HORIBA Scientific

Horiba Instruments Inc.

Particle Characterization

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System Verification

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Scope

- Is my analyzer working?
- Is my analyzer clean?
- Is my procedure OK?

- Not: Is my sample OK (that is method development)
- Prerequisite to running good sample data

Calibration vs. Verification

Calibration : enter standard sample(s), adjust instrument response to show expected result

Example: particle counters

Verification: enter standard sample(s), observe if response within accepted range

Example: DLS, laser diffraction

From ISO 13320, 6.5.1 Calibration: "Laser diffraction systems are based on first principles, though with idealized properties of the particles. <u>Thus, calibration in the strict sense is not required.</u> However, it is still necessary and desirable to confirm the correct operation of the instrument by a validation procedure."

Verification

From ISO 13320: "Primary validation can be made with any certified or standard reference material, acceptable to the practice of the end-users' industries."

"Certified or standard reference materials consisting of a known distribution having a range of spherical particles over one decade of size are preferred."

Note:

1. **This implies using a polydisperse standard**
2. **Most people still using monodisperse standards**
3. **Most polydisperse standards are not over one decade of size**

Monodisperse Standards

Very narrow distribution

Only tests central point

- **Not d10, d90**

Available in sizes 20 nm – 1000 μm

Mostly suspensions

Easy to use

Relatively inexpensive

Verifies optics only

1 μm particles will stay in suspension even if sampler pump broken

Will pass even if poorly suspended (for example, some particles floating on top)

www.thermo.com

www.nist.gov

1690	Polystyrene Spheres (1 μm)
1691	Polystyrene Spheres (0.3 μm)
1692	Polystyrene Spheres (3 μm)
1961	Polystyrene Spheres (30 μm)
1963a	Polystyrene Spheres (0.1 μm)
1964	Polystyrene Spheres (0.06 μm)
1965	Polystyrene Spheres (10 μm) (on slide)

www.polysciences.com

Monodisperse Standards

- **No official pass/fail criteria**
- **So make your own**
- **HORIBA IQ/OQ:**
  - **0.1, 1.0, 100 µm PSL (plus 3-30 µm polydisperse glass beads)**
  - **Mean +/- 5% from certified value**
- **Why measure so many sizes?**
  - **Two should cover all detectors**
  - **Larger sizes cost more**
- **Which sizes?**
  - **No one says measure near actual sample size**

20 nm
30 nm
40 nm
50 nm
60 nm
70 nm
80 nm
90 nm
100 nm
125 nm
150 nm
200 nm
220 nm
240 nm
270 nm
300 nm
350 nm
400 nm
450 nm
500 nm
500 nm
560 nm
600 nm
700 nm
800 nm
900 nm

1.0 µm
1.0 µm
1.1 µm
1.3 µm
1.6 µm
1.8 µm
2.0 µm
2.5 µm
3.0 µm
4.0 µm
5.0 µm
6.0 µm
7.0 µm
8.0 µm
9.0 µm
10 µm
12 µm
15 µm
20 µm
25 µm
30 µm
40 µm
50 µm
60 µm
70 µm
80 µm
100 µm
115 µm
140 µm
160 µm
200 µm
240 µm
280 µm
300 µm
400 µm
500 µm
550 µm
650 µm
750 µm
1000 µm

Sizes available from Thermo. Still Duke Scientific to me.

Polysdisperse Standards

- Defined (certified) distribution
- Defined procedure and pass/fail criteria (ISO and USP)
- Can buy directly from NIST (or other sources)
- Tests entire instrument

SRM	Description	Particle Diameter Distribution (µm)
1003c	Glass Beads	20 to 45 (635 to 325 mesh)
1004b	Glass Beads	40 to 150 (270 to 120 mesh)
1017b	Glass Beads	100 to 400 (140 to 45 mesh)
1018b	Glass Beads	220 to 750 (60 to 25 mesh)
1019b	Glass Beads	750 to 2450 (20 to 10 mesh)

www.nist.gov

SRM	Description	Particle Diameter, nominal (nm)
8011	Gold Nanoparticles	10 nm
8012	Gold Nanoparticles	30 nm
8013	Gold Nanoparticles	60 nm

Not really polydisperse?

