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HORIBA Scientific

Particle Characterization

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Key Points to Achieving Successful Laser Diffraction Method Development

September 26, 2018

Method Development

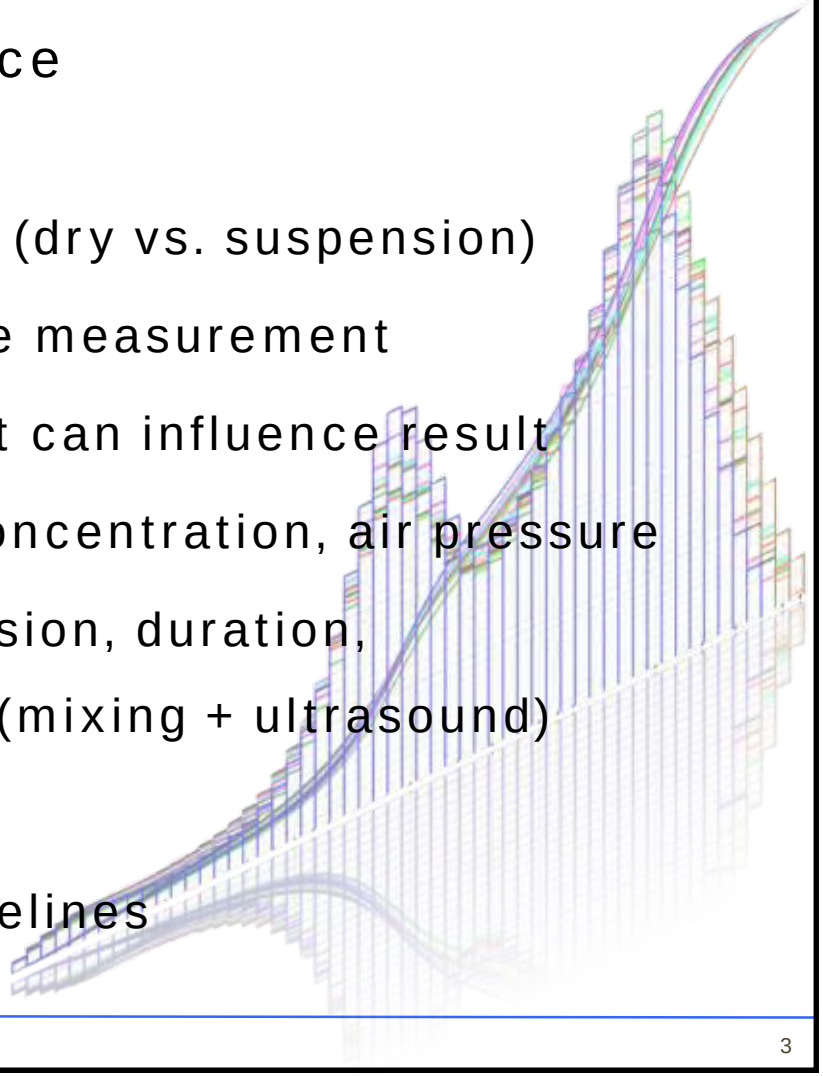
Goal: Reproducible method that tracks product performance

- Choose measurement approach (dry vs. suspension)
- Establish the parameters for the measurement
- Vary measurement settings that can influence result

  - Dry: measurement duration, concentration, air pressure

  - Wet: sampler selection, dispersion, duration, concentration, sample preparation (mixing + ultrasound)
- Test method reproducibility

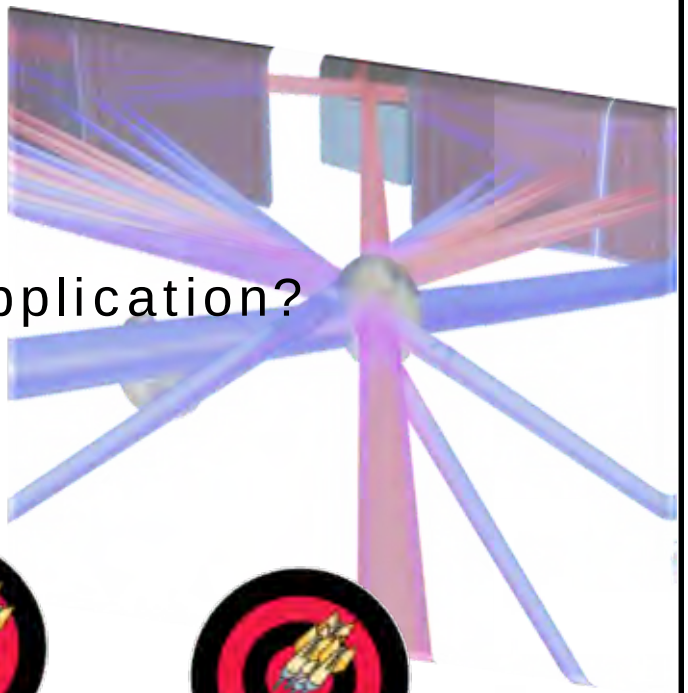
  - Meet ISO, USP or internal guidelines

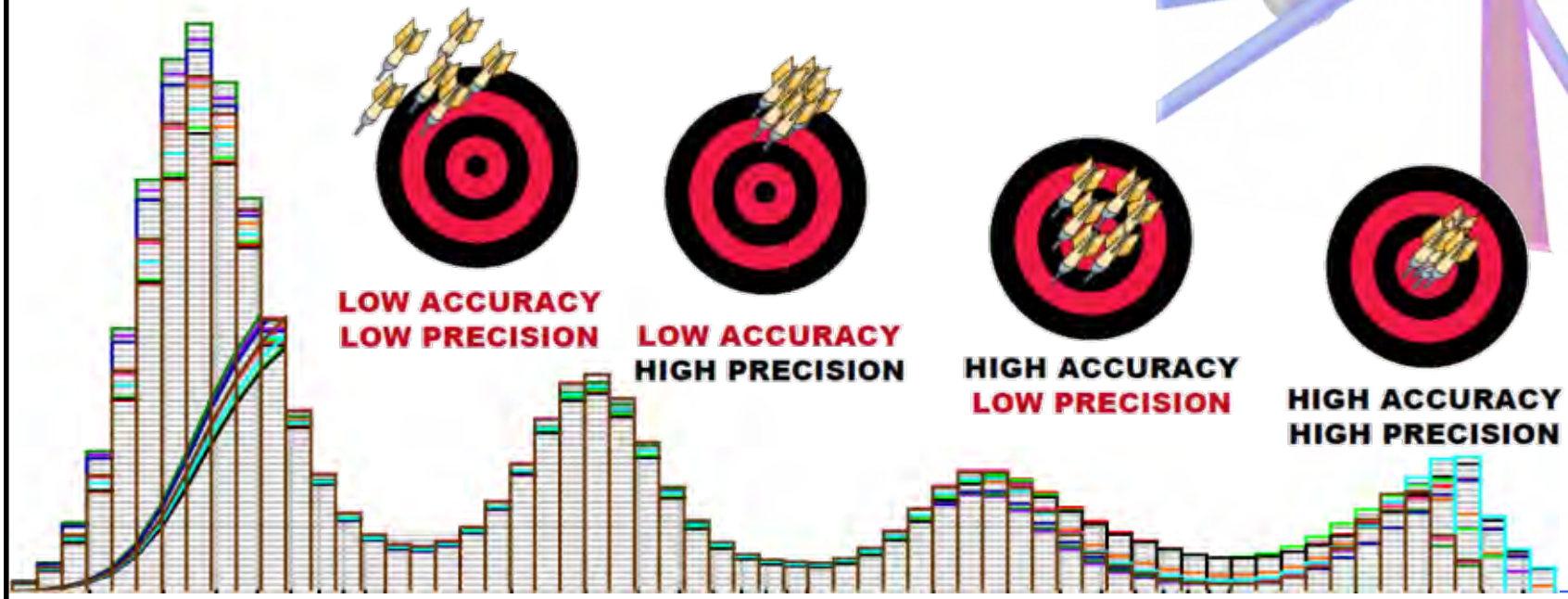


Method Development

Accuracy and Precision

- Is it the “real particle size”?
- Comparison to referee technique
- Which is more important to my application?

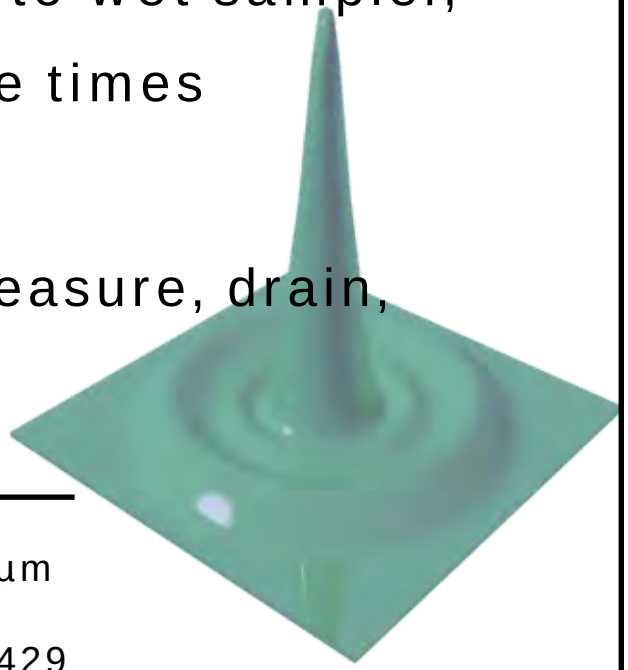




Method Development

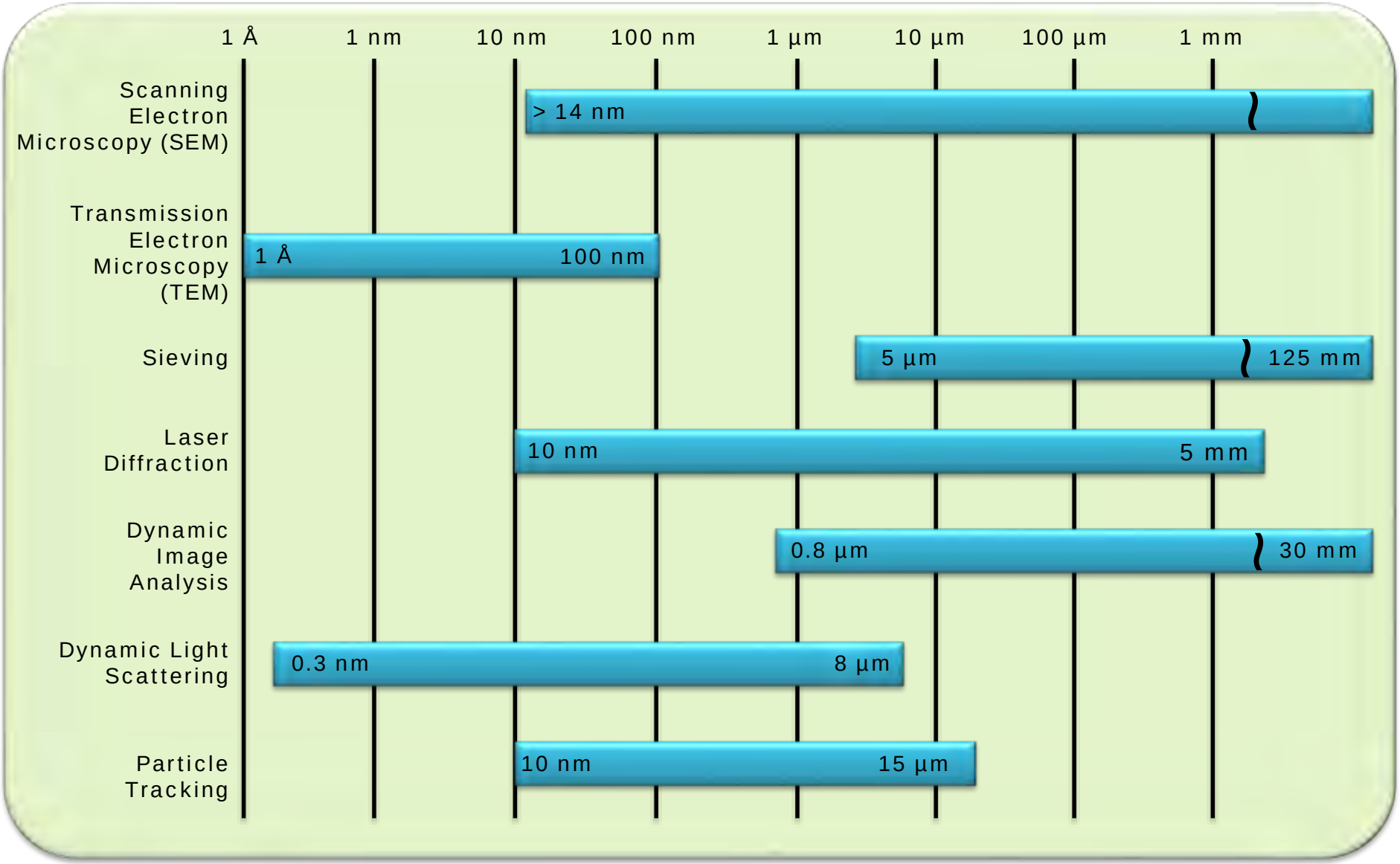
Repeatability and Reproducibility

- Repeatability: prepare sample, add to wet sampler, re-circulate, measure same multiple times (suspensions only)
- Reproducibility: prepare sample, measure, drain, repeat (suspensions + dry)

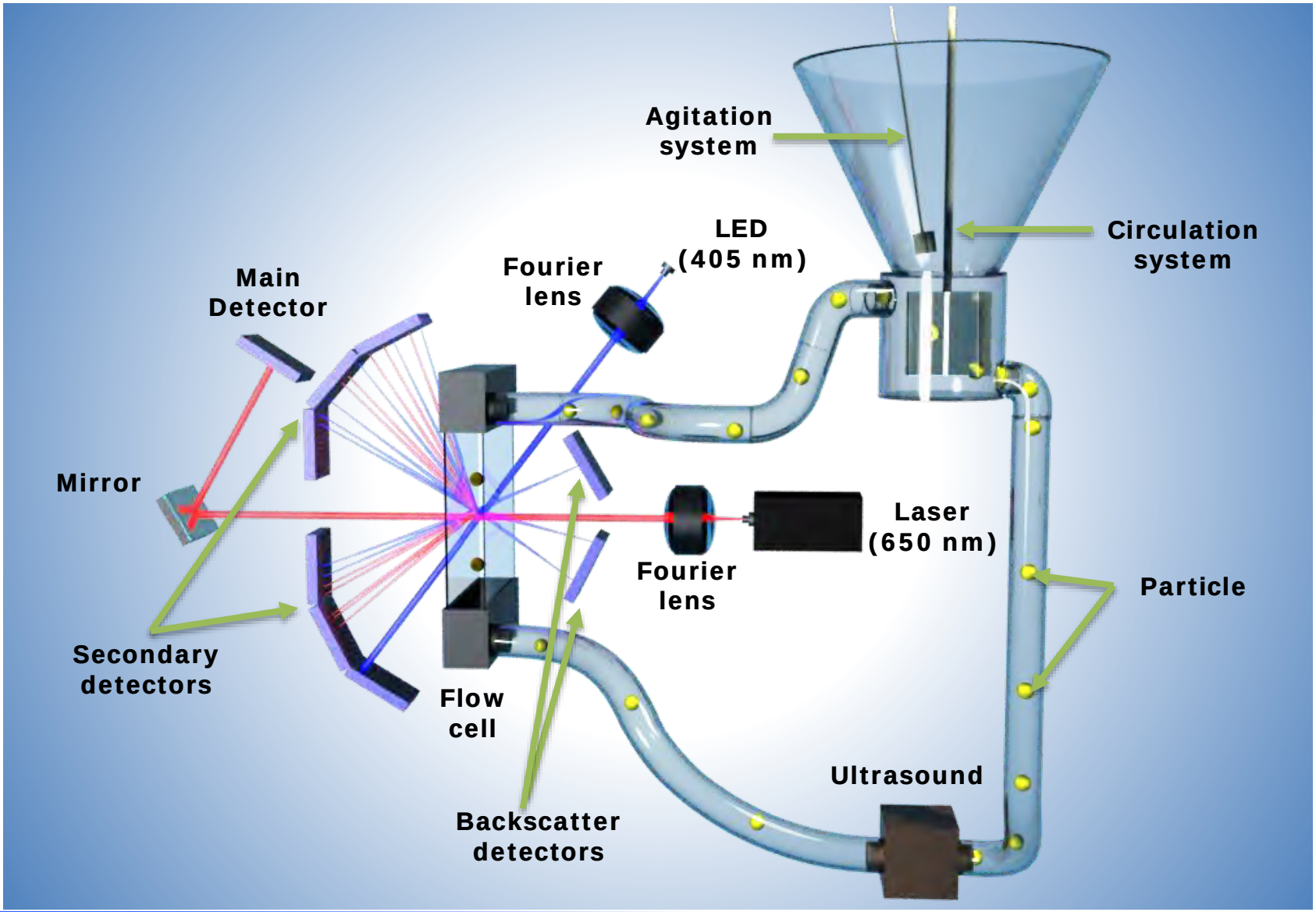


Coefficient of variance (CoV)	When D50 >10 µm		When D50 <10 µm	
	ISO 13320	USP 429	ISO 13320	USP 429
At median (D50)	3%	10%	6%	20%
At D10 and D90	5%	15%	10%	30%

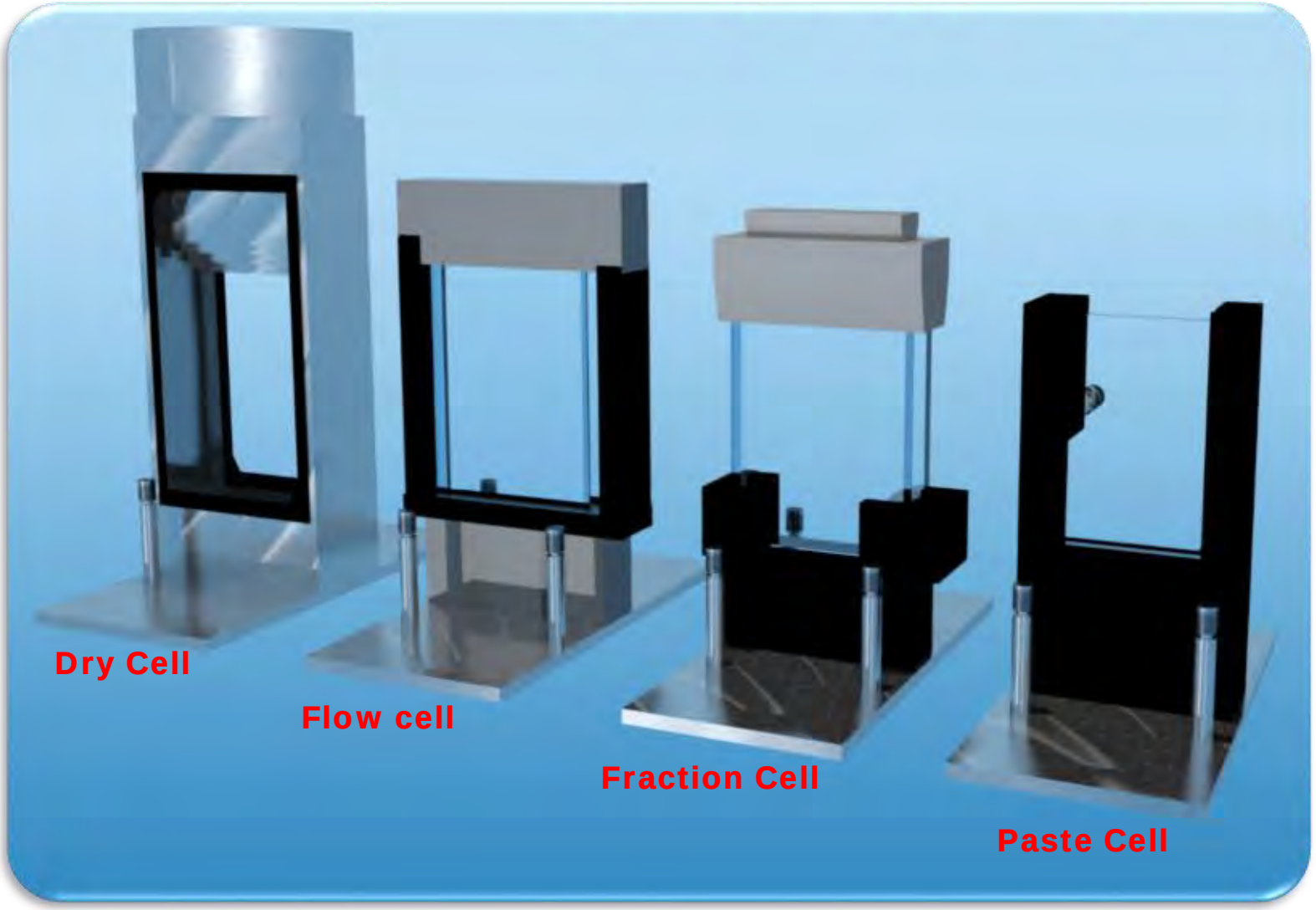
Measurement Range of the Main Techniques for Particle Characterization



