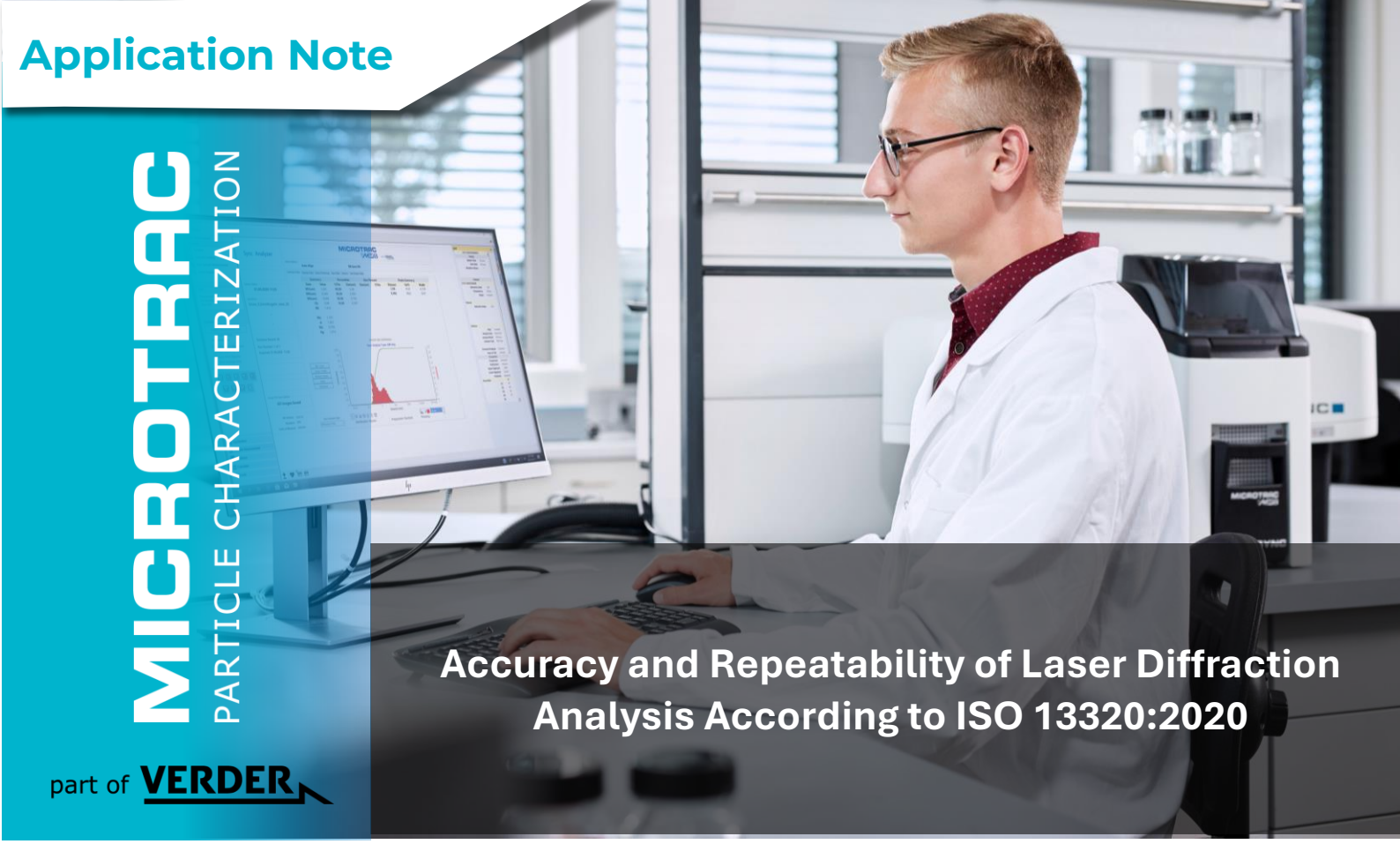
Application Note

MICROTRAC
PARTICLE CHARACTERIZATION

part of VERDER



Accuracy and Repeatability of Laser Diffraction Analysis According to ISO 13320:2020

Introduction

Laser diffraction is a widely recognized technique for particle size analysis in various industries, including pharmaceuticals, chemicals, and materials science. The accuracy and repeatability of this method are critical parameters that ensure reliable and reproducible results. ISO 13320:2020 defines the requirements for particle size analysis using laser diffraction. This standard describes the theory, instrument design principles, the operation, the evaluation and the interpretation of the data. It also includes aspects such as sample preparation and the requirements for the performance of the analyzer in terms of accuracy and reproducibility.