Polysdisperse Standards

- Now good range of sizes available
- Don’t recommend 0.1-1 μm
    - Also testing ability to disperse particles
- Can buy in proper quantities for given samplers
    - No sub-sampling concerns
- Only option for dry powder feeders
- No point in measuring more than one size range

Nominal Size (μm)	Catalogue Number	Nom Wt. Per Vial (g)	Sold in 10 bottle sets. Price per Set:		
			£	€*	$*
0.1 - 1μm	PS180	0.01	206	315	415
	PS181	0.02	240	365	485
1 - 10μm	PS190	0.025	69	105	140
	PS191	0.05	92	140	185
	PS192	0.10	115	175	235
	PS193	0.25	156	240	315
	PS194	0.50	206	315	415
3 - 30μm	PS200	0.025	59	90	120
	PS201	0.05	69	105	140
	PS202	0.10	92	140	185
	PS203	0.25	115	175	235
	PS204	0.50	156	240	315
	PS205	1.0	206	315	415
10 - 100μm	PS211	0.05	59	90	120
	PS212	0.10	80	125	165
	PS213	0.25	102	155	205
	PS214	0.50	146	225	295
	PS215	1.0	194	295	390

www.whitehousescientific.com/

Note: Whitehouse also supplies monodisperse

NIST 1003c

National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material® 1003c

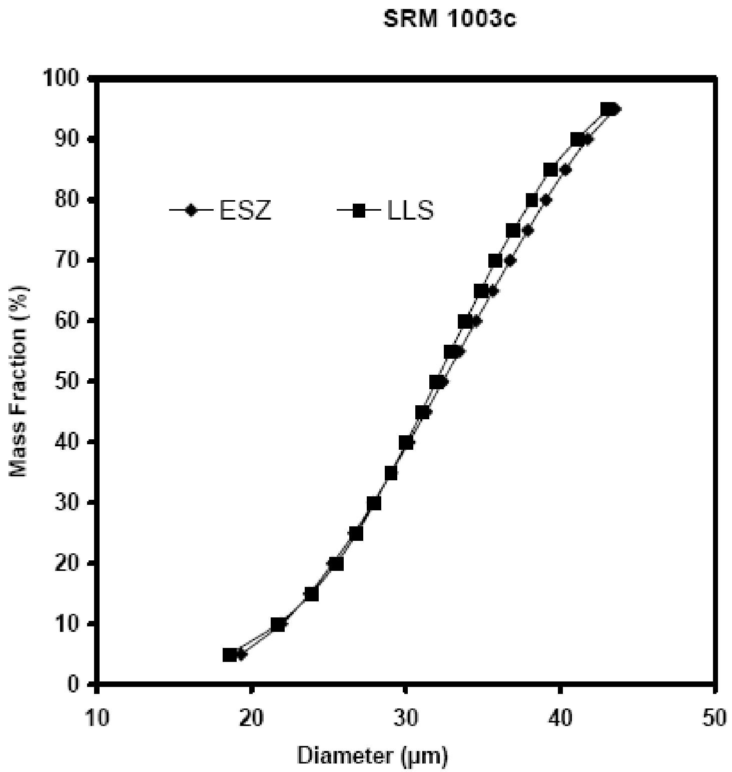

Table 1. Certified Diameter Values

Cumulative Mass Fraction Finer* (%)	Diameter (µm)	Standard Uncertainty Homogeneity (µm)	Standard Uncertainty Measurement (µm)	Type B Standard Uncertainty (µm)	Combined. Standard. Uncertainty (µm)	Expanded** Uncertainty (µm)
5	18.9	0.00	0.43	0.41	0.59	1.2
10	21.8	0.15	0.24	0.41	0.50	1.0
15	23.7	0.14	0.26	0.41	0.50	1.0
20	25.3	0.10	0.30	0.41	0.51	1.0
25	26.7	0.10	0.30	0.41	0.51	1.0
30	27.9	0.09	0.27	0.41	0.50	1.0
35	29.0	0.12	0.25	0.41	0.49	1.0
40	30.1	0.12	0.24	0.41	0.49	1.0
45	31.1	0.09	0.26	0.41	0.49	1.0
50	32.1	0.03	0.29	0.41	0.50	1.0
55	33.1	0.00	0.33	0.41	0.52	1.0
60	34.1	0.00	0.37	0.41	0.55	1.1
65	35.2	0.00	0.41	0.41	0.58	1.2
70	36.2	0.00	0.47	0.41	0.62	1.2
75	37.4	0.00	0.48	0.41	0.63	1.3
80	38.6	0.00	0.46	0.41	0.62	1.2
85	39.8	0.00	0.49	0.41	0.64	1.3
90	41.4	0.00	0.36	0.41	0.54	1.1
95	43.3	0.00	0.25	0.41	0.48	1.0