Double Beam Laser Diffraction Instrument Schematic

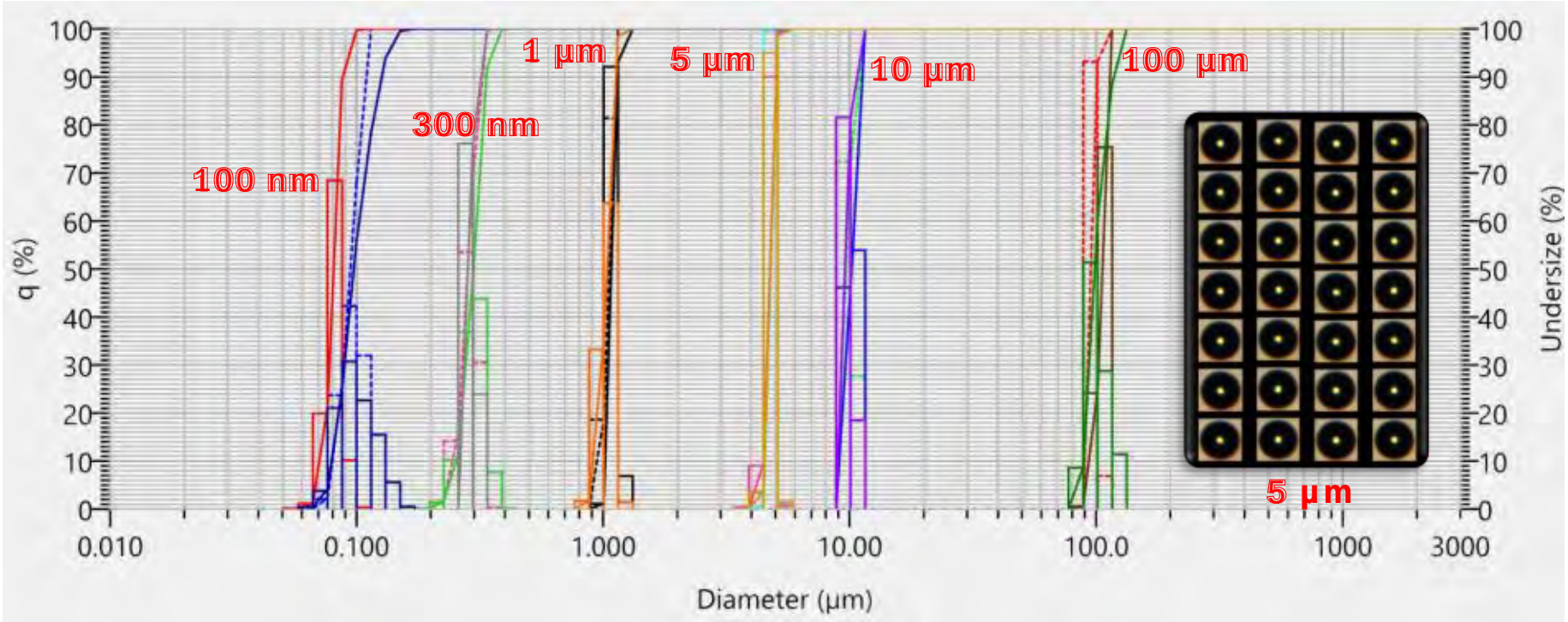


Different Measurement Options



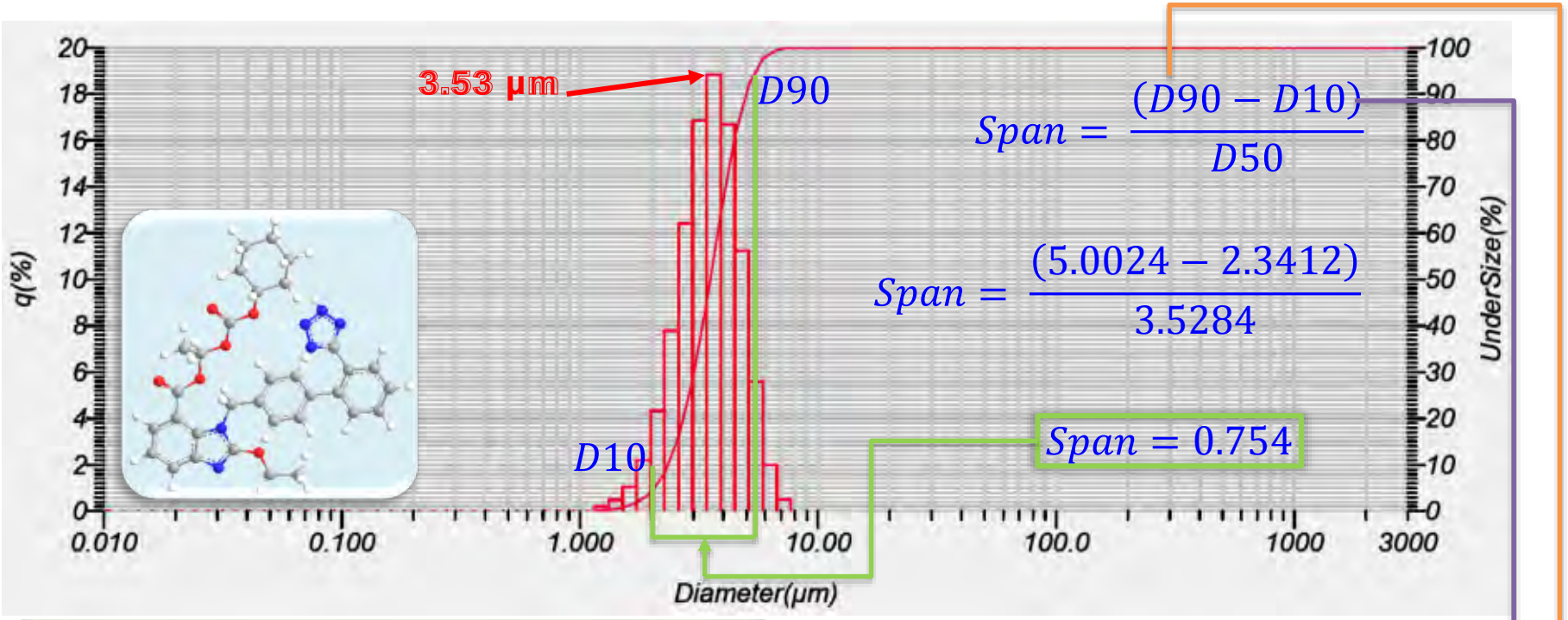
Instrument Validation/Verification

Polystyrene Standards for
Particle Size Calibration
(Flow, Fraction and Paste Cell)



Data Interpretation

Drug for high blood pressure



Product Specifications

D10 = 1.0 – 2.5 µm	*D10 = >2.5 µm*
D50 = 3.0 – 4.0 µm	*D50 = 3.0 – 4.0 µm*
D90 = 4.5 – 6.0 µm	*D90 = <5.5 µm*

Diameter on Cumulative %

(1)10.00 (%)- 2.3412(µm)
(2)20.00 (%)- 2.7154(µm)
(3)30.00 (%)- 3.0154(µm)
(4)40.00 (%)- 3.2685(µm)
(5)50.00 (%)- 3.5284(µm)
(6)60.00 (%)- 3.7922(µm)
(7)70.00 (%)- 4.0984(µm)
(8)80.00 (%)- 4.4461(µm)
(9)90.00 (%)- 5.0024(µm)

Method Development – Dry Dispersion

- First get sampling right & determine Refractive Index

Chute Riffling

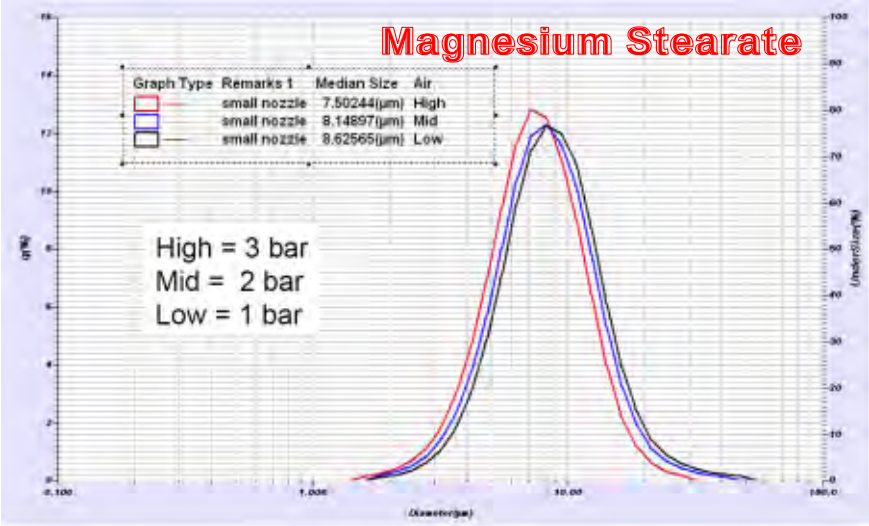
Rotary Riffling

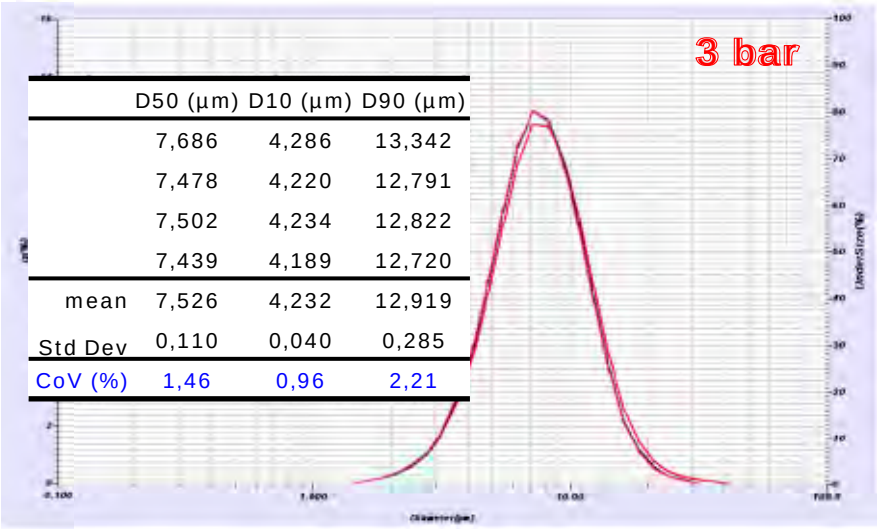
- Measure at 3 different pressures (low, medium, high)
- Determine optimum pressure based on good dispersion while not breaking particles
- You can also compare dry vs. wet measurements
- Adjust other settings to optimize sample concentration & duration
- Ideally measure all of powder placed into the sampler

(Segregation can occur on vibrating tray, constant mass flow rate important for stable concentration during measurement)

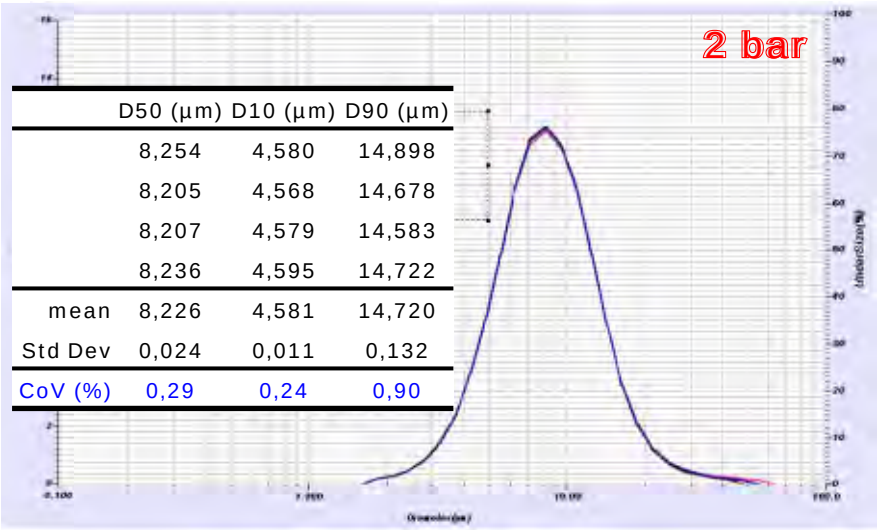
- Once settings chosen, test reproducibility

Pressure Effect on Sample Dispersion

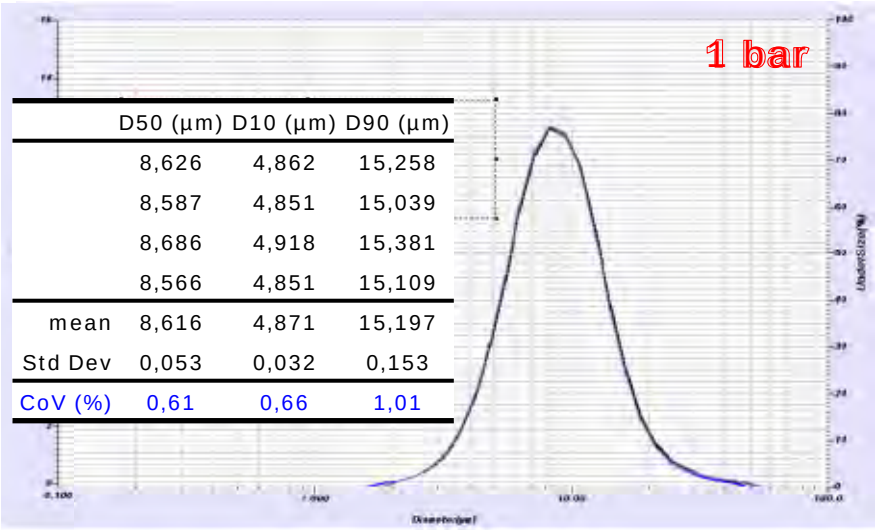




	D50 (µm)	D10 (µm)	D90 (µm)
	7,686	4,286	13,342
	7,478	4,220	12,791
	7,502	4,234	12,822
	7,439	4,189	12,720
mean	7,526	4,232	12,919
Std Dev	0,110	0,040	0,285
CoV (%)	1,46	0,96	2,21

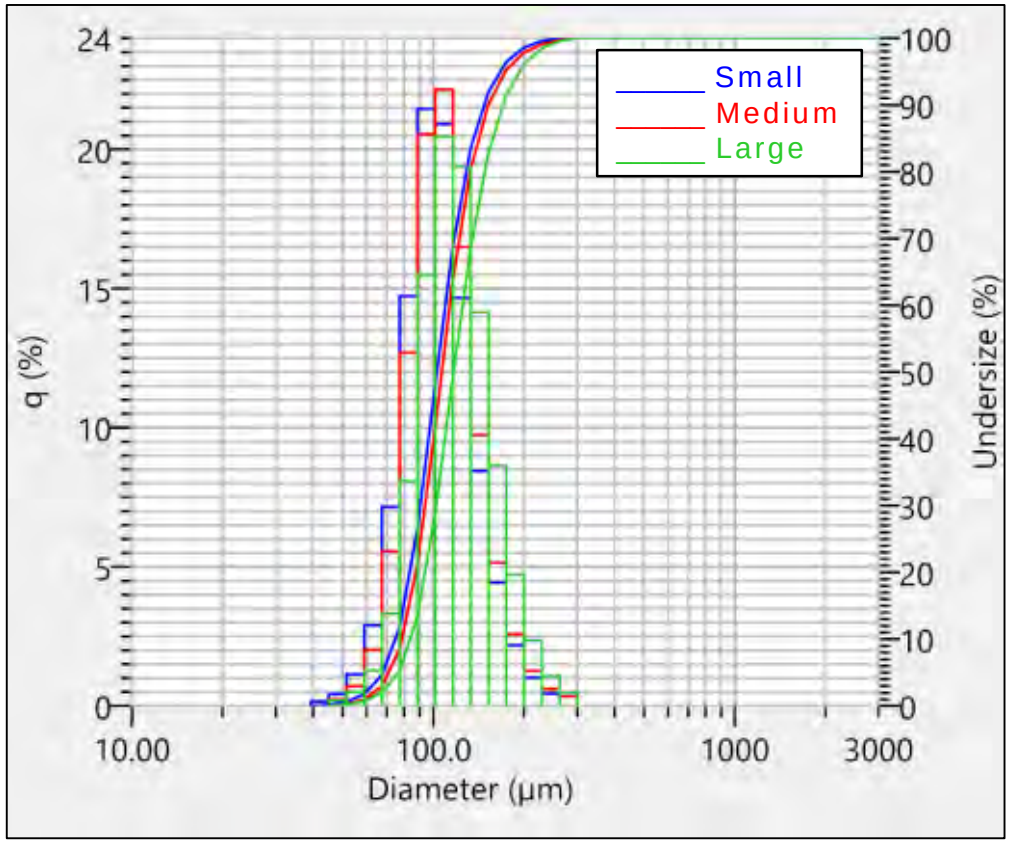


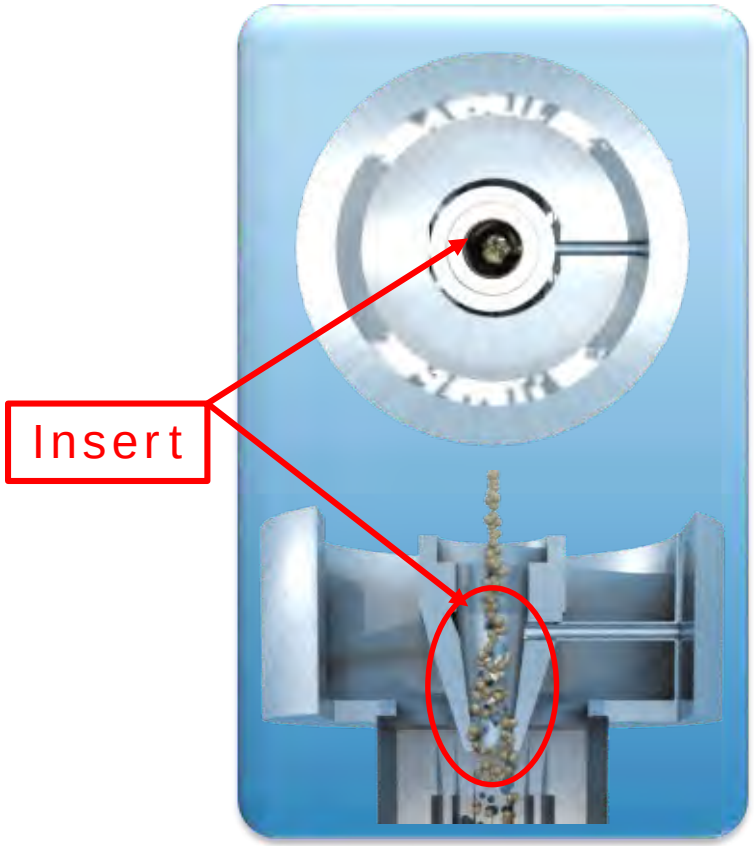
	D50 (µm)	D10 (µm)	D90 (µm)
	8,254	4,580	14,898
	8,205	4,568	14,678
	8,207	4,579	14,583
	8,236	4,595	14,722
mean	8,226	4,581	14,720
Std Dev	0,024	0,011	0,132
CoV (%)	0,29	0,24	0,90