ISO 13320:2020 provides comprehensive guidelines for the application of laser diffraction techniques, emphasizing the importance of using NIST traceable standards to achieve high precision. This white paper explores the concepts of accuracy and repeatability in the context of laser diffraction analysis with MICROTRAC equipment and outlines the role of NIST traceable standards in enhancing measurement reliability.

Laser diffraction is often used in quality control and regular proof of the proper functioning of the measuring equipment is essential. As part of the qualification and validation (IQ-OQ-PQ), the specifications of ISO13320:2020 define the acceptance criteria for laser diffraction measurements.

Microtrac was the first company to develop, produce and launch a commercial laser diffraction analyzer in the 1970s. Since then, Microtrac has stood for technological leadership in the field of particle analysis and has convinced customers from industry and science with innovative solutions.

Diffraction in Particle Analysis

The method of laser diffraction is based on the interaction of a laser beam with a particle collective, which is either dispersed in a liquid or an air stream. The diffraction or scattering

angles into which the laser light is scattered are characteristic of the particle size. Laser diffraction offers many practical advantages in its application, such as:

- **Wide measurement range:** modern laser diffraction analyzers measure particle size distributions from 20 nm to 4 mm, the best results are obtained in the range of 50 nm to 1 mm. Nevertheless, many applications can be operated with it.
- **Versatility:** Dry and wet measurements can be performed, the latter in water or various other solvents. In many cases, sample preparation can be done directly in the instrument.
- **Easy operation:** Thanks to largely automated processes, measurements can be carried out after only a short briefing. The measurements are also fast with a high sample throughput.
- **Robustness:** Laser diffraction instruments are characterized by low maintenance. The method is hardly susceptible to external interference and many devices are in production-related environments.

Despite all the advantages, however, various peculiarities of the method must be considered when interpreting the measurement results.

- **Size definition:** Laser diffraction uses a spherical particle model; the output size is an "Equivalent Sphere Diameter" (ESD). Particle shape cannot be measured.
- **Ensemble technique:** A measurement signal is evaluated that is generated by all particles in any orientation at the same time. Therefore, it is difficult to detect small amounts of oversize and undersize, as these particles only show a small contribution to the overall signal and the signal-to-noise ratio may not be sufficient at the corresponding detectors.
- **Volume distribution:** Laser diffraction outputs volume-based particle size distributions. The evaluation programs of the instruments usually offer a possibility of converting into number-based distributions. However, according to ISO 13320:2020, this is "not permitted"!
- **The sample quantity** is usually small in laser diffraction. Wet samples must be measured in strong dilution. For dry measurements, the sample quantity is usually between 0.1 – 1 g. Sampling errors can easily occur, especially with wide distributions.
- **Material properties:** the optical properties of the particles (refractive index) must be known for the evaluation. For large particles, the so-called Fraunhofer approximation can be applied to evaluate without a refractive index (from approx. 50 µm according to ISO 13320:2020, but in practice the Fraunhofer approximation is often successfully used for smaller particles).

Which measured values are considered?

Many parameters can be derived from a particle size distribution, e.g. mean particle size, standard deviation, span values, mode size, etc. Usually, percentile values are used to describe the size distribution. These are size values at which the cumulative distribution ("sum curve") reaches a certain value. According to ISO13320:2020, for laser diffraction percentile values between 5% and 95% should be reported. For the following tests, ISO 13320:2020 recommends looking at the percentile values at 10%, d 50% and 90%., also referred to as **$D_{10,3}$ / $D_{50,3}$ / $D_{90,3}$** or **$x_{10,3}$ / $x_{10,3}$ / $x_{10,3}$**. At this point, it should be noted that the specification of a $D_{100,3}$ or $x_{100,3}$ value is expressly prohibited in the standard.

Permissible Sample Material for Testing

The ISO13320:2020 defines a set of criteria for sample materials used for accuracy and reproducibility testing as part of equipment qualification. These criteria apply to both certified reference materials (CRM) and non-certified materials, such as in-house standards.