Note: different techniques always give different results

ISO 13320 : Real World Samples

- Test all samples 3 times for "repeatability"
- I call this "reproducibility"
  - 3 independent measurements
  - Prepare, measure, drain, repeat
- Calculate mean & coefficient of variation (COV) for d10, d50, d90
  - COV = (st dev/mean) * 100
  - COV < 3% at median d_{50}
  - COV < 5% at d_{10} & d_{90}
  - Double limits below 10 µm

Note: actual text reads
x_{10}, x_{50}, x_{90}
Only Germans use x,
ROW uses d
Guess who supervised
writing ISO 13320…

ISO 13320 “Validation”

“The response of a laser diffraction instrument is considered to meet this standard if the mean value of the *x*50 coming from at least three independent measurements deviates less than 3 % from the certified range of values of the Certified or Standard Reference Material, i.e. the mean value together with its standard deviation; the mean values for the *x*10 and *x*90 should deviate less than 5 % from the certified range of values.”

ISO 13320 “Validation”

6.3.2 Precautions e) Validate the instrument operation with respect to both precision and accuracy at regular time intervals by measuring a control sample of known size distribution (see 6.4 and 6.5.2).

Therefore, two parts to the verification test. Measure standard 3 times. Calculate mean value at d10, d50, d90 for accuracy. Calculate COV for precision.

Precision:

- **COV < 3% at median d_{50}**
- **COV < 5% at d_{10} & d_{90}**

Accuracy:

- **d 50 within 3% of “certified range of values”**
- **d10 & d90 within 5% of “certified range of values”**

Pass/Fail: Example: NIST 1003

Only need D10, D50, D90

What about uncertainty?

Use "Expanded Uncertainty" (95% confidence)

Include the bottle uncertainty. If the bottle uncertainty for D50 is over 3%, then you will often fail due to bottle-to-bottle variations.

Table 1. Certified Diameter Values

Cumulative Mass Fraction Finer[a] (%)	Diameter (µm)	Standard Uncertainty Homogeneity (µm)	Standard Uncertainty Measurement (µm)	Type B Standard Uncertainty (µm)	Combined. Standard. Uncertainty (µm)	Expanded Uncertainty[b] (µm)
5	18.9	0.00	0.43	0.41	0.59	1.2
10	21.8	0.15	0.24	0.41	0.50	1.0
15	23.7	0.14	0.26	0.41	0.50	1.0
20	25.3	0.10	0.30	0.41	0.51	1.0
25	26.7	0.10	0.30	0.41	0.51	1.0
30	27.9	0.09	0.27	0.41	0.50	1.0
35	29.0	0.12	0.25	0.41	0.49	1.0
40	30.1	0.12	0.24	0.41	0.49	1.0
45	31.1	0.09	0.26	0.41	0.49	1.0
50	32.1	0.03	0.29	0.41	0.50	1.0
55	33.1	0.00	0.33	0.41	0.52	1.0
60	34.1	0.00	0.37	0.41	0.55	1.1
65	35.2	0.00	0.41	0.41	0.58	1.2
70	36.2	0.00	0.47	0.41	0.62	1.2
75	37.4	0.00	0.48	0.41	0.63	1.3
80	38.6	0.00	0.46	0.41	0.62	1.2
85	39.8	0.00	0.49	0.41	0.64	1.2
90	41.4	0.00	0.36	0.41	0.54	1.1
95	43.3	0.00	0.25	0.41	0.48	1.0

(a) The cumulative mass fraction finer is the portion of SRM 1003c smaller than the certified diameter value.
(b) The uncertainty at each percentile, computed according to the ISO and NIST Guides [4,5], is an expanded uncertainty at the 95 % level of confidence.