	D50 (µm)	D10 (µm)	D90 (µm)
	8,626	4,862	15,258
	8,587	4,851	15,039
	8,686	4,918	15,381
	8,566	4,851	15,109
mean	8,616	4,871	15,197
Std Dev	0,053	0,032	0,153
CoV (%)	0,61	0,66	1,01

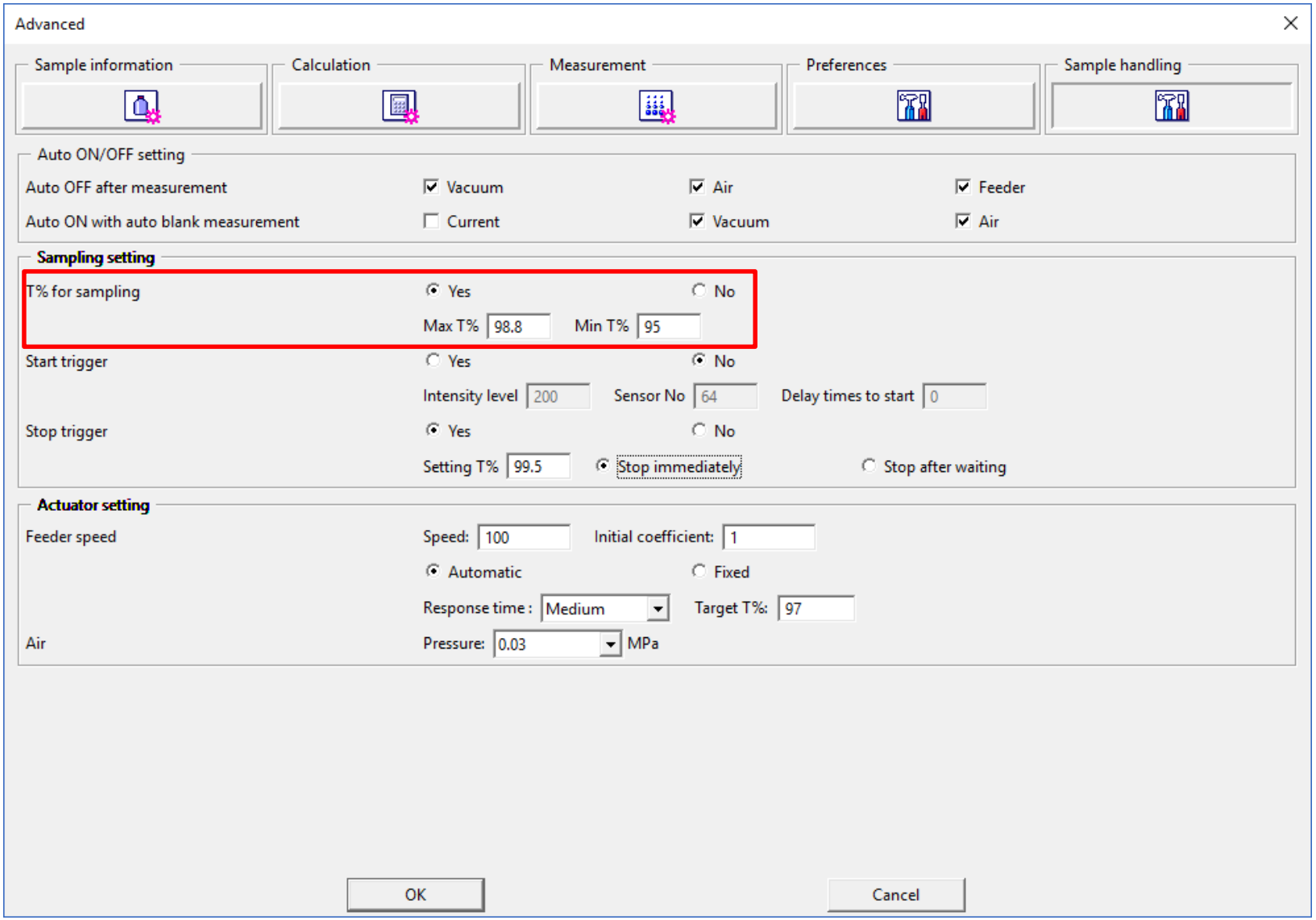
Insert Effect on Sample Dispersion





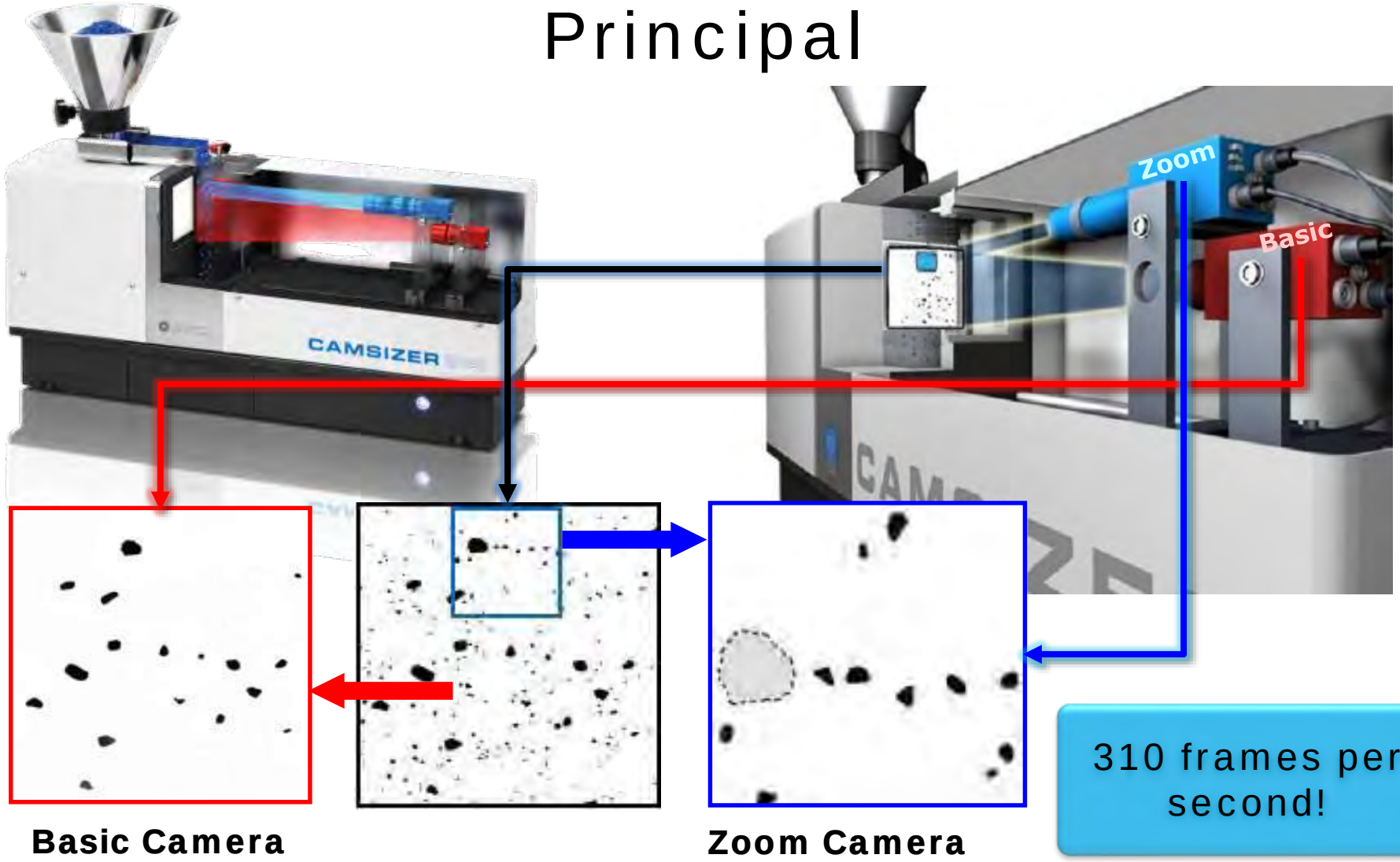
Top Insert	D10 (µm)	D90 (µm)	D50 (µm)		
Small	74.8	147.8	102.8	2.6%	9.0%
Medium	78.6	152.3	106.7	6.4%	
Large	83.7	170.8	116.8		

Sample Concentration



Dynamic Image Analysis

Principal



Basic Camera

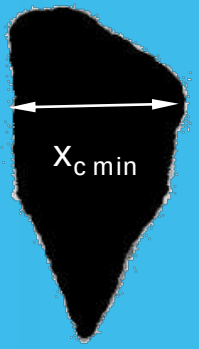
Zoom Camera

310 frames per second!

Dynamic Image Analysis

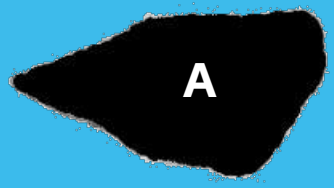
$X_{c\,min}$

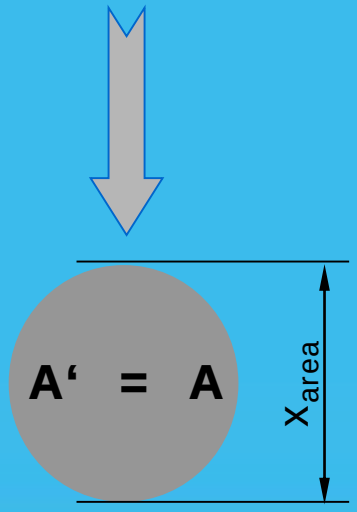
"Width"



X_{area}

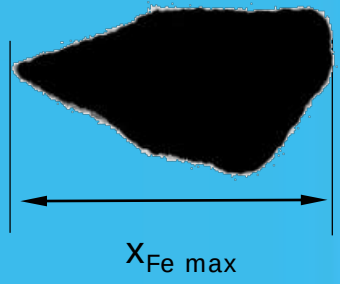
"Diameter over projection surface"





$X_{Fe\,max}$

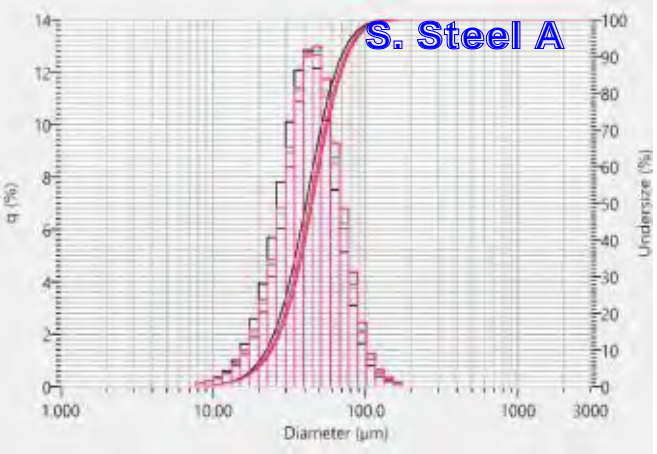
"Length"



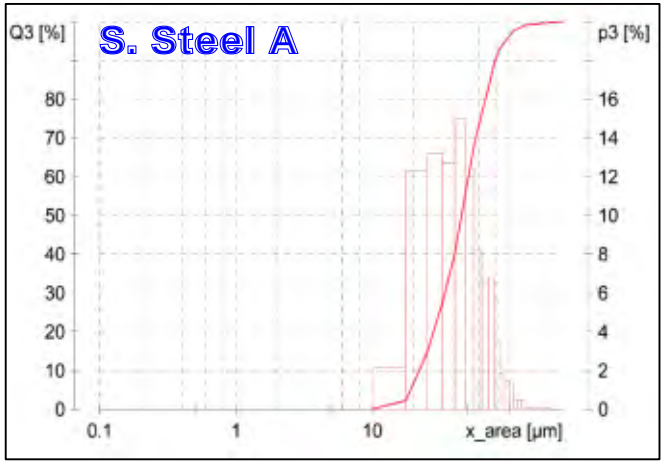
Result compatible with Laser diffraction*

Stainless Steel Powder for 3D Printers

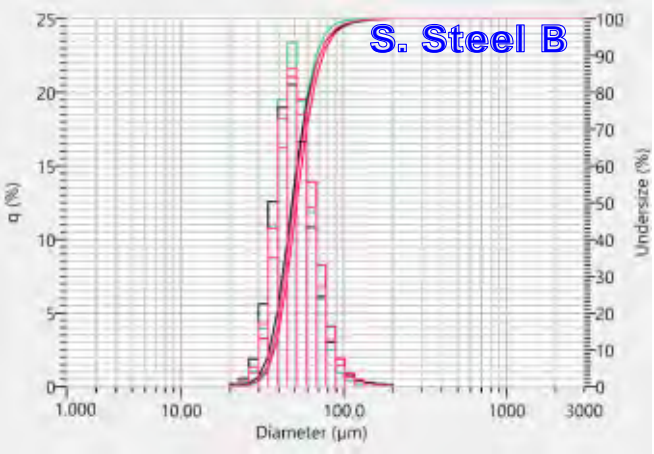
Laser Diffraction (LD)

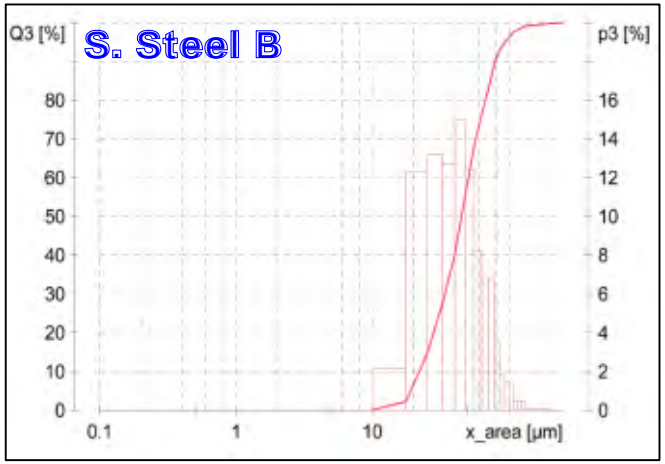


Dynamic Image Analysis (DIA)



	D50	D10	D90
LD	43.1	23.4	73.6
DIA	45.0	22.8	78.9
Std Dev	1.3	0.4	3.7
CoV	3.0%	1.8%	4.9%



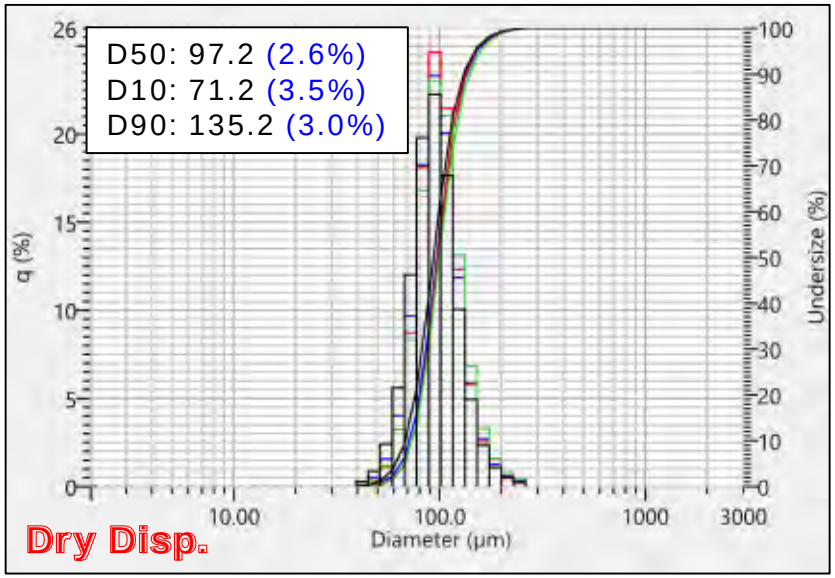


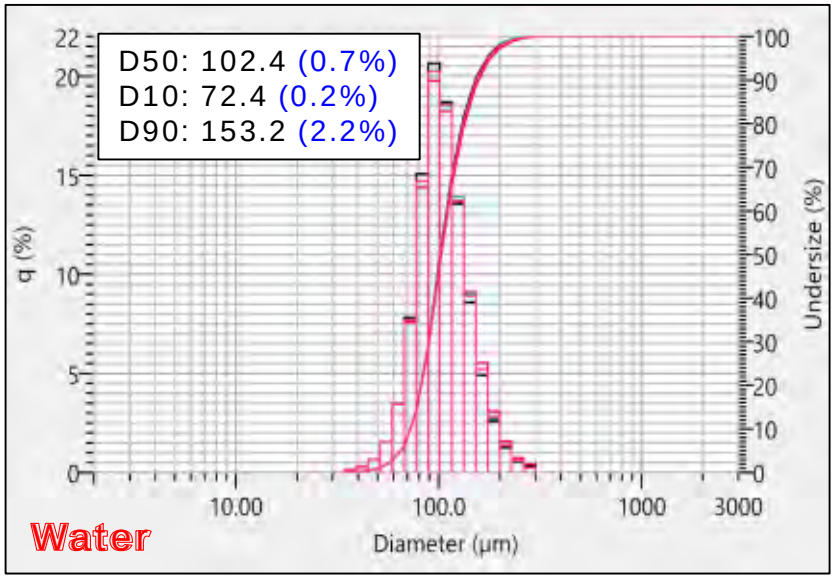
	D50	D10	D90
LD	49.4	36.0	71.4
DIA	50.2	33.7	76.2
Std Dev	0.6	1.6	3.4
CoV	1.1%	4.7%	4.6%

