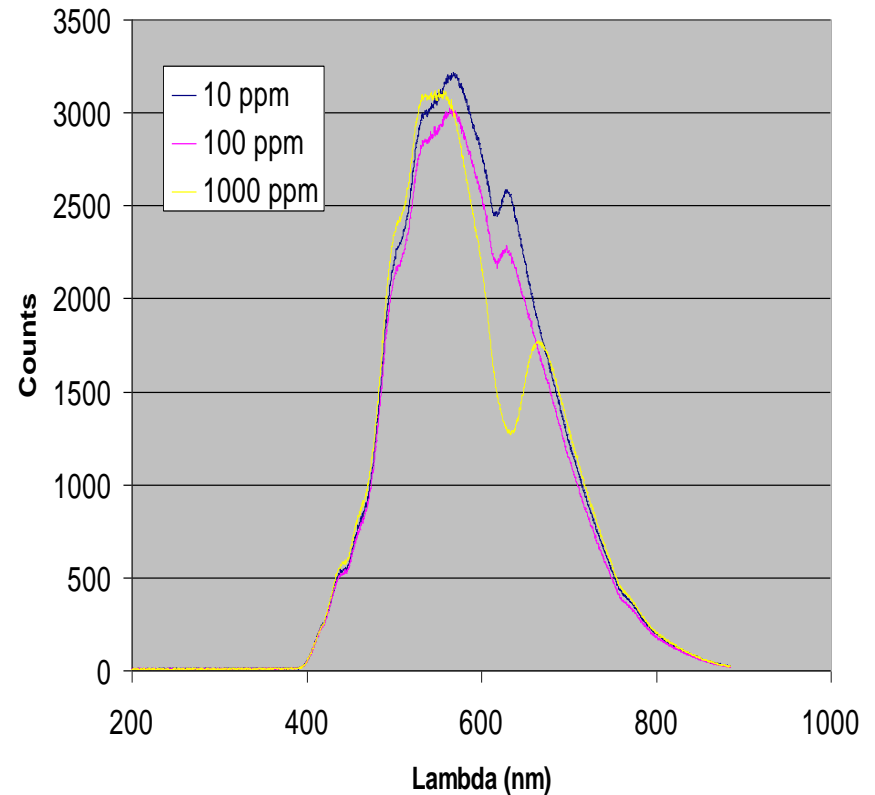
Container Closure Integrity: Dye Ingress Leak Detection

USP/PhEur Dye Ingress Test Samples



RxPax, LLC, PDA Metro Chapter, May 2011
H. Wolf, et al, PDA J Pharm Sci & Technol., 63, 2009, p. 489 - 498

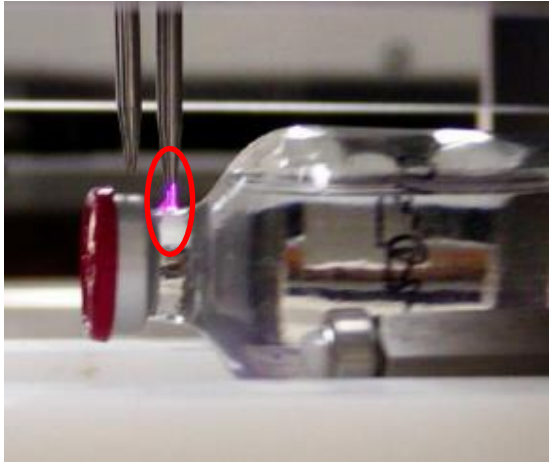
Dye Test not Sensitive enough
for Human Operator



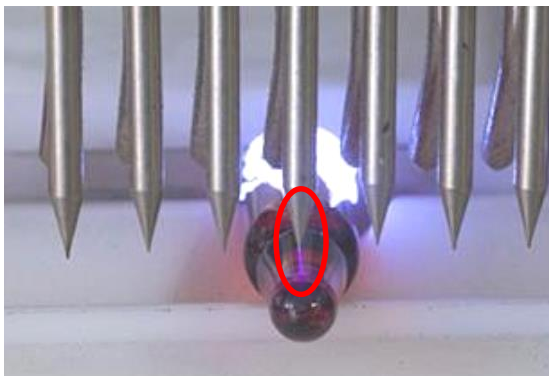
Dye Test Sensitive if in
Conjunction with Automatic
Spectrometer

Container Closure Integrity: High Voltage Leak Detection

- Superior to Dye Test
- Non destructive system
- Fast > 600 pcs/min
- HV accurate system very high efficiency
- No influence on protein products



Vial hole size (μ)	Packages tested (#)	# Packages ID'd as LEAKING DAY 1		# Packages ID'd as LEAKING DAY 29	
		Vacuum decay	HVLD	Vacuum decay	HVLD
PRODUCT-FILLED					
15	10	8	10	2	10
25	10	9	10	2	10
50	10	10	10	3	10
PLACEBO-FILLED					
15	10	10	10	10	10
25	10	10	10	10	10
50	10	10	10	10	10



HV Test Sensitive Enough for Integrity Assurance



A **Stevanato** Group Brand

Thank You for Your Attention!

Para maiores detalhes entre em contato:
gaetano.baccinelli@stevanatogroup.com

www.optrelinspection.com