Pass/Fail: Example: NIST 1003

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Note “Expanded Uncertainty”

- **Pass/fail:**
- **21.8*.95 = 20.71µm**
- **21.8*1.05 = 22.89 µm**
- **Range = 20.71 – 22.89 µm**

D10: d = 21.8 µm w/ 1.0 uncertainty

Pass/fail

(21.8 – 1)*.95 = 19.76 µm

(21.8 + 1)*1.05 = 23.94 µm

Range = 19.76 – 23.93 µm

Table 1. Certified Diameter Values

Cumulative Mass Fraction Finer[a] (%)	Diameter (µm)	Standard Uncertainty Homogeneity (µm)	Standard Uncertainty Measurement (µm)	Type B Standard Uncertainty (µm)	Combined. Standard. Uncertainty (µm)	Expanded Uncertainty[b] (µm)
5	18.9	0.00	0.43	0.41	0.59	1.2
10	21.8	0.15	0.24	0.41	0.50	1.0
15	23.7	0.14	0.26	0.41	0.50	1.0
20	25.3	0.10	0.30	0.41	0.51	1.0

Example: NIST 1003

- **d50 pass/fail (3%)**
  - **(32.1 - 1)*.97 = 30.17 μm**
  - **(32.1 + 1)*1.03 = 34.09 μm**
  - **Range = 30.17 – 34.09 μm**
- **d 90 pass/fail (5%)**
  - **(41.4 – 1)*.95 = 38.38 μm**
  - **(41.4+1)*1.05 = 44.52 μm**
  - **Range = 38.38 – 44.52 μm**
- **Note: d5 – d 95 range is 18.9 – 43.3, hardly “one decade”, being addressed in next version of ISO 13320**

Table 1. Certified Diameter Values

Cumulative Mass Fraction Finer* (%)	Diameter (μm)	Standard Uncertainty Homogeneity (μm)	Standard Uncertainty Measurement (μm)	Type B Standard Uncertainty (μm)	Combined Standard Uncertainty (μm)	Expanded** Uncertainty (μm)
5	18.9	0.00	0.43	0.41	0.59	1.2
10	21.8	0.15	0.24	0.41	0.50	1.0
15	23.7	0.14	0.26	0.41	0.50	1.0
20	25.3	0.10	0.30	0.41	0.51	1.0
25	26.7	0.10	0.30	0.41	0.51	1.0
30	27.9	0.09	0.27	0.41	0.50	1.0
35	29.0	0.12	0.25	0.41	0.49	1.0
40	30.1	0.12	0.24	0.41	0.49	1.0
45	31.1	0.09	0.26	0.41	0.49	1.0
50	32.1	0.03	0.29	0.41	0.50	1.0
55	33.1	0.00	0.33	0.41	0.52	1.0
60	34.1	0.00	0.37	0.41	0.55	1.1
65	35.2	0.00	0.41	0.41	0.58	1.2
70	36.2	0.00	0.47	0.41	0.62	1.2
75	37.4	0.00	0.48	0.41	0.63	1.3
80	38.6	0.00	0.46	0.41	0.62	1.2
85	39.8	0.00	0.49	0.41	0.64	1.3
90	41.4	0.00	0.36	0.41	0.54	1.1
95	43.3	0.00	0.25	0.41	0.48	1.0