CRMs can be made up of spherical or non-spherical particles. Spherical particles are a good choice because laser diffraction theory is based on spherical model particles and outputs an ESD. In this case, the particle size is independent of the measurement method and the results are directly traceable. Spherical CRMs are usually qualified using methods other than laser diffraction, mostly image analysis. For non-spherical CRMs, qualification must be carried out via interlaboratory (round robin) tests in which suitable laboratories perform laser diffraction analyses.

In-house reference materials can be spherical or non-spherical, and it is a good idea that the composition and size distribution correspond to what is usually measured by the respective user to best reflect the actual analysis conditions. Of course, the measuring instruments used to qualify the in-house standard must first be checked with CRMs.

In addition, the following provisions apply to all reference materials:

- **Distribution width** $x_{90.3} / x_{10.3} = 1.5 – 10$. Therefore, no broad distributions over several orders of magnitude should be considered, nor should you consider strictly monodisperse materials.
- **The aspect ratio** is intended to be no less than 0.5 in any orientation. Needle-shaped or flattened particles should therefore not be used.
- **Optical properties:** it must be an optically homogeneous material with a known refractive index for the wavelengths used.
- **Physical and chemical stability:** The material should not age within the intended period of use. In wet measurements, the particles should retain their properties (no dissolution or swelling) when in contact with the dispersion medium. In dry measurements, the particles should be so robust that they are not destroyed during the measurement.
- **Dispersibility:** A robust protocol must be in place to break up agglomerates and disperse the sample. For wet measurements, this includes the choice of the appropriate dispersion medium, possibly additives (surfactants, sodium phosphate, etc.) and ultrasonic use (power, duration). For dry measurements, this includes the settings for suction and dispersion pressure, as well as sample quantity and feed speed.
- **Sample quantity:** There must be a sufficient, homogeneous amount of material from which representative aliquot can be easily taken.

Repeatability

Repeatability refers to the **consistency of measurement results** when the same sample is analyzed multiple times under identical conditions. High repeatability indicates that the instrument produces reliable results with minimal variation. There are two types of repeatability:

- **instrument repeatability** in which and a sample aliquot is measured at least 6 times in the device (this means: the same particles are measured 6 times). This tests the ability of the instrument to provide consistent measurement data. Possible causes of poor instrument repeatability would be, for example, an error in the circulation system, or another hardware failure.
- **method repeatability**. In which at least 6 different sub-samples of a test material are measured. This checks also the repeatability of sampling and sample preparation.

In both cases, the measurements should be carried out one after the other without major interruptions on the same device, by the same operator with the same methodology and identical settings. This means that for dry measurements, only "method repeatability" is applicable, as sample material is not recovered after analysis. It would be possible to flowable bulk solids in a free-fall setup, but this approach is practically meaningless for laser diffraction. For wet measurements, both types of repeatability can be tested.

Repeatability test can be carried out with any suitable “in-house” material that fulfils the guidelines for suitable test and reference material given in the ISO13320:2020 (see previous chapter).

The x10, x50 and x90 values of the individual measurements should be logged. No individual value in the measurement series should deviate from the mean value of the measurement series by more than a fixed percentage. The corresponding tolerances are listed in the table:

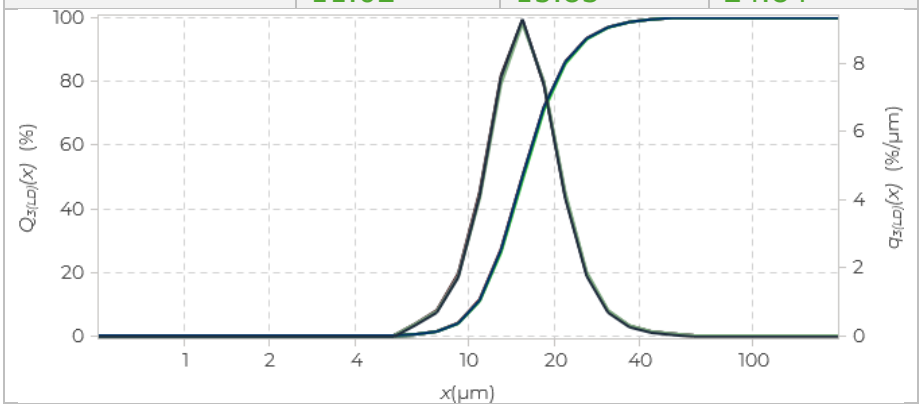
	Instrument repeatability	**Method repeatability**
D10	± 2 %	± 3 %
D50	± 1.5 %	± 2.5 %
D90	± 3 %	± 4 %

The following examples illustrate the excellent instrument repeatability of the MICROTRAC SYNC laser diffraction analyzer.