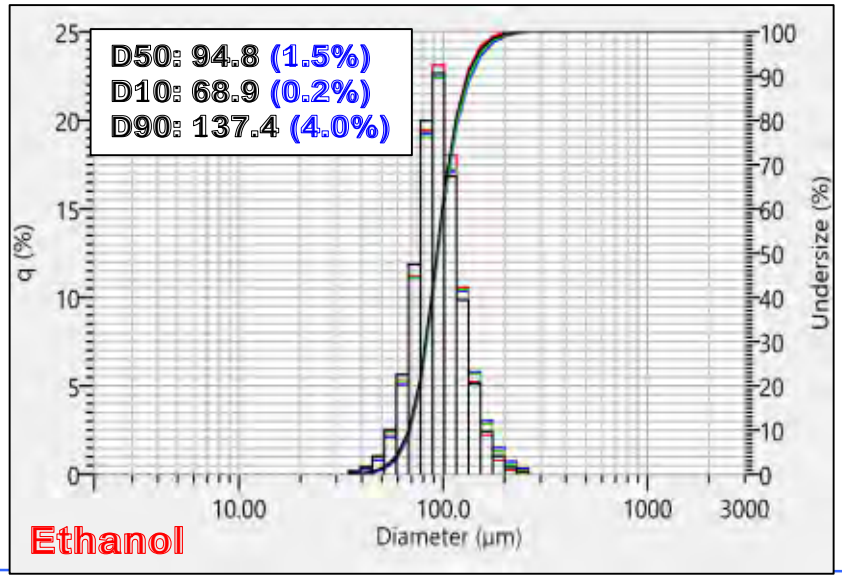
Method Development – Wet Dispersion

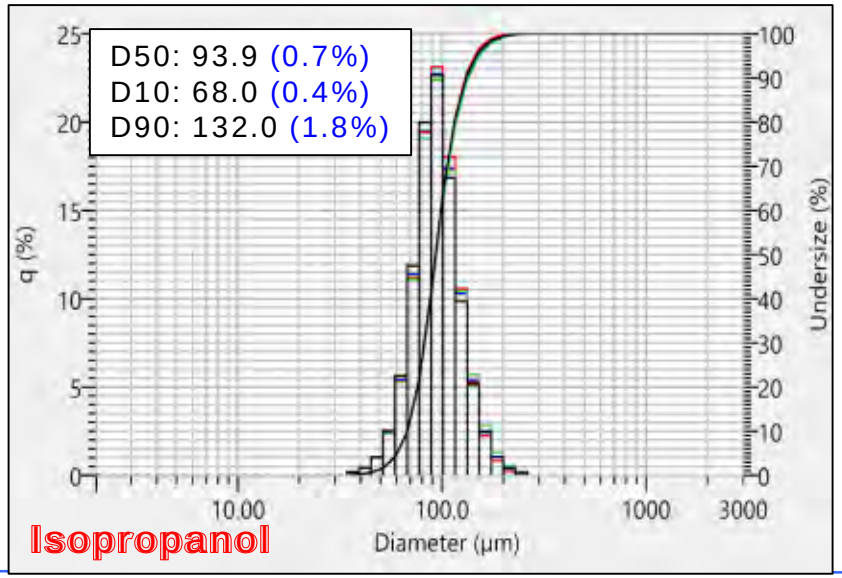
- First determine RI
- Choose solvent (water, surfactants, hexane, etc.)
- Sampler selection: sample volume
- Pump & stirrer settings
- Concentration
- Measurement duration
- Does the sample need ultrasound?
- Document size-time plot
- Disperse sample, but don't break particles
- Check for reproducibility

Alumina in Different Dispersants

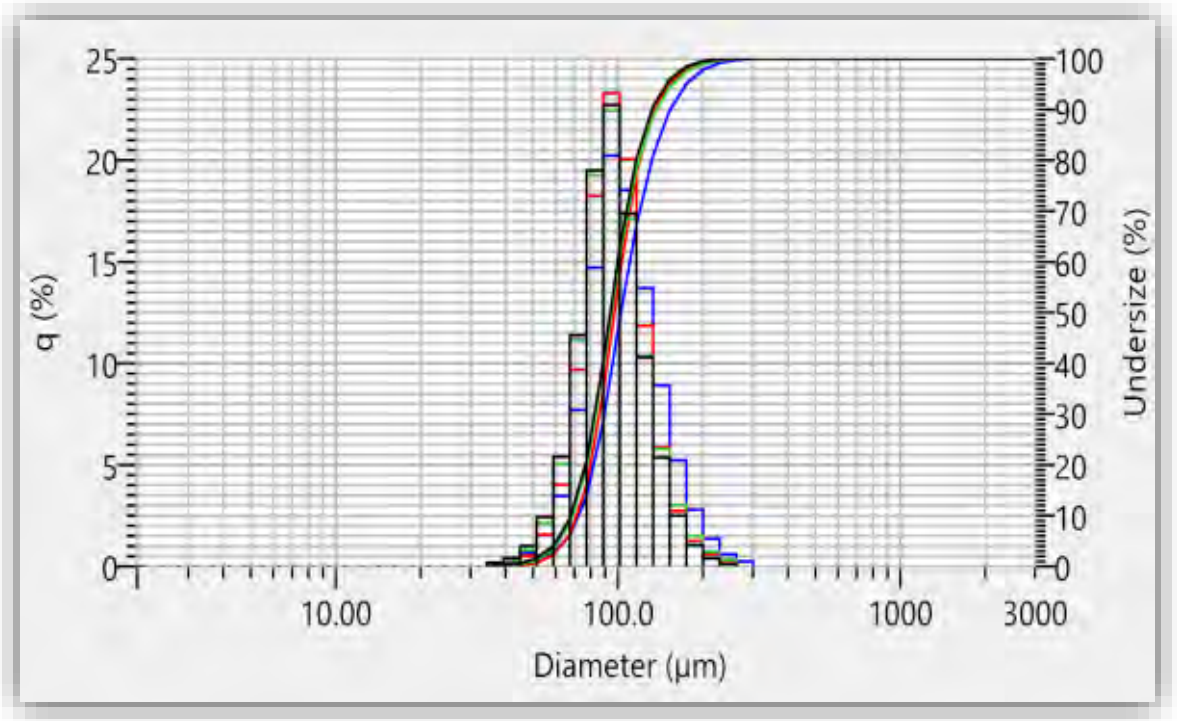








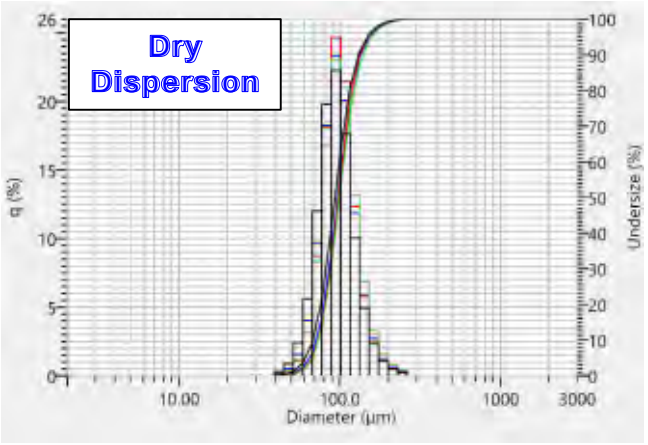
Alumina in Different Dispersants



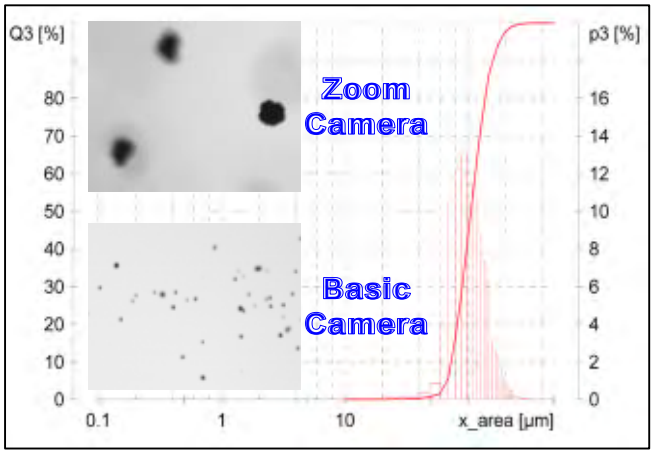
Dispersion	D50	D10	D90	Span
Dry	97.2	71.2	135.2	0.659
Water	102.4	72.4	153.2	0.789
Ethanol	94.8	68.9	137.4	0.722
iso-propanol	93.8	68.0	132.0	0.662
Std Dev	3.84	2.03	9.43	0.06
CoV	3.96%	2.89%	6.76%	

Alumina – Via Orthogonal Techniques

Laser Diffraction (LD)

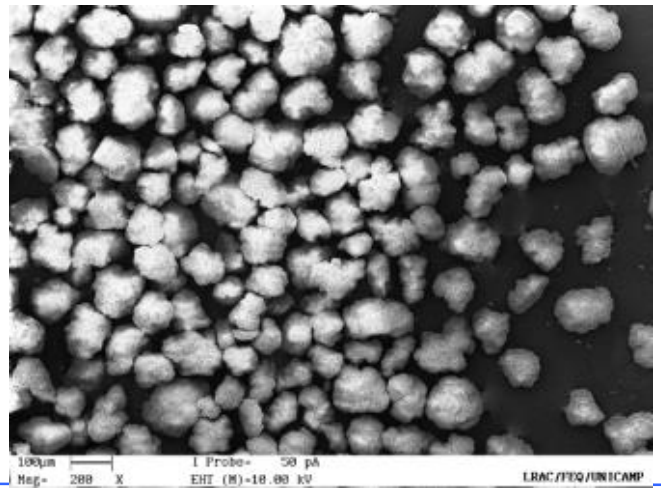


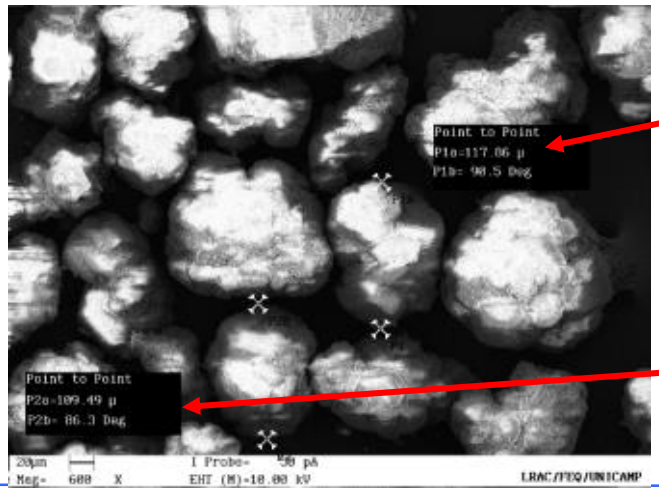
Dynamic Image Analysis (DIA)



	D50	D10	D90
LD (Dry)	97.2	71.2	135.2
LD (H_2O)	102.4	72.4	153.2
DIA	105.7	73.5	159.3
CoV	4.2%	1.6%	8.4%

Scanning Electron Microscopy (SEM)





Point to Point
P1a=117.86 µ
P1b= 90.5 Deg

Point to Point
P2a=109.49 µ
P2b= 86.3 Deg

Case of Study

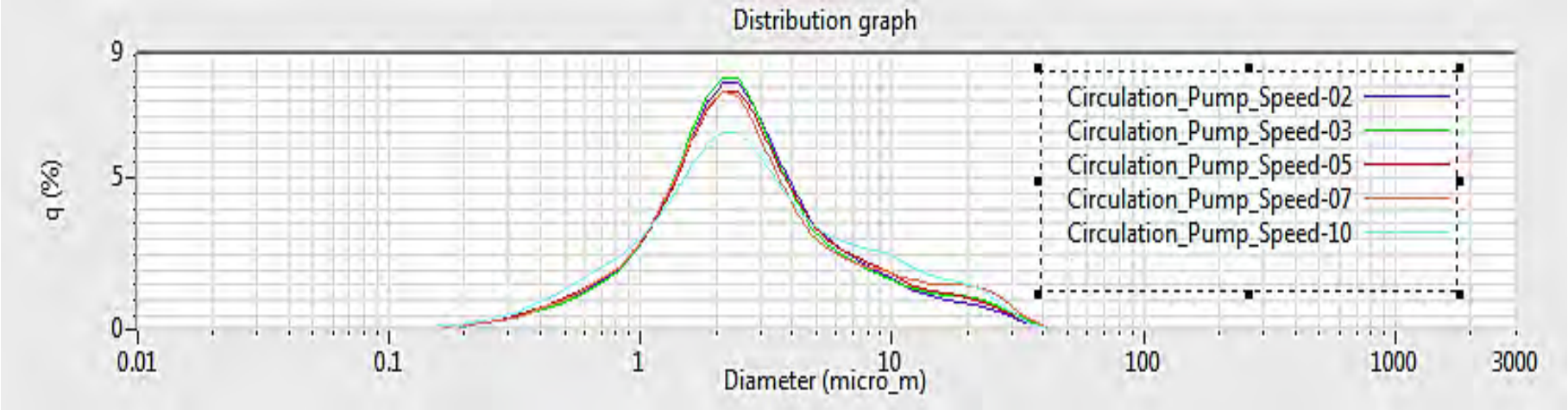
Unknown sample of fertilizer

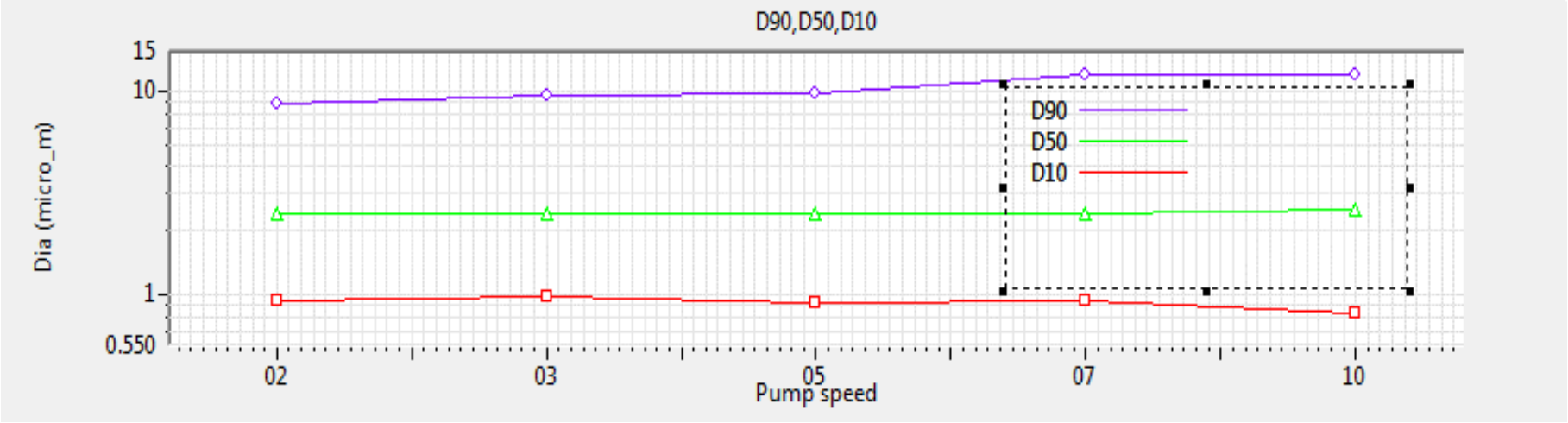
What is know?

Emulsion containing CuO

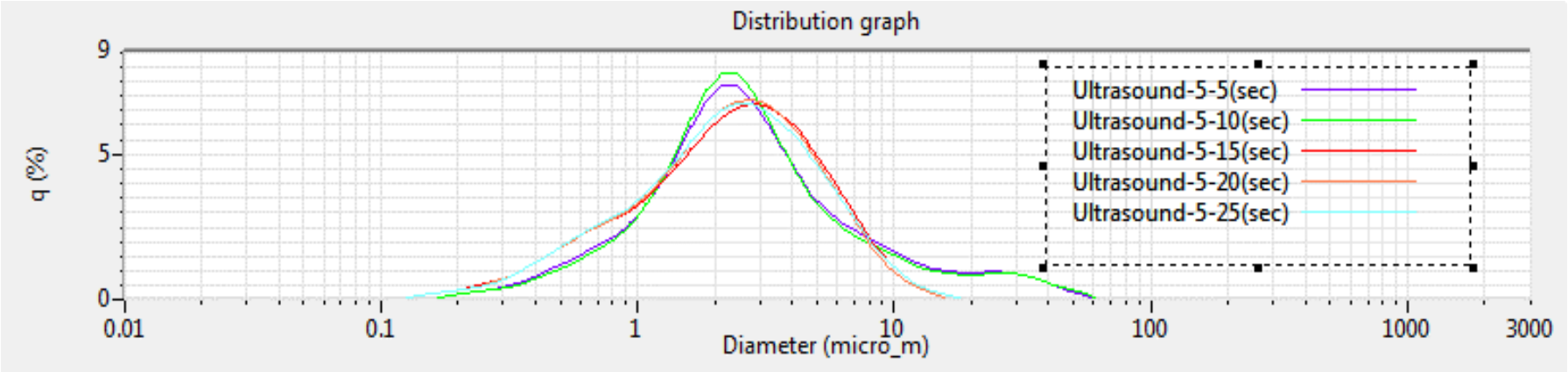
CuO Refractive Index: 2.63

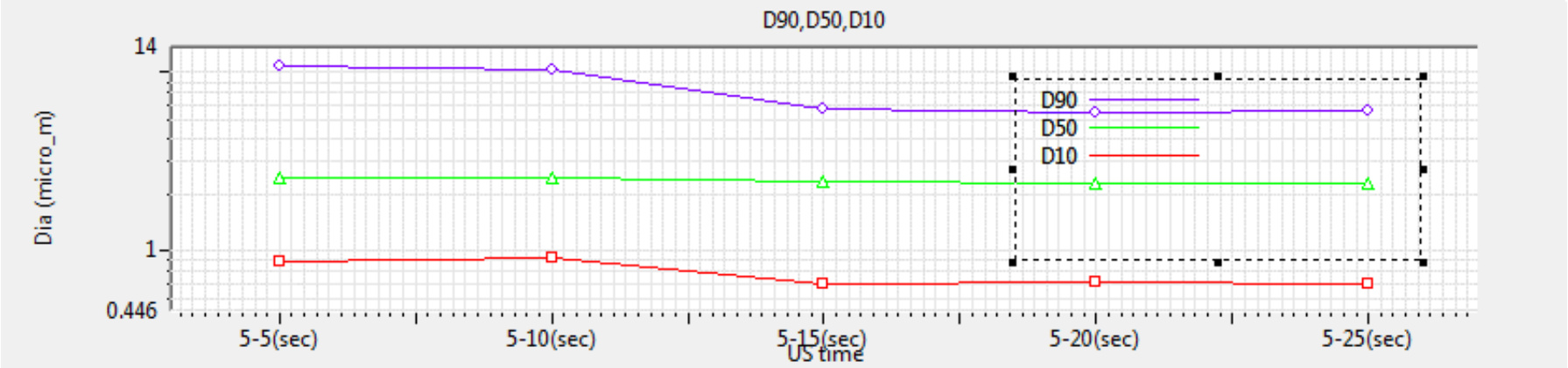
Circulation Speed





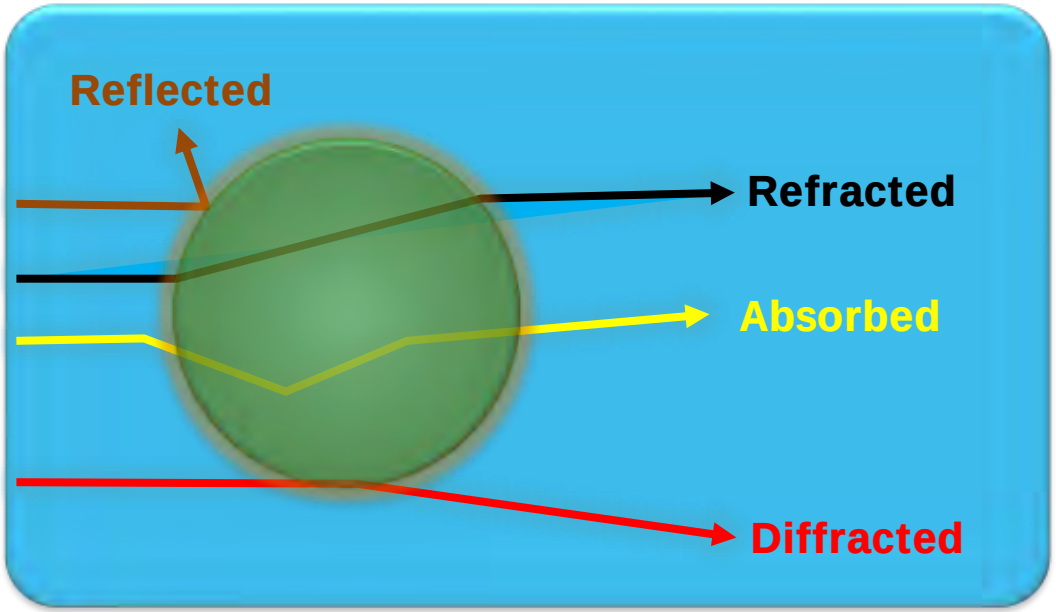
Ultrasound

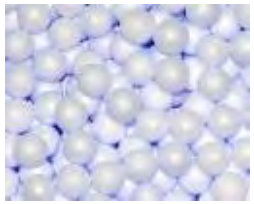




	Ultrasound-5-5(sec)	Ultrasound-5-10(sec)	Ultrasound-5-15(sec)	Ultrasound-5-20(sec)
D90	10.5021	10.0176	6.10109	5.8281
D50	2.48897	2.46775	2.38183	2.32004
D10	0.840432	0.891544	0.637004	0.642828