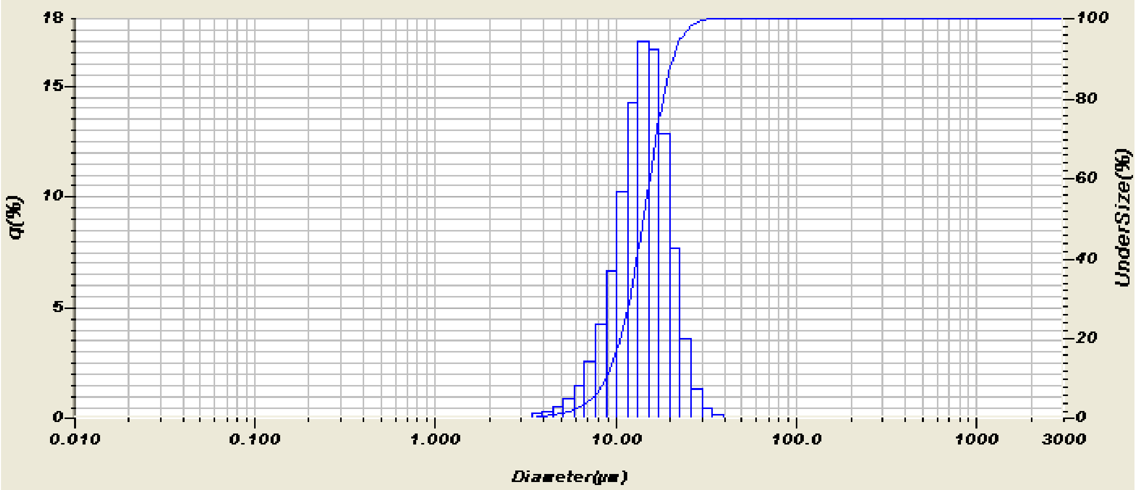
* The cumulative mass fraction finer is the portion of SRM 1003c smaller than the certified diameter value.
** The uncertainty at each percentile, computed according to the ISO and NIST Guides [4,5], is an expanded uncertainty at the 95% level of confidence.

Watch your mixing!

- Had a customer that was measuring a 100 micron polystyrene bead.
- Needed a LOT of sample (1/2 of a bottle) for a test and scattering was very weak.
- Agitation was set low and beads floated to top of cup.
- Set agitation higher to ensure that beads were entrained.
- Also should have considered some surfactant.

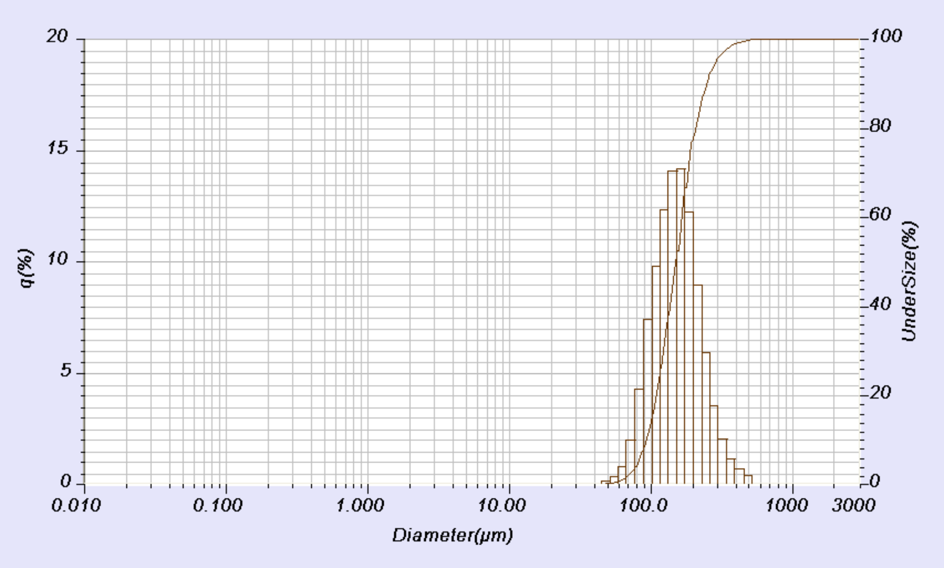
HORIBA LA-960 Data: PS202

PS202 (3-30µm)	D10	D50	D90
Standard Value (µm)	9.14	13.43	20.34
Uncertainty (µm)	0.86	0.86	1.44
ISO standard error	5%	3%	5%
Lower limit (µm)	7.866	12.193	17.955
Measured Result (µm)	9.721	13.916	18.959
Upper Limit (µm)	10.500	14.719	22.869