Instrument repeatability SiC powder (wet measurement)

While the previous example is spherical material, here is the instrument repeatability for a non-spherical SiC powder with a particle size is in a similar range as PS201.

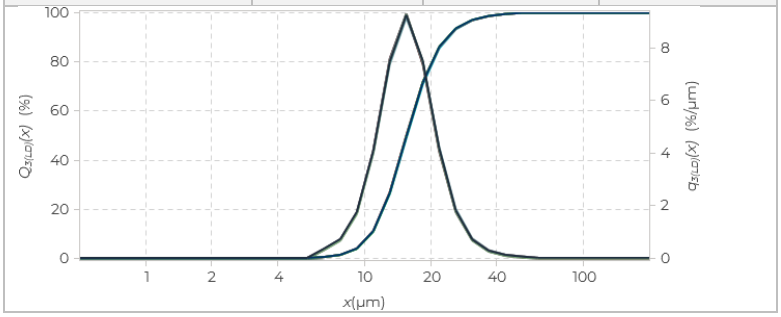
SiC	**D10 (µm)**	**D50 (µm)**	**D90 (µm)**
Run 1	10.78	15.56	23.71
Run 2	10.75	15.53	23.68
Run 3	10.80	15.59	23.76
Run 4	10.82	15.63	23.80
Run 5	10.86	15.70	23.95
Run 6	10.81	15.56	23.74
Mean	10.80	15.60	23.77
SD	0.034	0.056	0.087
CV	0.31 %	0.36 %	0.37 %
Min Tolerance	10.58	15.37	23.06
Max Tolerance	11.02	15.83	24.84



Method repeatability SiC (wet measurement)

Multiple samplings of the SiC powders have been performed to check the method repeatability. Results below.

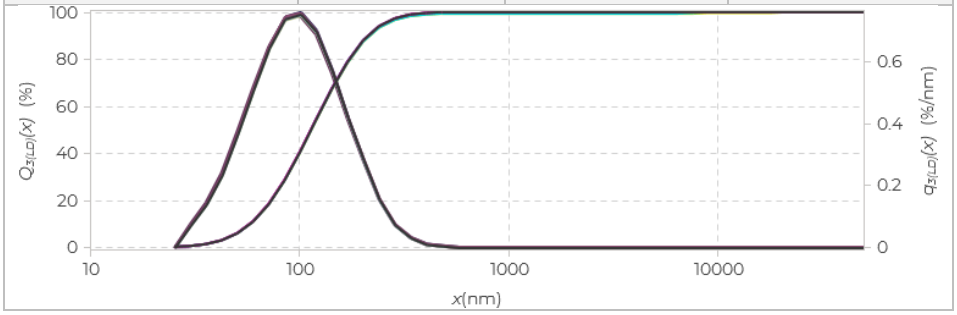
SiC	D10 (µm)	D50 (µm)	D90 (µm)
Run 1	10.86	15.70	23.95
Run 2	10.81	15.56	23.74
Run 3	10.81	15.59	23.74
Run 4	10.81	15.58	23.72
Run 5	10.85	15.61	23.66
Run 6	10.82	15.62	23.68
Mean	10.83	15.61	23.75
SD	0.021	0.045	0.095
CV	0.19 %	0.29 %	0.40 %
Min Tolerance	10.51	15.22	22.80
Max Tolerance	11.16	16.00	24.70



Instrument repeatability Diamond (wet measurement)

This is example shows the instrument repeatability of a fine diamond powder, which is used as a polishing agent. The sample has been prepared with a 200 W ultrasonic probe for 1 minute. For very fine materials, the repeatability is also excellent.