Optical Events





Polystyrene
1.60 – 0.000i

Copper
0.60 – 3.600i

$Cu(OH)_2$
1.72 – 0.100i

Emulsion
1.75 – 0.001i

The use of the Mie Theory requires the knowledge of sample optical properties
(Complex Refractive Index)

1.67-0.10i
Refractive Index (Real valor)
Imaginary Index (absorption)

- For transparent particles use 0 for the imaginary component
- For slightly opaque materials use 0.01 or 0.1
- For opaque materials use 1.0 or higher

Refractive Index Effect

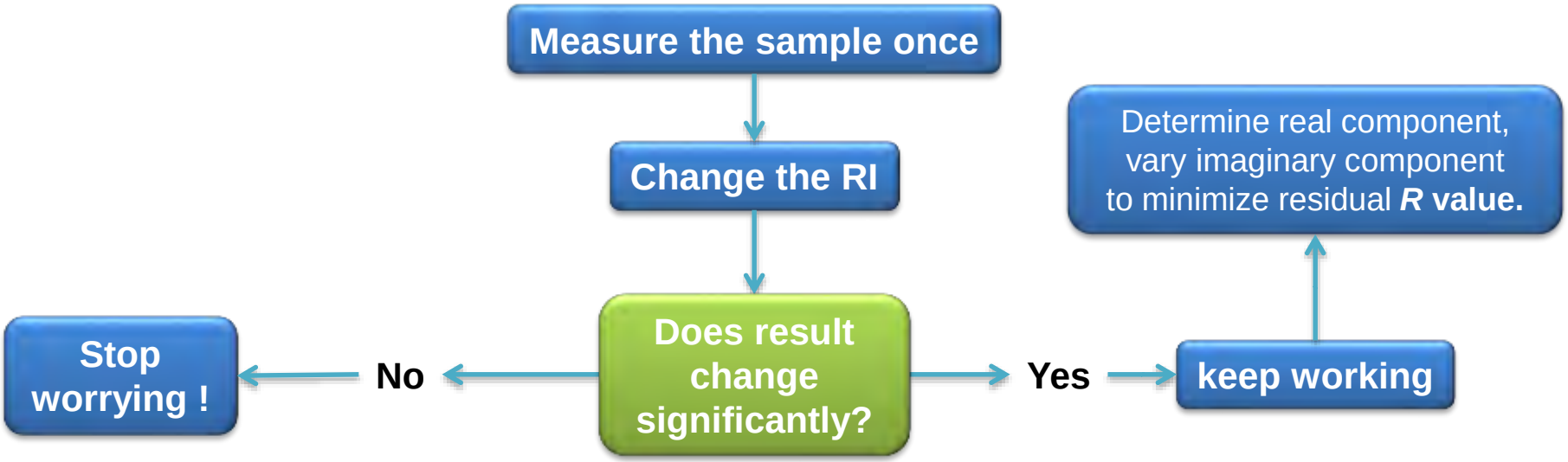
Most pronounced when:

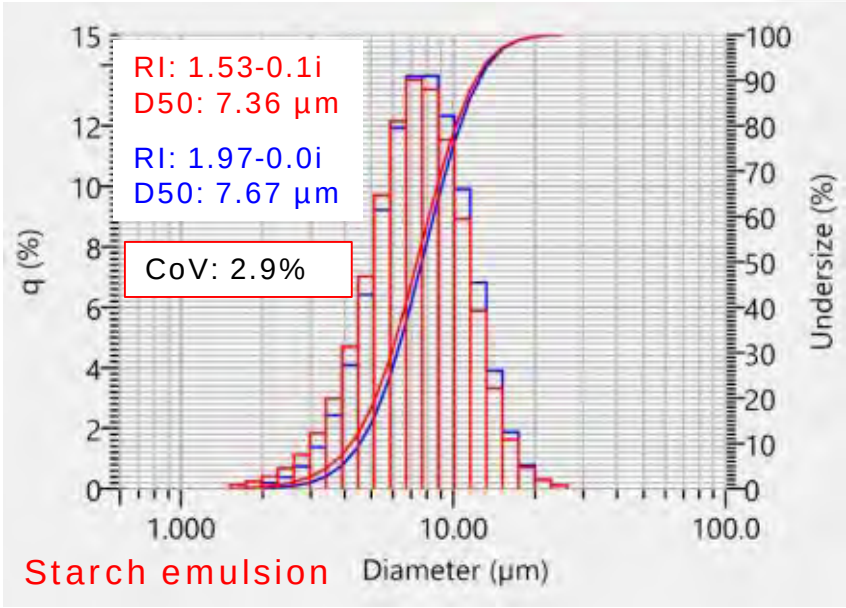
- Particles are spherical
- Particles are transparent
- RI of particle is close to RI of fluid
- When particles are smaller than ~35-40 µm

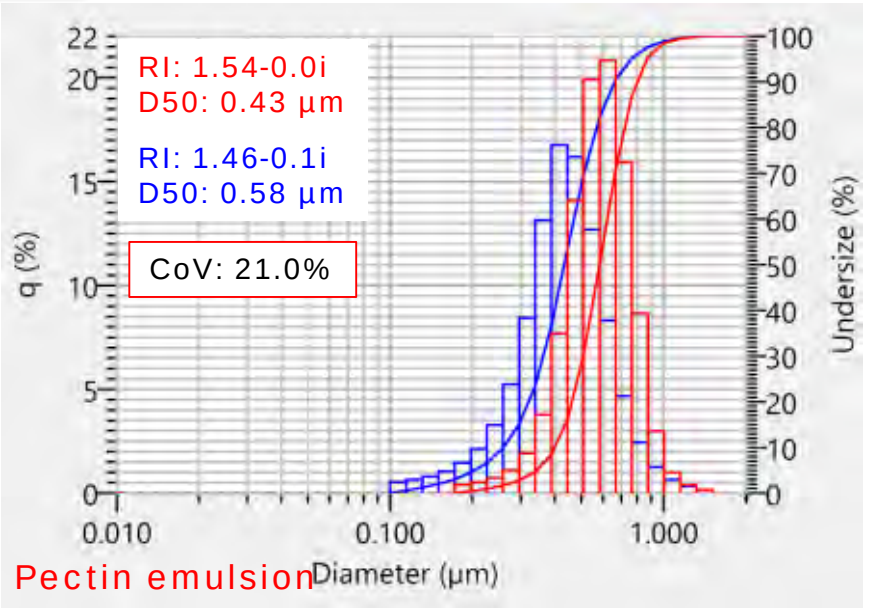
Least pronounced when:

- Particles are not spherical
- Particles are opaque
- RI of particle is larger than RI of the fluid
- When particles are larger than ~35-40 µm