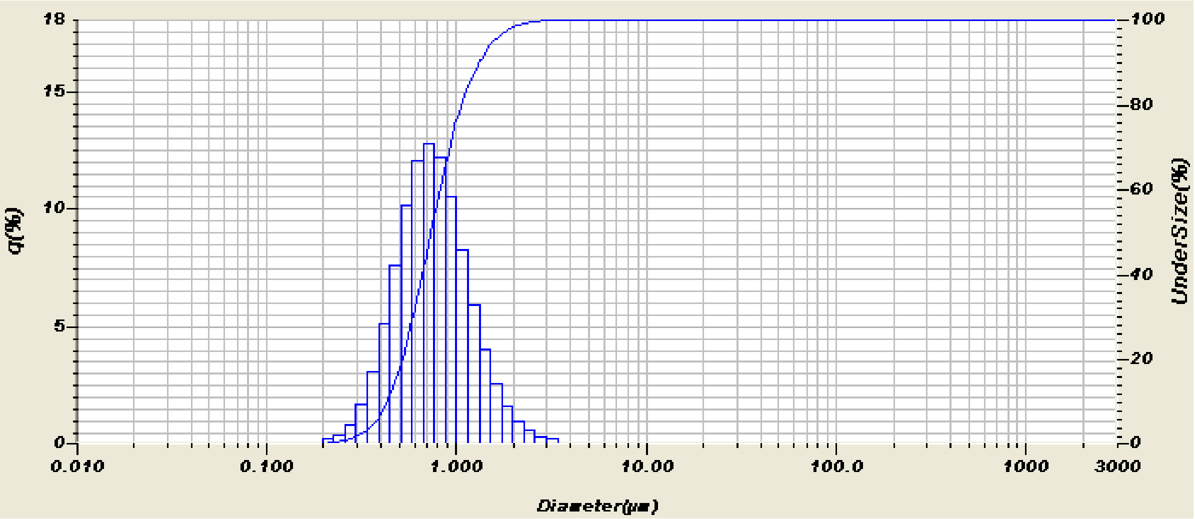
HORIBA LA-950 Data : PS 225

PS225 (50-350μm)	D10	D50	D90
Standard Value (μm)	93.7	150.5	238.8
Uncertainty (μm)	3.54	2.52	6.02
ISO standard error	5%	3%	5%
Lower limit (μm)	85.652	143.541	221.141
Measured Result (μm)	94.217	153.815	252.542
Upper Limit (μm)	102.102	157.611	257.061



HORIBA LA-950 Data : PS 181

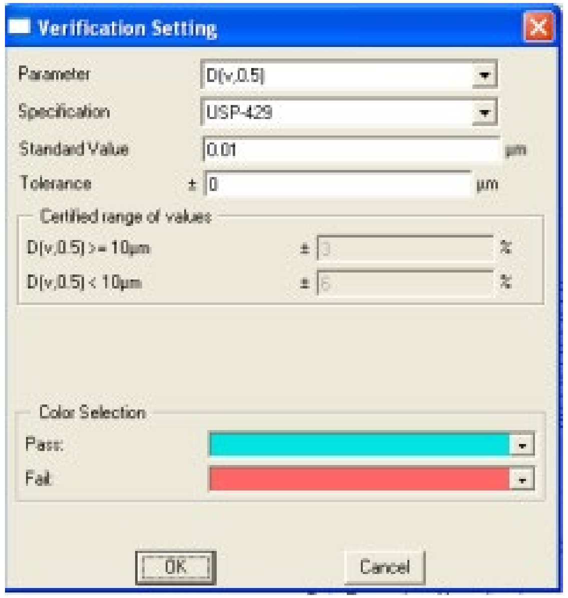
PS181 (0.1-1µm)	D10	D50	D90
Standard Value (µm)	0.36	0.65	1.11
Uncertainty (µm)	0.06	0.06	0.13
ISO standard error	5%	3%	5%
Lower limit (µm)	0.285	0.5723	0.931
Measured Result (µm)	0.434	0.709	1.296
Upper Limit (µm)	0.441	0.7313	1.302