Diamond	D10 (nm)	D50 (nm)	D90 (nm)
Run 1	59.04	115.24	215.94
Run 2	59.64	115.93	218.14
Run 3	59.57	115.68	217.94
Run 4	59.42	115.08	214.25
Run 5	59.34	115.13	214.63
Run 6	59.56	115.54	215.07
Mean	59.43	115.43	216.00
SD	0.2	0.31	1.54
CV	0.34	0.27%	0.71 %
Min Tolerance	58.24	113.70	209.56
Max Tolerance	60.62	117.16	222.52

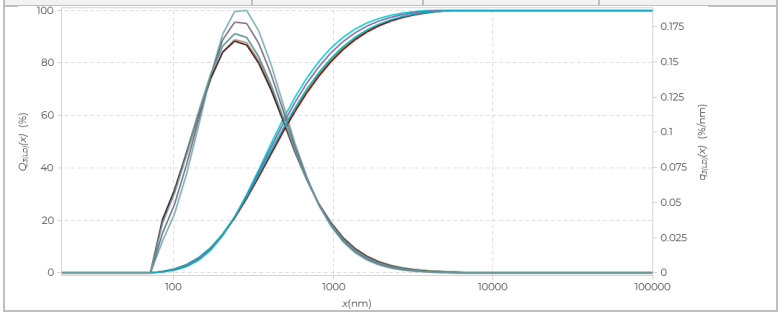


Instrument repeatability Alumina (wet measurement, failed)

Instrument repeatability for an alumina sample. First, the alumina powder was stirred into water and treated with a 200 W ultrasonic probe for 1 minute. A suitable aliquot was

withdrawn from the well-stirred suspension and transferred into the analyzer. The result of 6 consecutive measurements is shown below. The instrument repeatability test is failed!

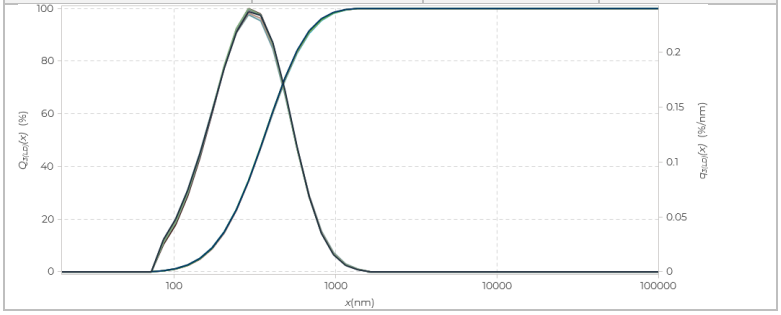
Alumina	D10 (nm)	D50 (nm)	D90 (nm)
Run 1	176.37	451.44	1449
Run 2	174.80	442.57	1406
Run 3	180.64	416.57	1171
Run 4	175.06	452.30	1467
Run 5	178.09	427.68	1269
Run 6	175.12	441.48	1395
Mean	176.68	438.67	1359.5
SD	2.1	12.79	105.4
CV	1.19 %	2.91 %	6.02 %
Min Tolerance	173.15	432.09	1305
Max Tolerance	180.21	445.25	1400



Instrument repeatability Alumina (wet measurement, success)

The above experiment was repeated with slight modification: Both sample preparation and measurement were made in 3 mmol/l sodium pyrophosphate solution. The phosphate stabilizes the suspension and prevents agglomeration. Now, the repeatability test is a success! This shows the importance of good sample preparation. Repeatability tests can help to establish a robust measurement protocol. Note that the d50 and d90 values are significantly smaller than without sodium pyrophosphate due to the more efficient sample preparation.