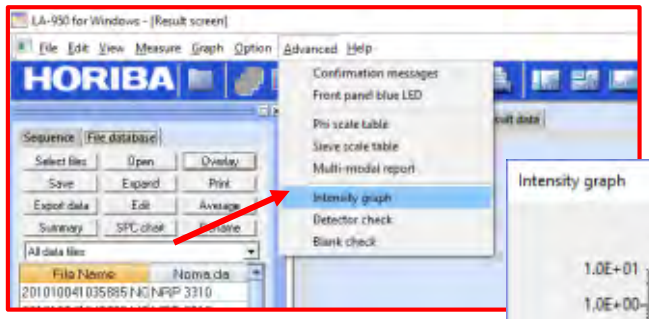
Practical Approach

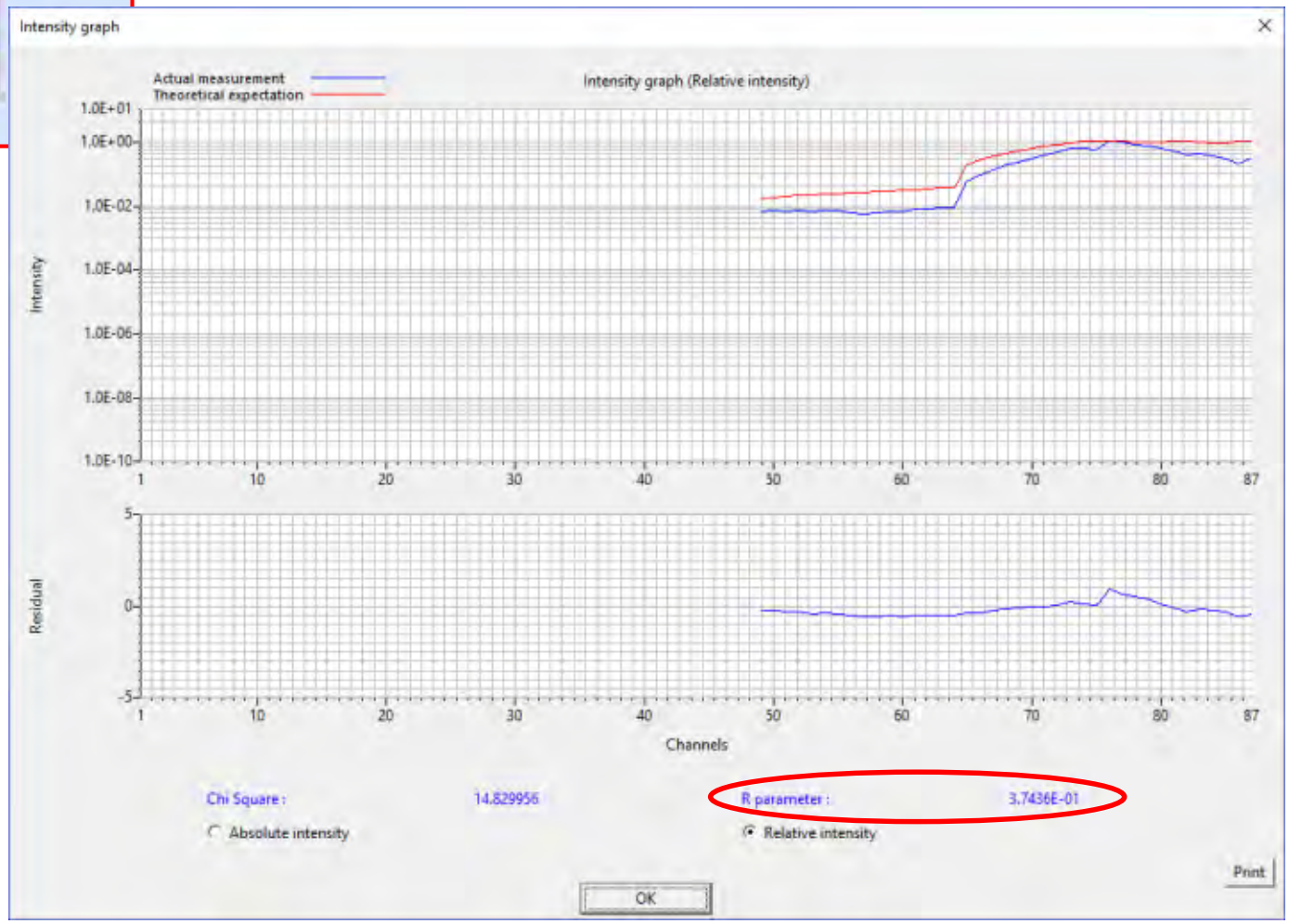




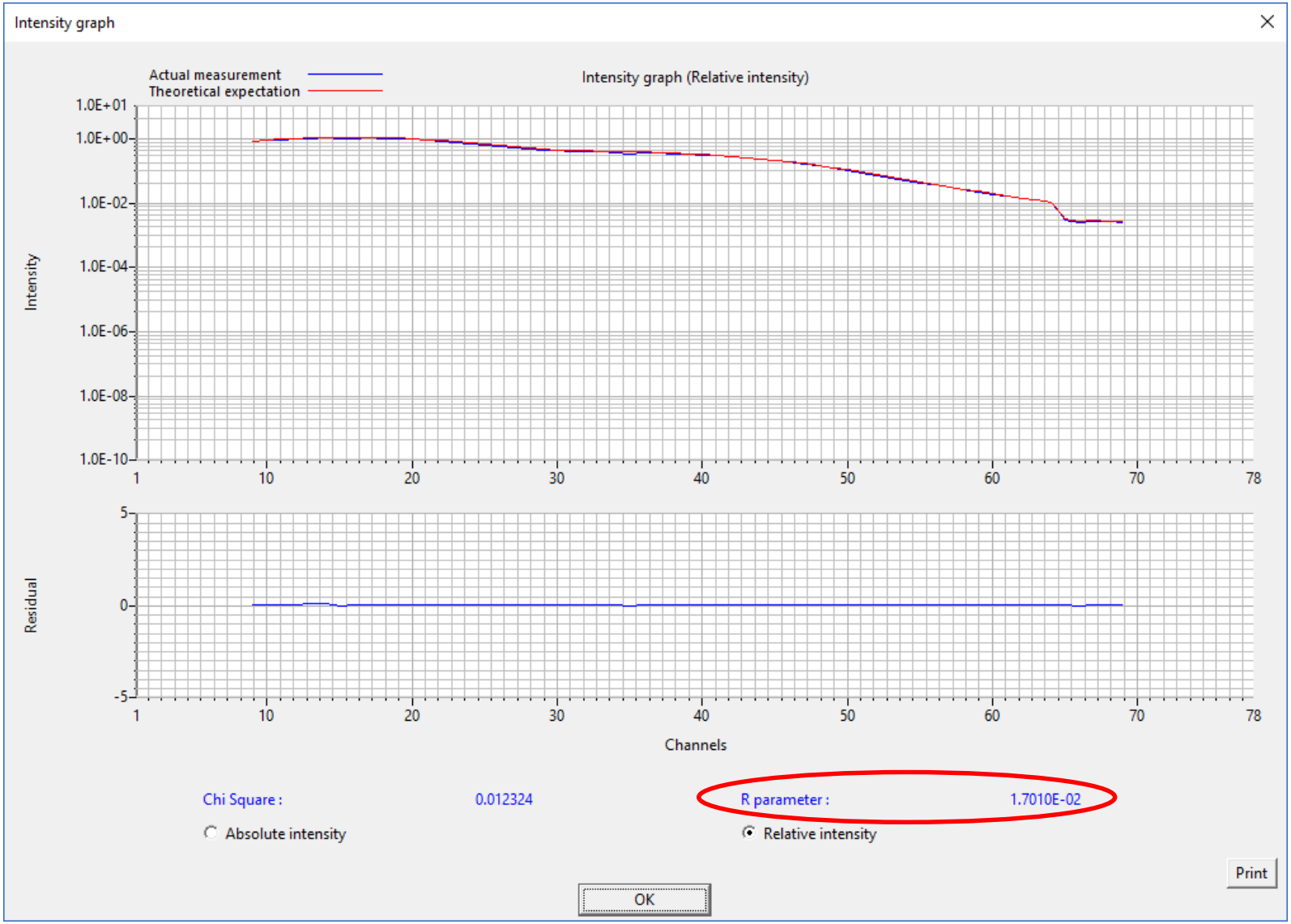


Intensity Graph

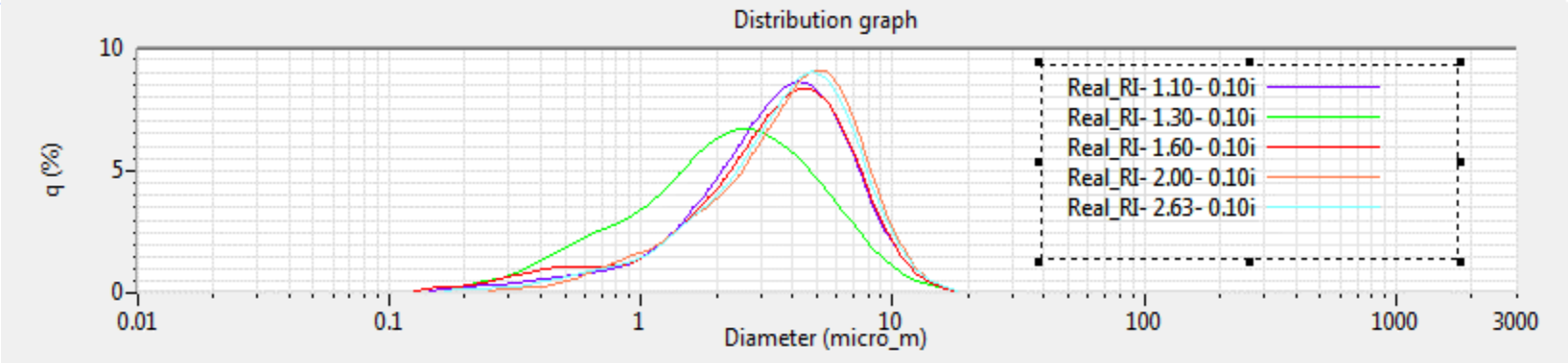


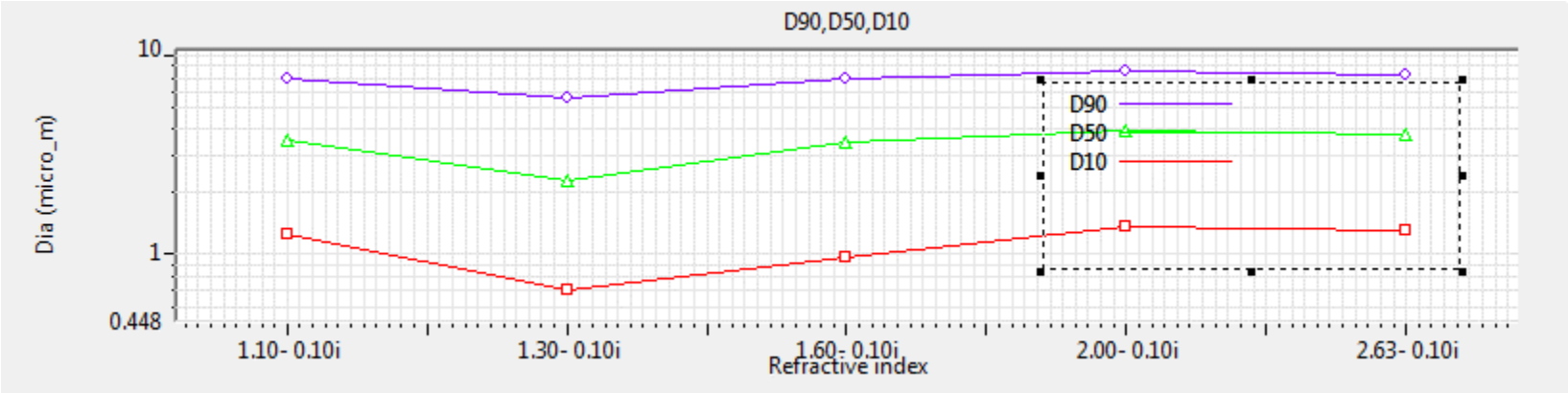


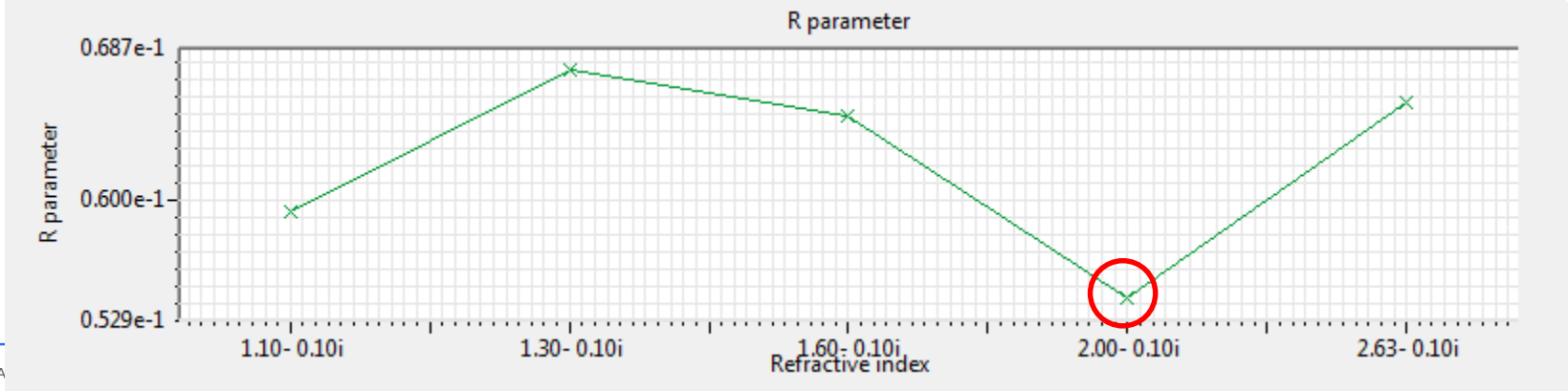
Intensity Graph – Good Correlation



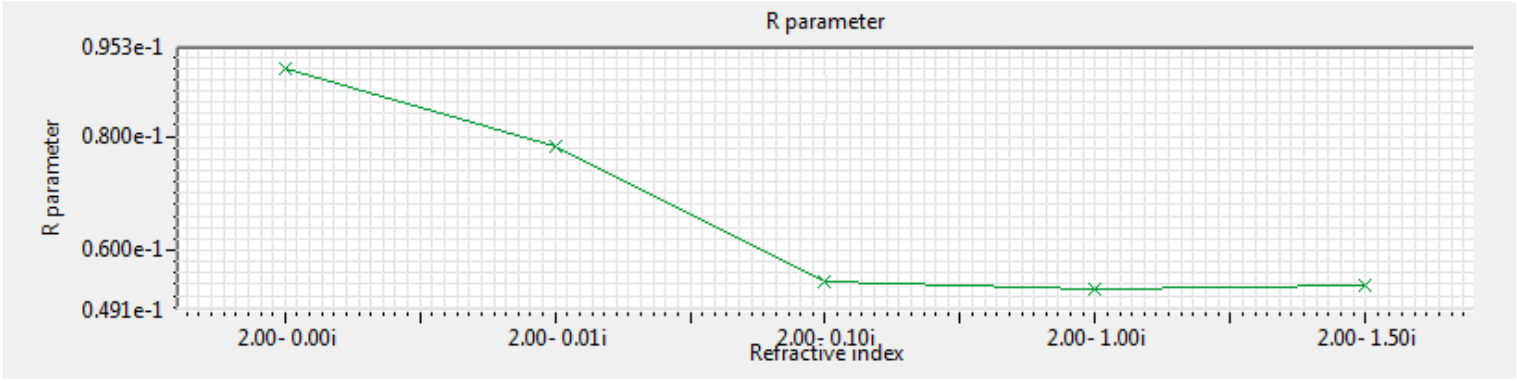
Refracting Index – *Real Valor*

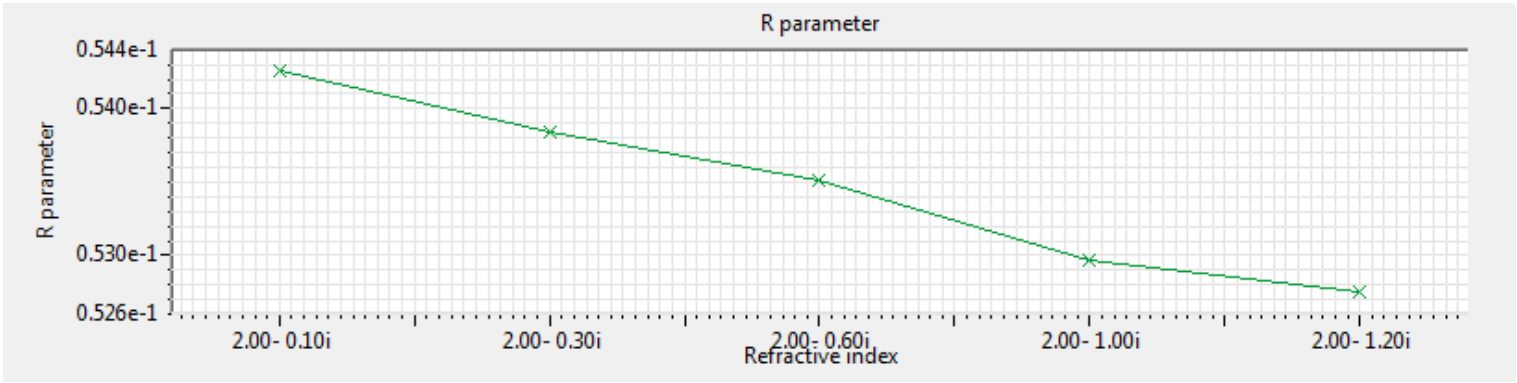


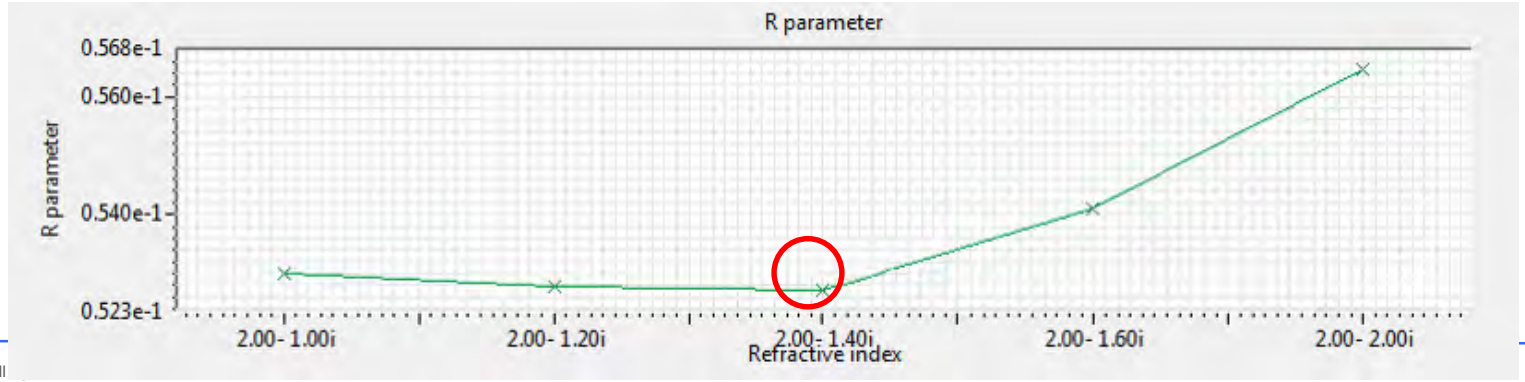




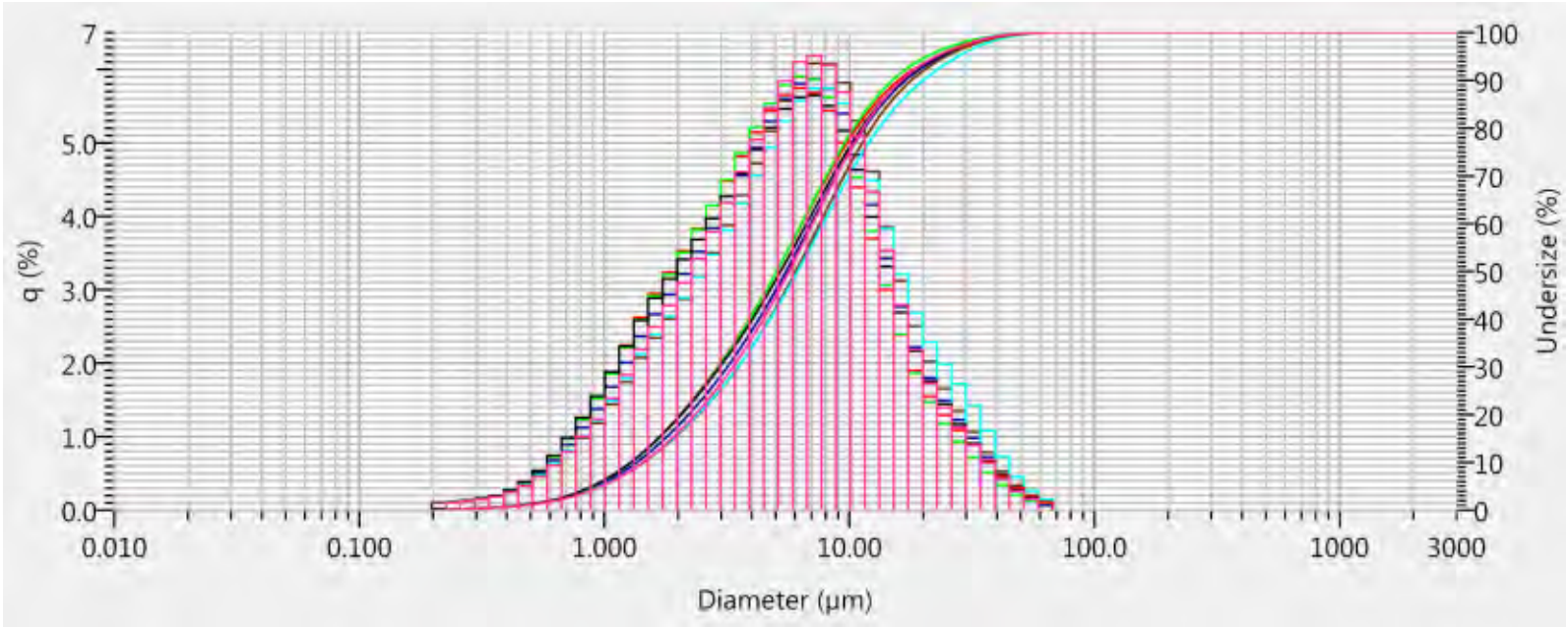
Refracting Index – *Imaginary Valor*







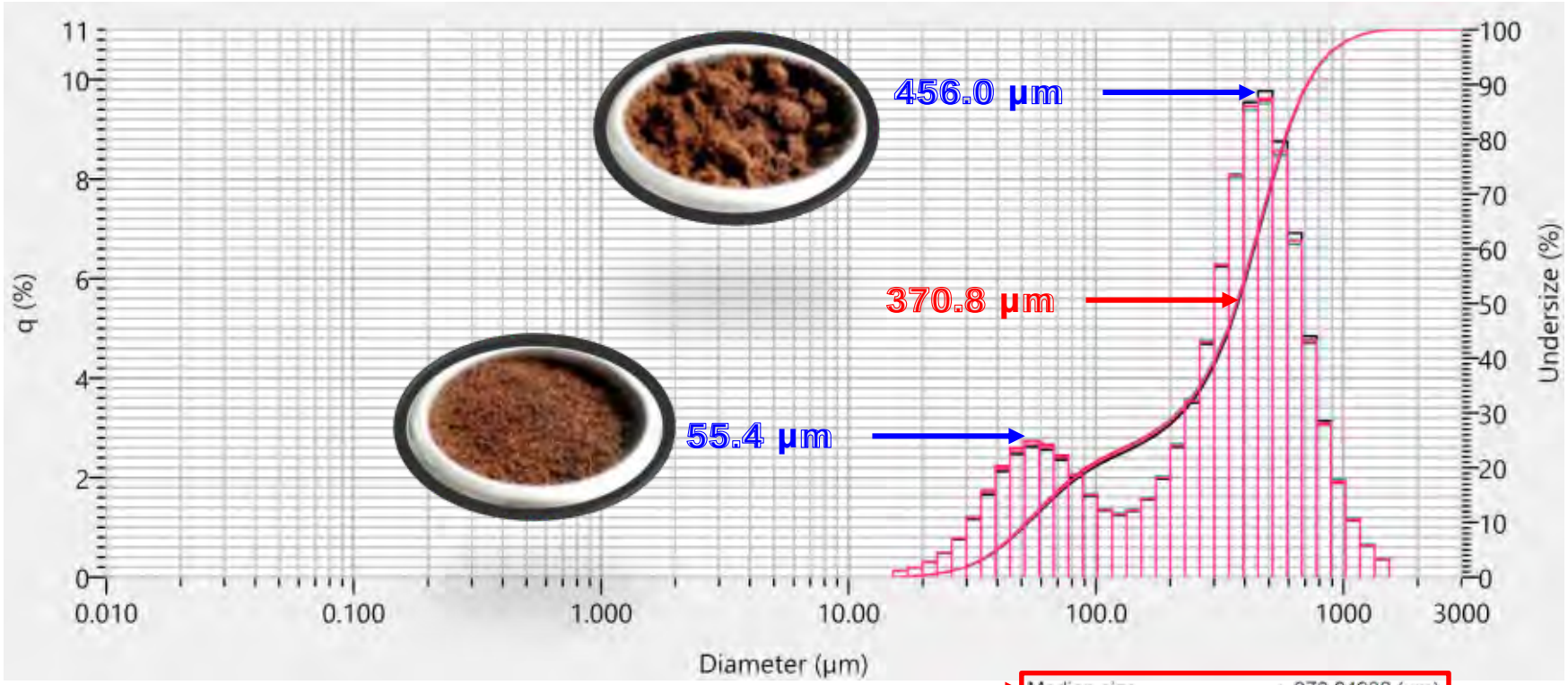
Final Results



Transmittance (R)	:	96.5 (%)
Transmittance (B)	:	96.1 (%)
Circulation speed	:	3
Agitation speed	:	3
Ultrasound	:	00:25 (5)
Distribution base	:	Volume
Refractive index (R)	:	Copper oxide [Copper oxide(2.000 - 1.400i),1.33(1.333)]

Median size	:	5.51560 (µm)
Span	:	2.8228
Diameter on cumulative %	:	(1)10.00 (%)- 1.3595 (µm)
	:	(2)20.00 (%)- 2.2084 (µm)
	:	(3)30.00 (%)- 3.1765 (µm)
	:	(4)40.00 (%)- 4.2724 (µm)
	:	(5)50.00 (%)- 5.5156 (µm)
	:	(6)60.00 (%)- 6.9811 (µm)
	:	(7)70.00 (%)- 8.8260 (µm)
	:	(8)80.00 (%)- 11.5047 (µm)
	:	(9)90.00 (%)- 16.9289 (µm)