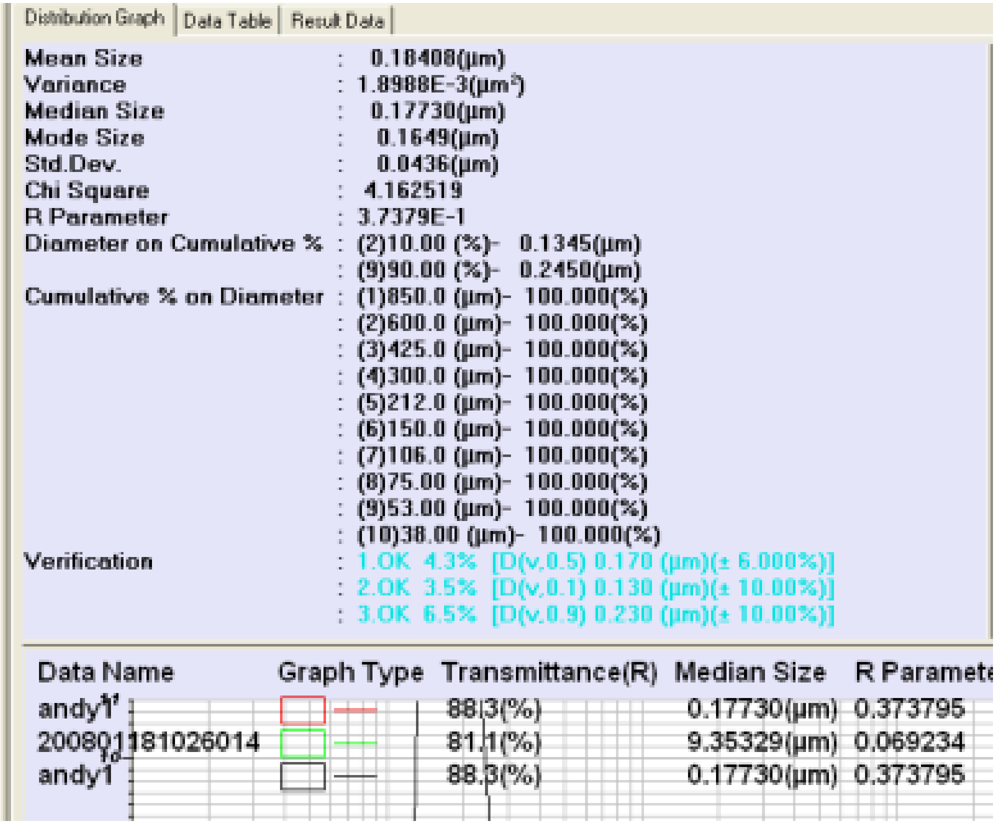


USP<429>

- Used only in the pharmaceutical industry
- Based on ISO 13320
- Broader limits for reproducibility
- Same limits for verification

LA-960 Calculation Automation





Aqueous vs. Solvent

- All results shown were run in H_2O
- What if system is used for solvent?
- Switch over to water – test – back to solvent
- Always form emulsion when switching to H_2O
- Watch your background!
- Test until system passes???

SAMPLE ID	RUN 1	RUN 2	RUN 3	RUN 4	RUN 5	AVG	Spec*
PS-202 in IPA							
D10	9.31	9.32	9.37	9.37	9.37	9.35	7.87 - 10.50
D50	13.87	13.88	13.95	13.96	13.95	13.92	12.19 - 14.72
D90	19.88	19.89	19.98	20	19.97	19.94	17.96 - 22.87
PS-202 in Hexanes							
D10	10.07	10.13	10.16	10.18	10.24	10.16	7.87 - 10.50
D50	14.96	15.05	15.1	15.12	15.21	15.09	12.19 - 14.72
D90	21.37	21.47	21.51	21.53	21.62	21.50	17.96 - 22.87

Passes in IPA

Doesn't in hexane

LA-920 data

Conclusions

- Verify system on a regular basis
  - Current practice: daily to annually
  - Should be risk based decision
    - Run plant on particle size = daily
    - Use for research 3 times/year = annually
- Switch to using polydisperse standards to also test samplers
- Most companies still using monodisperse latex – but be aware of risk and “paper trail” not strong

Thank-you

HORIBA Scientific

Thank you

Thank you

Omoshiro-okashiku
Joy and Fun

감사합니다

Cảm ơn

ありがとうございました

Dziękuję

धन्यवाद

Grazie

Merci

谢谢

நன்ற

ขอบคุณครับ

Obrigado

Σας ευχαριστούμε

Tack ska ni ha

شُكْرا

Большое спасибо

Danke

Gracias