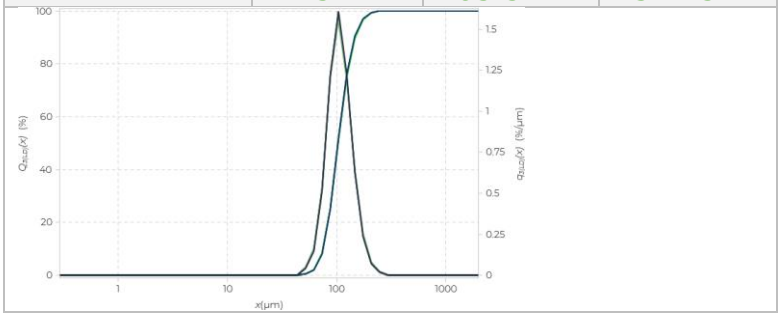
Alumina	D10 (nm)	D50 (nm)	D90 (nm)
Run 1	176.83	357.75	677.06
Run 2	179.42	356.11	665.65
Run 3	177.59	357.36	670.53
Run 4	178.61	356.21	663.29
Run 5	178.00	355.02	664.36
Run 6	177.22	355.96	657.97
Mean	177.95	356.40	666.48
SD	0.87	0.91	6.00
CV	0.49 %	0.26 %	0.90 %
Min Tolerance	174.39	340.22	646.49
Max Tolerance	181.51	361.75	686.47



Method repeatability: Corundum (dry measurement)

The same requirements and tolerances apply to dry measurements as to wet measurements. However, only a determination of method repeatability is possible, because the sample is passed through the device in an air stream, and generally cannot be recovered. Measurements in freefall with almost 100% recovery are conceivable but have no practical relevance for laser diffraction analysis. The example shows the method repeatability using a corundum sample with a d50 of about 100 µm, a typical sample that can be analyzed well with laser diffraction dry.

Corundum	D10 (µm)	D50 (µm)	D90 (µm)
Run 1	75.95	103.95	148.32
Run 2	75.87	103.57	147.46
Run 3	75.93	103.61	147.52
Run 4	76.07	103.59	149.43
Run 5	75.78	104.07	146.82
Run 6	76.33	103.70	147.80
Mean	75.99	103.75	147.89
SD	0.18	0.19	0.82
CV	0.23 %	0.19 %	0.55 %
Min Tolerance	74.47	102.19	143.37
Max Tolerance	77.51	105.31	152.23



Instrument Accuracy

Accuracy refers to the degree to which a measurement aligns with the true value or accepted reference standard. In the context of laser diffraction, accuracy is determined by comparing the particle size distribution obtained from the instrument with known, traceable standards. On the calibration certificates of such materials, the measured values including the uncertainty, are usually at a 95 % confidence interval.
In the instrument accuracy test, the measurements are to be carried out within a short time interval on the same instrument by the same operator using the same method.

ISO 13320:2020 outlines specific protocols for verifying the accuracy of laser diffraction instruments. These protocols include:

- Using certified reference materials (CRMs) with known particle size distributions.
- Performing regular instrument checks and calibrations as per the manufacturer's recommendations.
- Documenting and reviewing the calibration and verification processes to ensure traceability and compliance.

ISO 13320:2020 states that the final limits shall be calculated from the joined standard uncertainty (standard deviation) of the certified material $u_{\mathrm{crm}}$and the standard uncertainty of the diffraction system u_{p}:

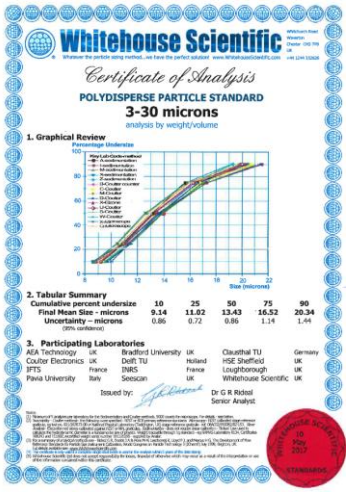
$$U_{\mathrm{lim}} = CF \pm \sqrt{u_{\mathrm{crm}}^2 + u_{\mathrm{p}}^2}$$

Parameter	Maximum acceptable instrument uncertainty	Coverage factor, CF
D10	< 2 %	2-3
D50	< 1.5 %	2-3
D90	< 2.5 %	2-3

Table 1 Parameters for the calculation of the tolerance limits as listed in ISO13320:2020.

The coverage factor is a numerical factor used in measurement uncertainty analysis to widen the uncertainty interval to a specific confidence level. Typically, this confidence level is chosen to be 95%, but it can vary depending on the requirements. The coverage factor is determined by the desired confidence level and the distribution of the uncertainty components. For normally distributed uncertainties, a coverage factor of 2 approximately corresponds to a 95% confidence level, meaning there's about a 95% chance that the true value lies within the expanded uncertainty range.