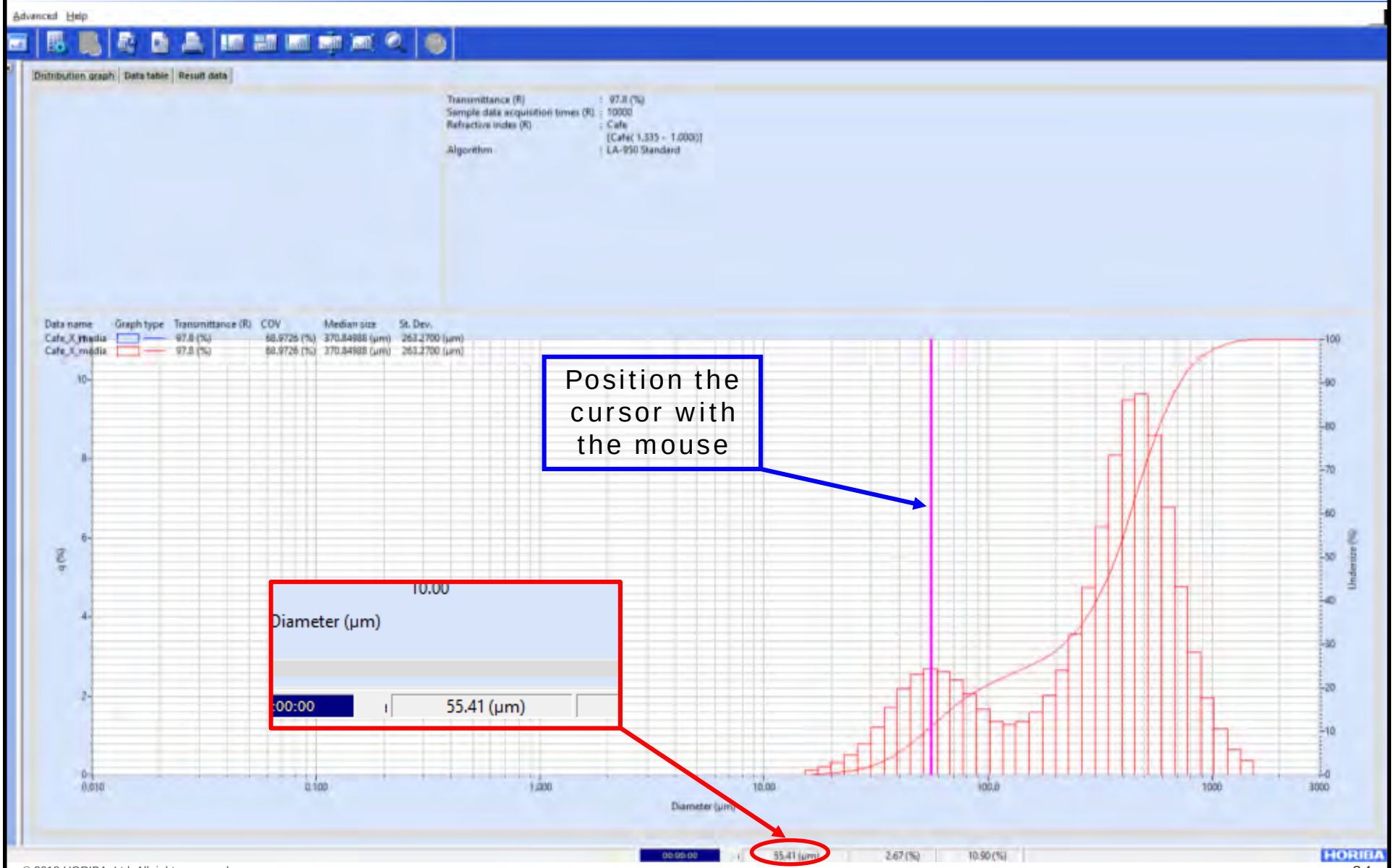
Dry Dispersion – Coffee



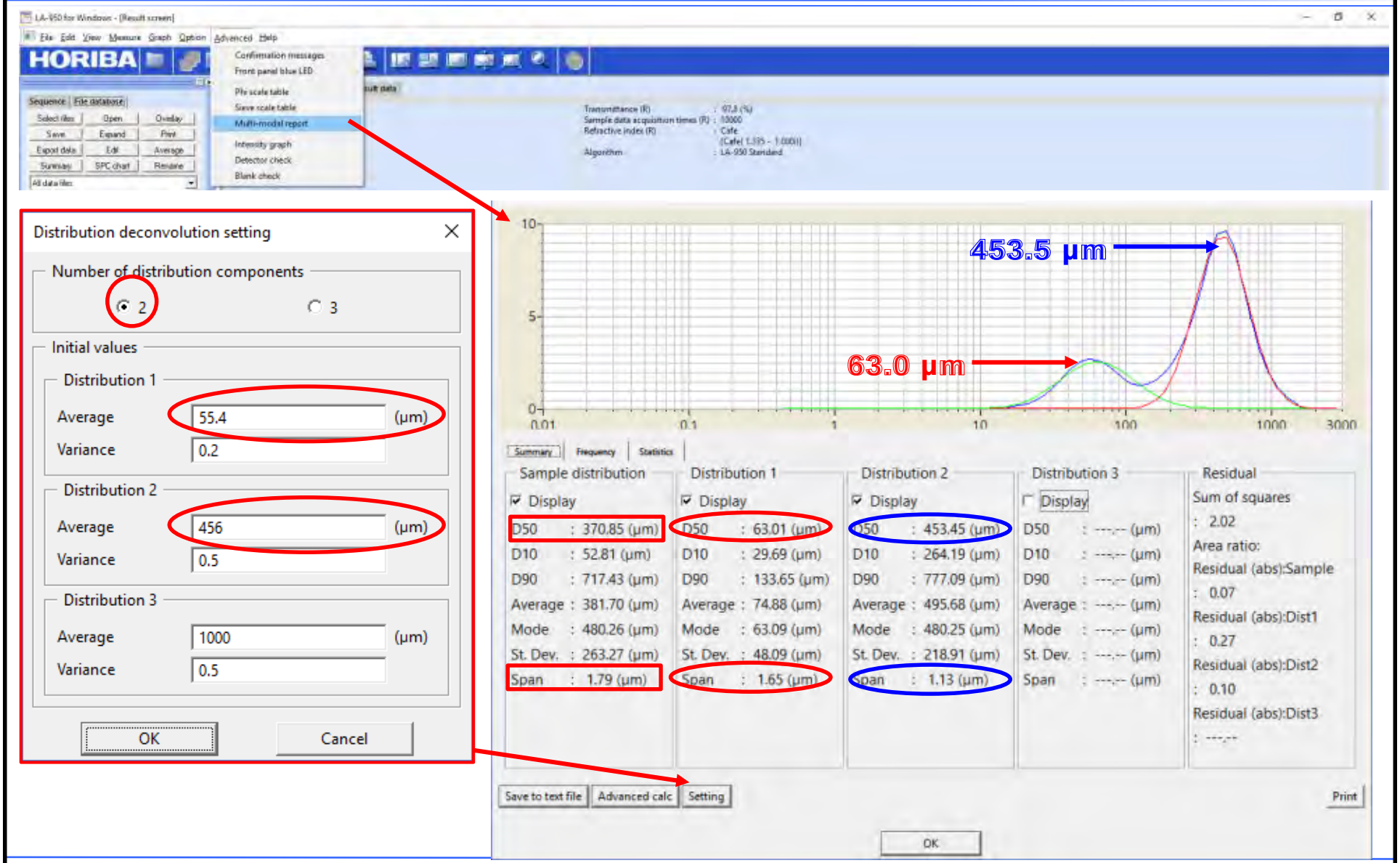
Measurement	D10	D90	D50
1	52.3	714.0	368.5
2	52.7	719.3	369.0
3	53.5	719.0	375.1
mean	52.8	717.4	370.8
Std Dev	0.61	3.00	3.65
CoV	1.16	0.42	0.98

Median size	: 370.84988 (µm)
Mean size	: 381.70218 (µm)
St. Dev.	: 263.2700 (µm)
Geo. mean size	: 268.6917 (µm)
Geo. St. Dev.	: 2.6470 (µm)
Mode size	: 480.2568 (µm)
Span	: 1.7922
Diameter on cumulative %	: (1)10.00 (%)- 52.8112 (µm)
	: (2)20.00 (%)- 94.4257 (µm)
	: (3)30.00 (%)- 217.0729 (µm)
	: (4)40.00 (%)- 305.0816 (µm)
	: (5)50.00 (%)- 370.8499 (µm)
	: (6)60.00 (%)- 431.9580 (µm)
	: (7)70.00 (%)- 497.8002 (µm)
	: (8)80.00 (%)- 580.4877 (µm)
	: (9)90.00 (%)- 717.4302 (µm)

Data Treatment – Bimodal Distribution

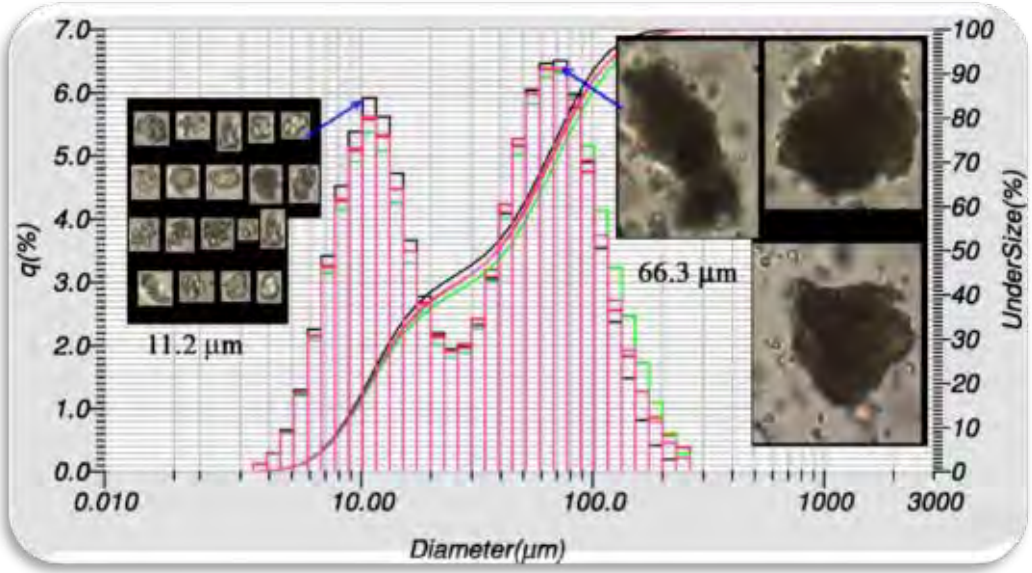


Coffee – Multimodal Report



Clay – Multimodal Report

Natural Clay

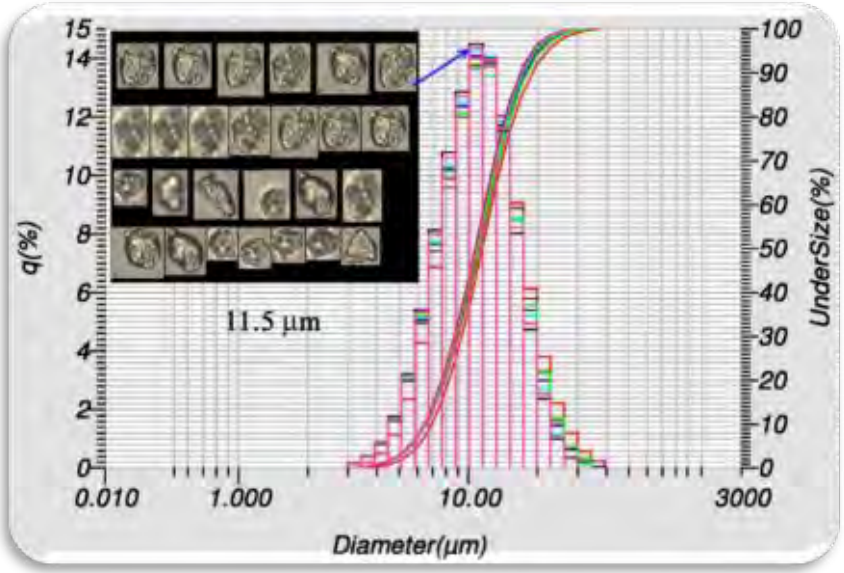


Peak # 1 (0.0100 - 26.1111 µm)
Median Size : 11.18102(µm)
Mean Size : 12.16924(µm)
Diameter on % : (1)10.00 (%)- 6.6
: (2)50.00 (%)- 11.
: (3)90.00 (%)- 19.

Peak # 2 (26.1111 - 3000.0000 µm)
Median Size : 67.06469(µm)
Mean Size : 75.64296(µm)
Diameter on % : (1)10.00 (%)- 36.
: (2)50.00 (%)- 67.
: (3)90.00 (%)- 12

Aspect ratio
Peak 1:2 : 5.913

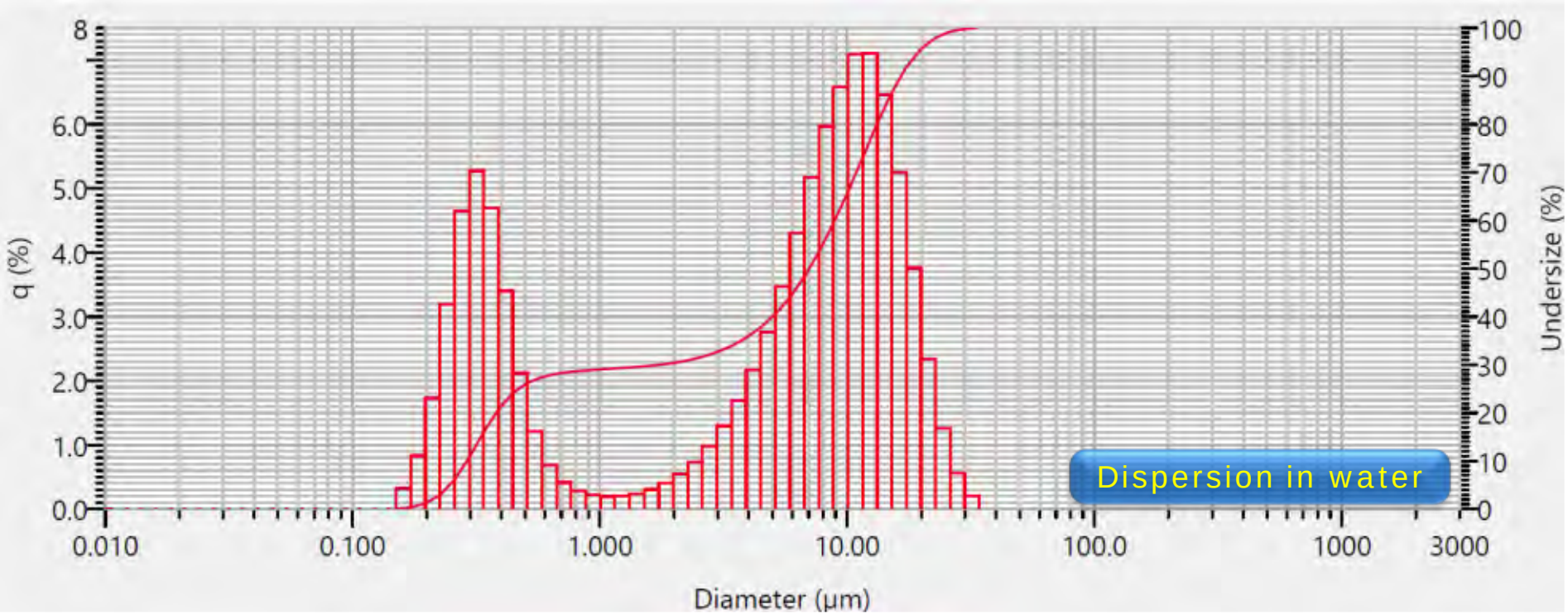
Modified Clay



Median Size : 11.47206(µm)
Mean Size : 12.39214(µm)
Std.Dev. : 5.0446(µm)
Geo.Mean Size : 11.4809(µm)
Geo.Std.Dev. : 1.4769(µm)
Mode Size : 10.9106(µm)
Span : OFF
Diameter on Cumulative % : (1)10.00 (%)- 6.9324(µm)
: (2)50.00 (%)- 11.4721(µm)
: (3)90.00 (%)- 19.0407(µm)

Case of Study - Wafer Filler

First trial: Water dispersion

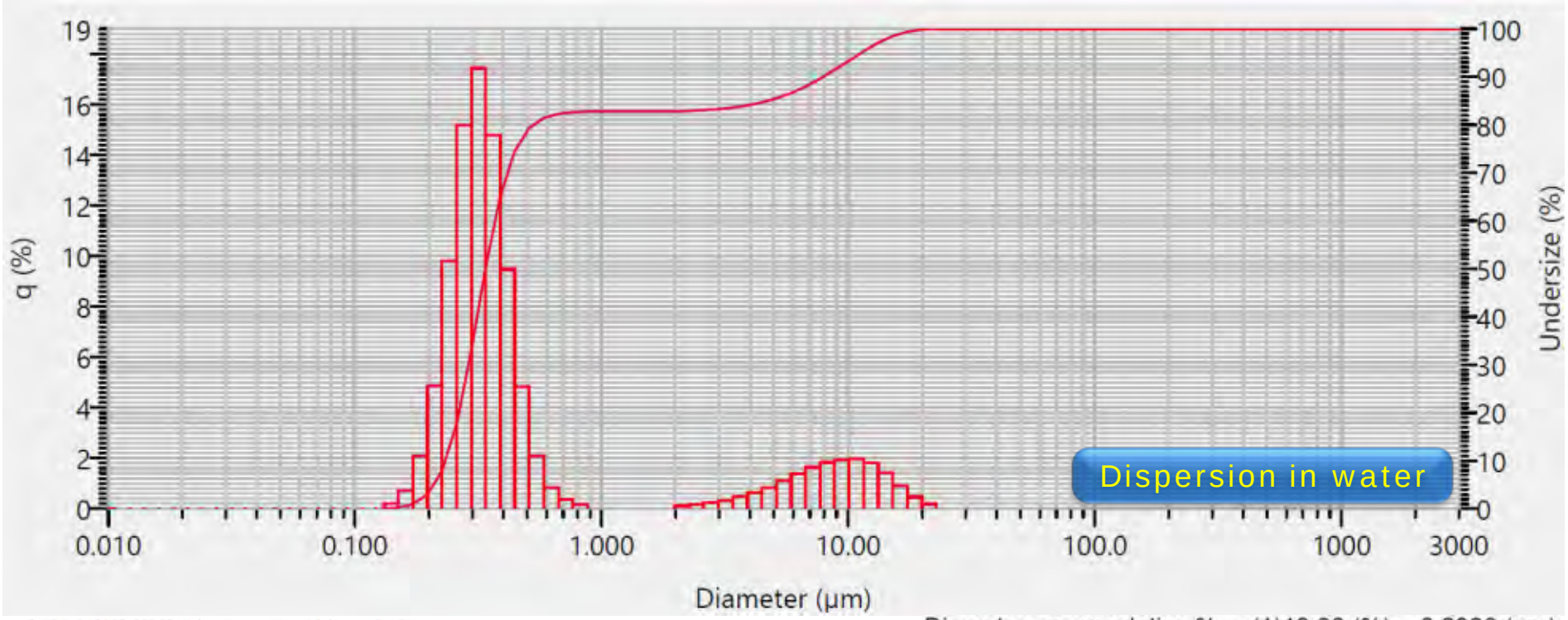


Transmittance (R)	: 93.4 (%)
Transmittance (B)	: 86.6 (%)
Circulation speed	: 3
Agitation speed	: 10
Ultrasound	: Off
Refractive index (R)	: 1.6-0.1 [1.6-0.1(1.600 - 0.100i),Water(1.333)]

Diameter on cumulative %	: (1)10.00 (%)- 0.2901 (µm)
	: (2)20.00 (%)- 0.3810 (µm)
	: (3)30.00 (%)- 1.7706 (µm)
	: (4)40.00 (%)- 5.0007 (µm)
	: (5)50.00 (%)- 7.0334 (µm)
	: (6)60.00 (%)- 8.9242 (µm)
	: (7)70.00 (%)- 10.9027 (µm)
	: (8)80.00 (%)- 13.1999 (µm)
	: (9)90.00 (%)- 16.5488 (µm)

Case of Study - Wafer Fillers

After 5 min of circulation (3)

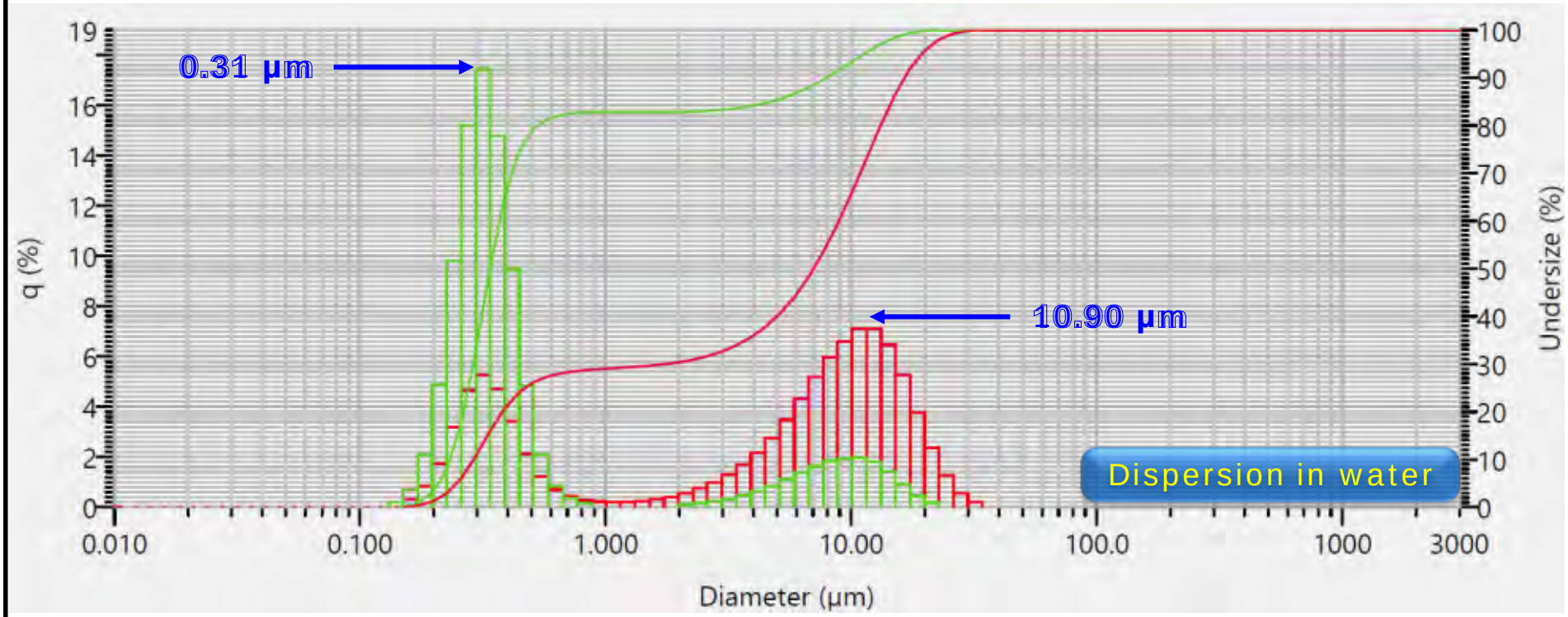


Transmittance (R)	: 96.7 (%)
Transmittance (B)	: 90.2 (%)
Circulation speed	: 3
Agitation speed	: 10
Ultrasound	: Off
Refractive index (R)	: 1.6-0.1 [1.6-0.1(1.600 - 0.100i),Water(1.333)]

Diameter on cumulative %	: (1)10.00 (%)- 0.2326 (µm)
	: (2)20.00 (%)- 0.2641 (µm)
	: (3)30.00 (%)- 0.2888 (µm)
	: (4)40.00 (%)- 0.3132 (µm)
	: (5)50.00 (%)- 0.3386 (µm)
	: (6)60.00 (%)- 0.3710 (µm)
	: (7)70.00 (%)- 0.4172 (µm)
	: (8)80.00 (%)- 0.5324 (µm)
	: (9)90.00 (%)- 7.9434 (µm)

Case of Study - Wafer Fillers

Partial sample solubilization



Time: 0

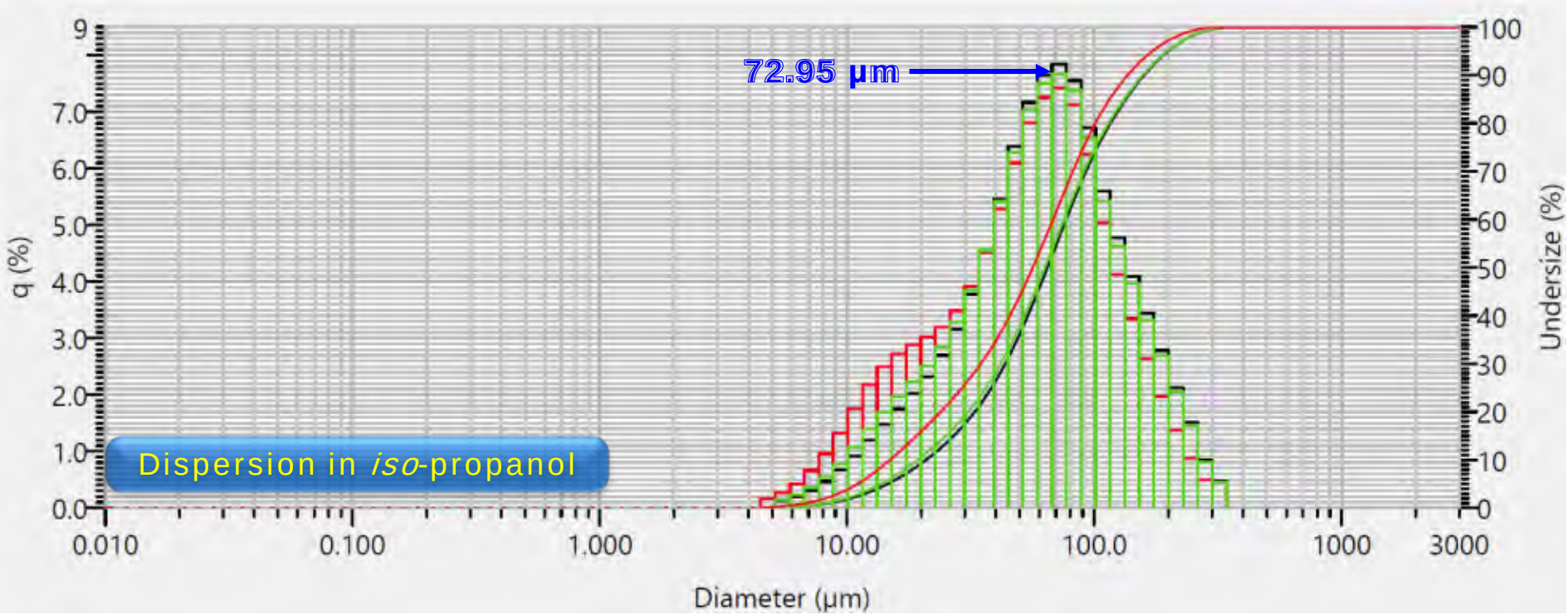
Transmittance (R)	: 93.4 (%)
Transmittance (B)	: 86.6 (%)
Circulation speed	: 3
Agitation speed	: 10
Ultrasound	: Off
Refractive index (R)	: 1.6-0.1 [1.6-0.1(1.600 - 0.100i),Water(1.333)]

After 5 min

Transmittance (R)	: 96.7 (%)
Transmittance (B)	: 90.2 (%)
Circulation speed	: 3
Agitation speed	: 10
Ultrasound	: Off
Refractive index (R)	: 1.6-0.1 [1.6-0.1(1.600 - 0.100i),Water(1.333)]

Case of Study - Wafer Fillers

Second trial: Isopropanol dispersion + Ultrasound



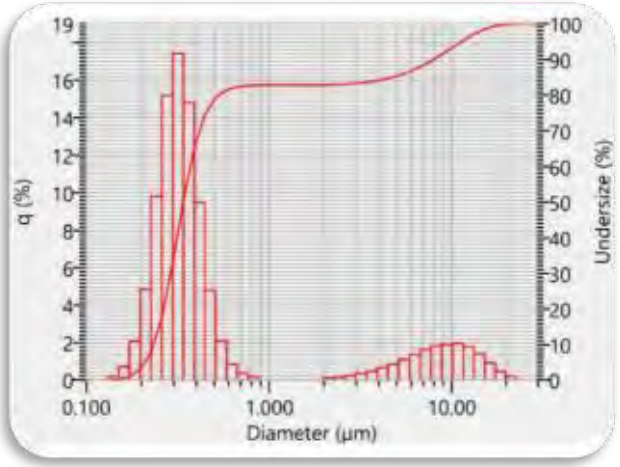
After 5 min

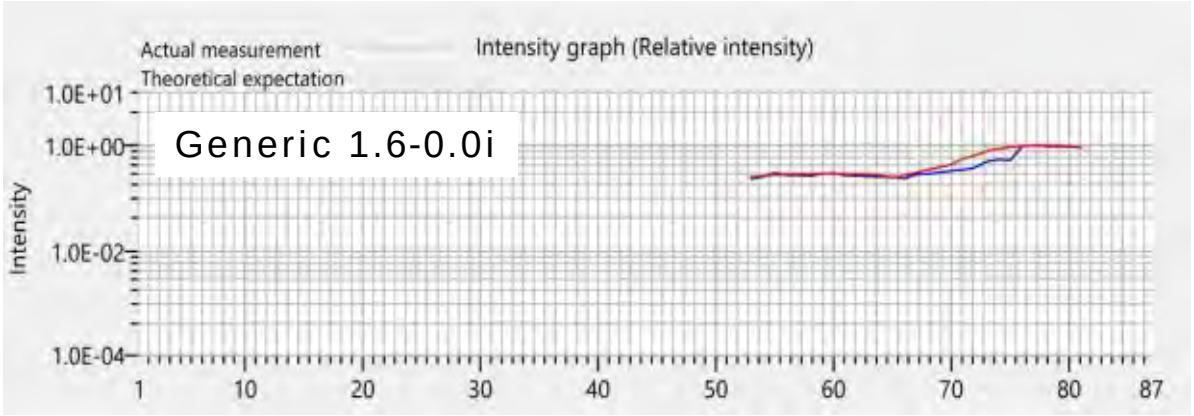
Transmittance (R)	: 96.6 (%)
Transmittance (B)	: 97.7 (%)
Circulation speed	: 3
Agitation speed	: 10
Ultrasound	: 00:50 (7)
Refractive index (R)	: Recheio em iso-propanol [Recheio(1.600 - 0.000i),isopropanol(1.378)]

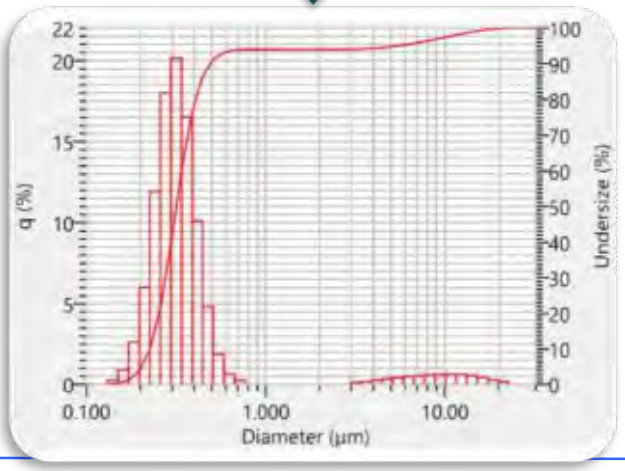
Diameter on cumulative %	: (1)10.00 (%)- 20.9681 (µm)
	: (2)20.00 (%)- 32.9725 (µm)
	: (3)30.00 (%)- 43.7598 (µm)
	: (4)40.00 (%)- 54.0146 (µm)
	: (5)50.00 (%)- 64.8526 (µm)
	: (6)60.00 (%)- 77.1788 (µm)
	: (7)70.00 (%)- 92.8493 (µm)
	: (8)80.00 (%)- 116.2566 (µm)
	: (9)90.00 (%)- 159.5376 (µm)

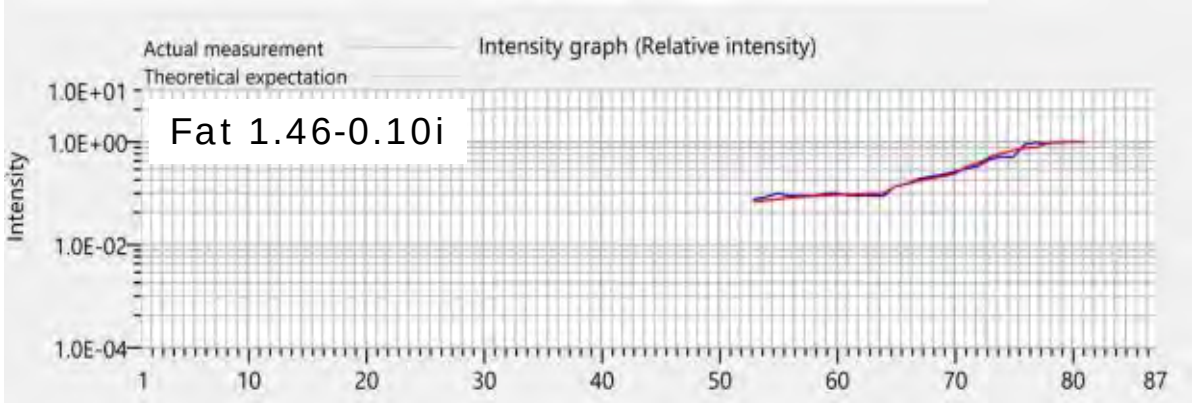
Data Treatment – Refraction Index Improvement

Dispersion in Water



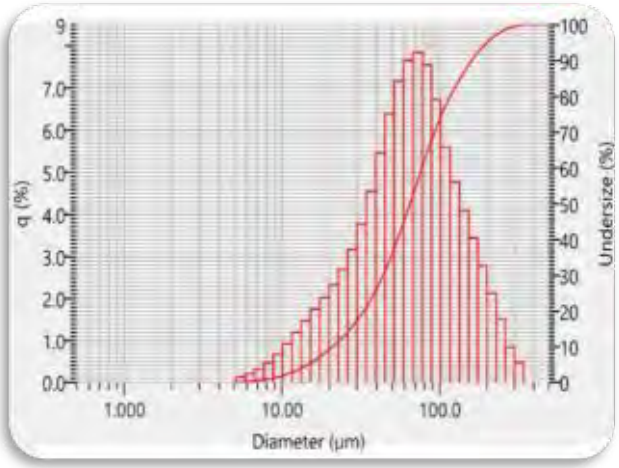


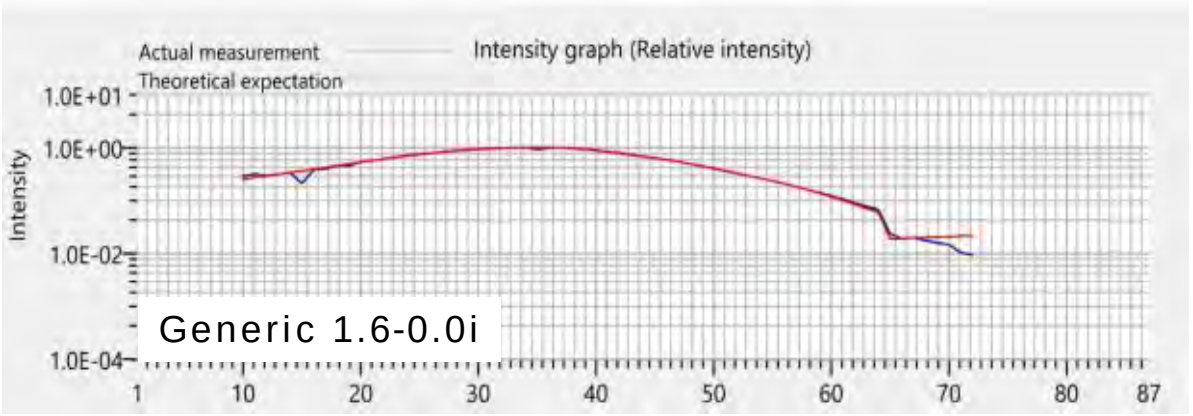


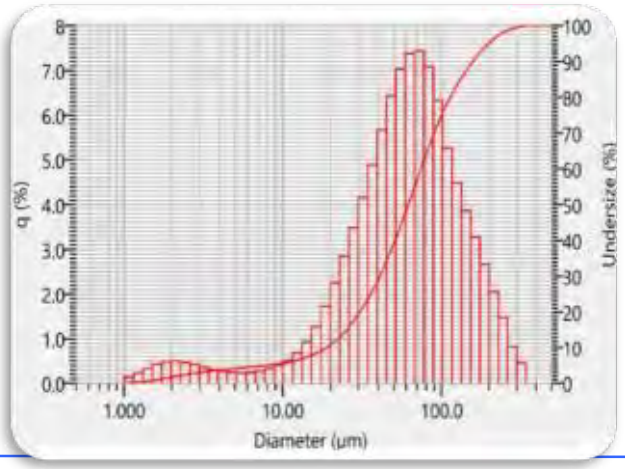


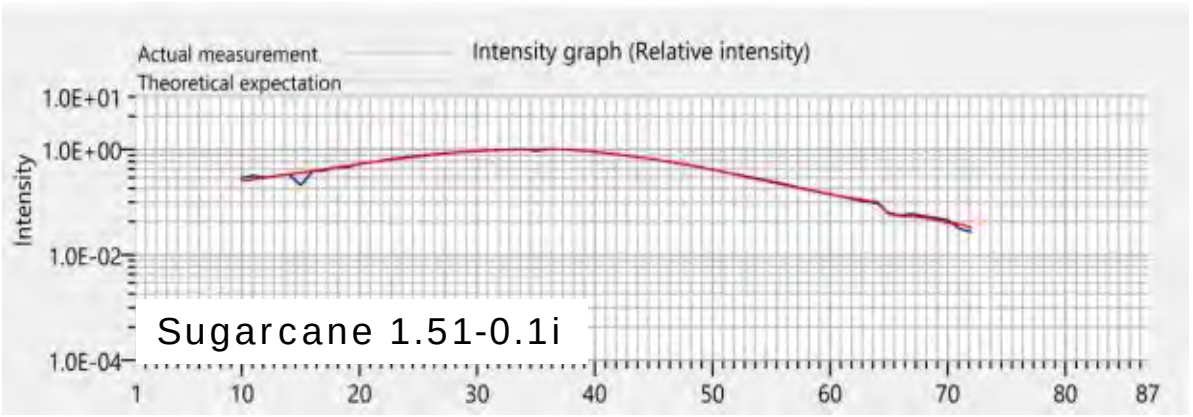
Data Treatment – Refraction Index Improvement

Dispersion in *iso*-propanol



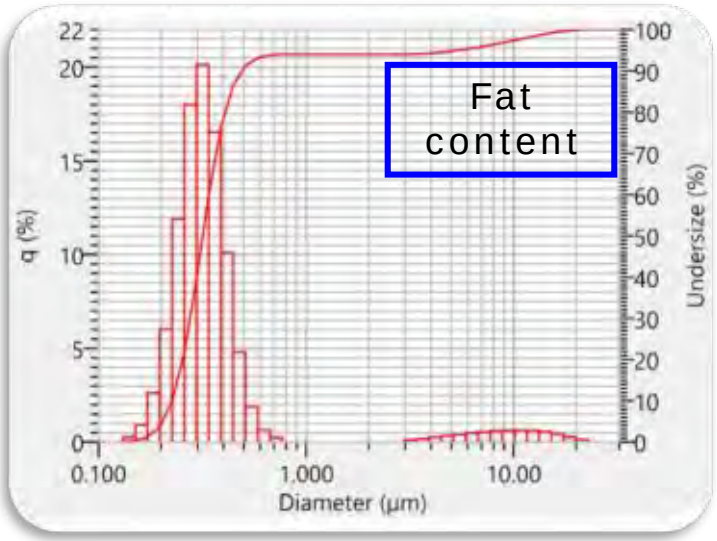






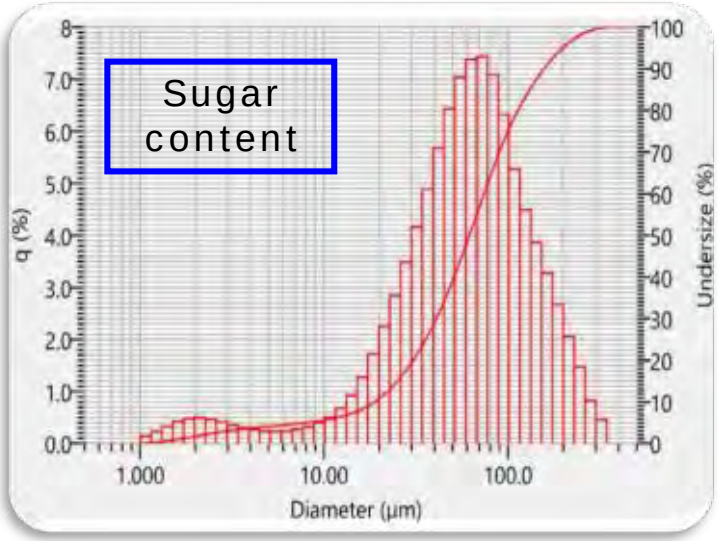
Different Targets in the Same Sample

Dispersion in Water



Sample distribution		Distribution 1		Distribution 2	
Display		Display		Display	
D50	0.32 (µm)	D50	0.31 (µm)	D50	9.30 (µm)
D10	0.23 (µm)	D10	0.23 (µm)	D10	4.78 (µm)
D90	0.49 (µm)	D90	0.43 (µm)	D90	18.09 (µm)
Average	0.89 (µm)	Average	0.32 (µm)	Average	10.63 (µm)
Mode	0.32 (µm)	Mode	0.32 (µm)	Mode	9.43 (µm)
St. Dev.	2.51 (µm)	St. Dev.	0.08 (µm)	St. Dev.	5.88 (µm)
Span	0.84 (µm)	Span	0.66 (µm)	Span	1.43 (µm)

Dispersion in *iso*-propanol



Sample distribution		Distribution 1		Distribution 2	
Display		Display		Display	
D50	61.81 (µm)	D50	3.38 (µm)	D50	65.83 (µm)
D10	18.89 (µm)	D10	0.99 (µm)	D10	26.52 (µm)
D90	157.20 (µm)	D90	11.56 (µm)	D90	163.85 (µm)
Average	76.40 (µm)	Average	5.36 (µm)	Average	84.67 (µm)
Mode	72.07 (µm)	Mode	3.19 (µm)	Mode	63.19 (µm)
St. Dev.	58.14 (µm)	St. Dev.	6.60 (µm)	St. Dev.	68.46 (µm)
Span	2.24 (µm)	Span	3.13 (µm)	Span	2.09 (µm)

Conclusions

- Must have representative sample
- Powders: select air pressure
- Suspensions: wet, disperse
- Check accuracy w/microscope
- Investigate system settings: concentration, agitation, ultrasound
- Design for maximum precision
- Follow guidelines in standards

Thank you

감사합니다

Cảm ơn

ありがとうございました

Dziękuję

धन्यवाद

Grazie

Merci

谢谢

நன்ற

ขอบคุณ ครับ

Obrigado

Σας ευχαριστούμε

شُكْرا

Tack ska ni ha

Большое спасибо

Danke

Gracias

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