For our test of accuracy, the CRM "PS201" from the company Whitehouse Scientific was used. These are glass spheres in a size range of 3 µm – 30 µm.


Whitehouse Scientific

Certificate of Analysis

POLYDISPERSE PARTICLE STANDARD

3-30 microns

analysis by weight/volume

1. Graphical Review

2. Tabular Summary

Cumulative percent undersize	10	25	50	75	90
Final Mean Size – microns	9.14	11.02	13.43	16.52	20.34
Uncertainty – microns	0.86	0.72	0.86	1.14	1.44

3. Participating Laboratories

AEA Technology	UK	Bradford University	UK	Clausthal TU	Germany
Coulter Electronics	UK	Delft TU	Holland	HSE Sheffield	UK
IFTS	France	INRS	France	Loughborough	UK
Pavia University	Italy	Sesscan	UK	Whitehouse Scientific	UK

Issued by: Dr G R Rideal, Senior Analyst

	Percentile				
Laboratory	**10**	**25**	**50**	**75**	**90**
A	8.63	10.85	13.18	15.61	19.90
I	8.80	11.21	13.94	16.96	20.16
M	8.70	10.82	13.78	17.01	20.41
X	8.60	10.98	13.70	16.72	19.93
Z	9.50	11.36	13.65	16.34	19.29
Mean	**8.85**	**11.04**	**13.65**	**16.53**	**19.94**
SD*	0.33	0.21	0.25	0.52	0.37
B	9.17	10.93	13.27	16.36	20.14
C	9.33	11.09	13.44	16.79	20.69
M	8.77	10.47	12.69	15.81	19.76
D	9.70	11.51	13.85	17.20	21.40
X	9.24	11.03	13.55	17.28	21.51
U	9.19	10.92	13.21	16.22	20.01
S	9.59	11.47	13.91	17.20	21.18
W	8.75	10.42	12.59	15.74	19.19
Mean	**9.21**	**10.98**	**13.33**	**16.58**	**20.49**
SD*	0.32	0.37	0.45	0.59	0.79
X	10.0	11.6	13.7	16.6	20.4
O	9.1	10.7	13.0	15.9	21.1
Mean	**9.6**	**11.2**	**13.4**	**16.3**	**20.8**
$X_{(n=15)}$	**9.14**	**11.02**	**13.43**	**16.52**	**20.34**
XS_n	0.41	0.35	0.41	0.55	0.69
XS_{n-1}	0.43	0.36	0.43	0.57	0.72
95% confidence	**0.86**	**0.72**	**0.86**	**1.14**	**1.44**

Excerpt from the certificate of a PS201 standard.

The permissible limits are calculated as follows for the D50 value as an example:
The standard deviation is indicated on the certificate as 0.43 µm, thus u_{CRM} = 0.43 µm.
The uncertainty u_p of the system is calculated from the certified D50 value and the maximum permissible uncertainty of 1.5 %, thus. u_p = 13.43 µm * 0.015 = 0.20 µm.
If the values are inserted into the formula above and multiplied by CF=2, the measured values may deviate by +/- 0.95 µm from the certified value.

$$u_{lim} = \pm 2\sqrt{0.43^2 + 0.20^2}$$

PS201	Mean (µm)	Certified uncertainty, standard deviation (µm)	Lower Limit (µm)	Upper Limit (µm)
D10	9.14	0.43	8.21	10.07
D50	13.43	0.43	12.48	14.38
D90	20.34	0.72	18.58	22.10

Certified values according to the Certificate of Analysis of the PS201 standard. Limits are calculated using a coverage factor of CF=2 and the maximum acceptable instrument uncertainty as listed in Table 1.

For the following example of verifying the accuracy of the measurements, the certified material PS201 from Whitehouse Scientific was used. The samples are packed in individual vials, each containing 0.1 g of powder. This amount is just enough for a wet measurement with the SYNC. Larger aliquots are also available, but it must be strongly advised against taking samples randomly from a larger quantity, as the sampling error is inevitable.
ISO 13320:2020 stipulates that at least 3 aliquots should be used to determine the accuracy, but preferably 5.
Accordingly, five bottles are tested separately in this case. The average of all tests must be compared with the calculated limits.

PS201	D10 (µm)	D50 (µm)	D90 (µm)
Bottle 1	9.36	13.00	20.46
Bottle 2	9.02	12.95	20.08
Bottle 3	9.30	13.43	20.07
Bottle 4	9.26	13.41	20.02
Bottle 5	9.06	13.21	18.86
Average	9.20	13.20	19.90

Percentiles as measured for different samples on the same machine

Accuracy under intermediate precision conditions (or: the influence of location and operator)

In addition to pure instrument accuracy, it is often of interest to evaluate the results obtained by operators with different levels of expertise, or even instruments at different locations Such tests can be carried out with CRMs, but also with sufficiently qualified "in-house" reference materials may be used. These tests have high practical relevance, as CRMs are not always available in the size ranges of the users' sample material and a larger number of possible "sources of error" that can occur during an analysis will be checked.

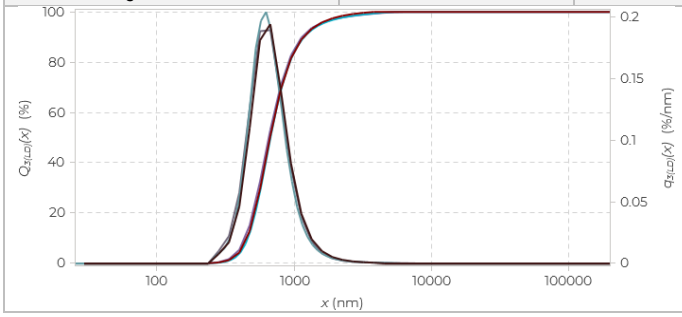
This procedure can be used to test:

1. Instrument-to-instrument comparability
2. Ability of operators
3. Comparability of sample preparation
4. Comparability of sampling / sample splitting

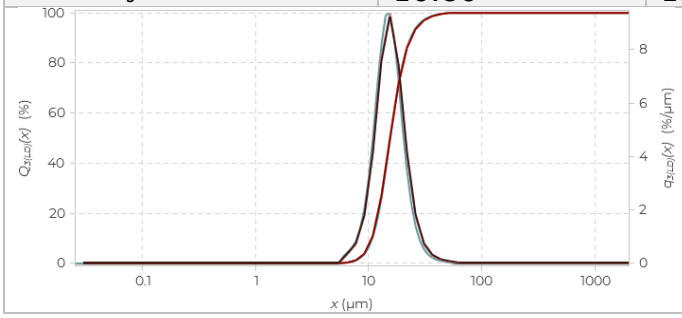
In the following examples, different samples were tested on three different SYNC devices at different locations (USA, Japan, Germany) by various users.

The results shown there were determined in the context of round robin tests, which are carried out by the German Federal Institute for Materials Research (Bundesanstalt für Materialforschung, BAM) at regular intervals. Microtrac laboratories and analyzers achieve excellent scores in these tests, which underlines the reliability of the measurement technology.

Barium Titanate	**D10 (µm)**	**D50 (µm)**	**D90 (µm)**
Japan	0.451	0.669	1.17
USA	0.466	0.679	1.19
Germany	0.460	0.684	1.18



SiC	**D10 (µm)**	**D50 (µm)**	**D90 (µm)**
Japan	10.86	15.64	23.55
USA	10.78	15.51	23.59
Germany	10.80	15.60	23.79



Summary

Laser diffraction is a recognized technique for particle size analysis across various industries, including pharmaceuticals, chemicals, and materials science. The accuracy and repeatability of this method are essential for ensuring reliable and reproducible results. ISO 13320:2020 defines the requirements for particle size analysis using laser diffraction, covering the theory, instrument design, operation, data evaluation, and interpretation, along with sample preparation and analyzer performance.
Microtrac, as a pioneer in developing and launching the first commercial laser diffraction analyzer in the 1970s, has been at the forefront of technological advancements in particle analysis. Examples of repeatability and accuracy tests using MICROTRAC SYNC laser diffraction analyzers showcase the instrument's reliability across different materials.
ISO 13320:2020 also addresses instrument accuracy, defining it as the alignment of measurements with true values or accepted reference standards This article presents examples that demonstrate the MICROTRAC SYNC analyzer's precision.