Technical
Specification

ISO/TS 5973

Laser diffraction measurements — Good practice

Mesures par diffraction laser — Bonnes pratiques

First edition
2024-07

Reference number
ISO/TS 5973:2024(en)

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights.

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 24, *Particle characterization including sieving*, Subcommittee SC 4, *Particle characterization*.

Any feedback or questions on this document should be directed to the user’s national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

The laser diffraction technique has evolved such that it is now a dominant method for determination of particle size distributions (PSDs). The success of the technique is because it can be applied to a wide variety of particulate systems. The technique is fast and can be automated, and a variety of commercial instruments are available. Nevertheless, the proper use of the instrument and the interpretation of the results require caution. ISO 13320 has had multiple revisions to date and covers the principles of the technology and information on evaluating the accuracy of the instrument with a view to qualification. ISO 13320 does not, however, cover the use of the technology on samples in great detail, and therefore, this document is intended to be used in conjunction with ISO 13320, as this document provides practical advice for the measurement of real samples, guidance on obtaining consistent results with good quality data and data interpretation.

Laser diffraction measurements — Good practice

1 Scope

This document gives guidance on the determination criteria for when laser diffraction is the most appropriate method for the analysis of samples, the appropriate preparation of samples, the verification of the correct functioning of instruments, the interpretation of data, and the assessment of data quality. This document focuses on the practical steps needed to obtain results of good quality, rather than on theoretical considerations, and covers not only the measurement of solid particles (in wet and dry measurement configurations), but also emulsions and bubbles. Result variation expectations of real samples are also considered in this document.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
absorption
reduction of intensity of a light beam not due to *scattering* (3.14)

[SOURCE: ISO 13320:2020, 3.1.1]

3.2
accuracy
closeness of agreement between a test result or measurement result and the true value

Note 1 to entry: In practice, the accepted reference value is substituted for the true value.

Note 2 to entry: The term “accuracy”, when applied to a set of test or measurement results, involves a combination of random components and a common systematic error or bias component.

Note 3 to entry: Accuracy refers to a combination of trueness and *precision* (3.8).

[SOURCE: ISO 3534-2:2006, 3.3.1]

3.3
intermediate precision
precision (3.8) under *intermediate precision conditions/reproducibility conditions* (3.4)

Note 1 to entry: Reproducibility is an alternative term for intermediate precision used in a specific case where a comparison of different instruments in different locations is required.

[SOURCE: ISO 3534-2:2006, 3.3.15, modified — Note 1 to entry has been added.]

3.4
intermediate precision conditions

<laser diffraction> measurement conditions where independent test results or measurement results are obtained on different laser diffraction instruments and in different test or measurement facilities, with different operators using the same prescribed method

Note 1 to entry: There are four elements to the operating condition: time, calibration, operator and equipment. Tests involving varying the first three are technically intermediate *precision* (3.8) tests, most notably when the operator is changed, however when the equipment location is varied then it is a reproducibility test.

Note 2 to entry: Method transfer between sites is a test of reproducibility. The conditions described above would be termed reproducibility conditions in this case.

[SOURCE: ISO 13320:2020, 3.1.11, modified — the conditions to different equipment and measurement facilities have been expanded.]

3.5
multiple scattering

consecutive *scattering* (3.14) of light by more than one particle, causing a *scattering pattern* (3.15) that is no longer the sum of the patterns from all individual particles

[SOURCE: ISO 13320:2020, 3.1.12]

3.6
transmission

<particle size analysis> fraction of incident light that remains un-attenuated by the particles

Note 1 to entry: Transmission can be expressed as a percentage.

Note 2 to entry: When expressed as fractions, *obscuration* (3.7) plus transmission equals unity.

[SOURCE: ISO 13320:2020, 3.1.29]

3.7
obscuration

fraction of incident light that is attenuated due to extinction [*scattering* (3.14) and/or *absorption* (3.1)] by particles

Note 1 to entry: Obscuration can be expressed as a percentage.

Note 2 to entry: When expressed as fractions, obscuration plus *transmission* (3.6) equals unity.

[SOURCE: ISO 8130-13:2019, 3.1, modified — words "percentage" and "during a laser diffraction measurement" have been removed from the definition and Notes 1 and 2 to entry have added.]

3.8
precision

closeness of agreement between independent test/measurement results obtained under stipulated conditions

Note 1 to entry: Precision depends only on the distribution of random errors and does not relate to the true value or the specified value.

Note 2 to entry: The measure of precision is usually expressed in terms of imprecision and computed as a standard deviation of the test results. Less precision is reflected by a larger standard deviation.

Note 3 to entry: Quantitative measures of precision depend critically on the stipulated conditions. *Repeatability conditions* (3.10) and reproducibility conditions are particular sets of extreme stipulated conditions.

[SOURCE: ISO 3534-2:2006, 3.3.4, modified —"measurement results" has been removed from Note 2 to entry.]

3.9

repeatability

precision (3.8) under *repeatability conditions* (3.10)

Note 1 to entry: Repeatability can be expressed quantitatively in terms of the stability characteristics of the particulates in the *dispersing medium* (3.17).

[SOURCE: ISO 3534-2:2006, 3.3.5, modified — "dispersion characteristics of the results" has been replaced with "particulates in the *dispersing medium*" in Note 1 to entry.]

3.10

repeatability conditions

observation conditions where independent test/measurement results are obtained with the same method on identical test/measurement items in the same test or measuring facility by the same operator using the same equipment within short intervals of time

Note 1 to entry: Repeatability conditions include:

- the same measurement procedure or test procedure;
- the same operator;
- the same measuring or test equipment used under the same conditions;
- the same location;
- repetition over a short period of time.

[SOURCE: ISO 3534-2:2006, 3.3.6]

3.11

instrument repeatability

closeness of agreement between multiple measurement results of a given property in the same aliquot of a sample under *repeatability conditions* (3.10)

Note 1 to entry: The variability includes the variability from only the instrument itself.

3.12

method repeatability

closeness of agreement between multiple measurement results of a given property in different aliquots of a sample, executed by the same operator using the same instrument under identical conditions within a short period of time

Note 1 to entry: Various pharmaceutical monographs dictate the measurement of six separate preparations.

Note 2 to entry: The variability includes the variabilities of the sub sampling technique, the sampled material, the sample handling when adding the sample to the instrument and the instrument itself.

Note 3 to entry: Method repeatability is usually determined as standard deviation of a number of measurement results

[SOURCE: ISO 13320:2020, 3.1.22, modified — "the sample handling when adding the sample to the instrument" has been added to Note 2 to entry, and Notes 1 and 3 to entry have been added.]

3.13

optical properties

refractive index and absorption parameters used in the analysis of the sample

3.14

scattering

change in propagation of light at the interface of two media having different *optical properties* (3.13)

[SOURCE: ISO 13320:2020, 3.1.23]

3.15
scattering pattern
angular pattern of light intensity, $I(\theta)$, or spatial pattern of light intensity, $I(r)$, originating from *scattering* (3.14), or the related readings of energy values taking into account the sensitivity and the geometry of the detector elements

[SOURCE: ISO 13320:2020, 3.1.25, modified with addition of “readings of”]

3.16
single scattering
scattering (3.14) whereby the contribution of a single member of a particle population to the total *scattering pattern* (3.15) remains independent of the other members of the population

[SOURCE: ISO 13320:2020, 3.1.26]

3.17
dispersing medium
liquid or gas used to suspend particles during measurement that reduces their concentration for measurement

Note 1 to entry: For measurements in liquid, the term "diluent" is often used as a synonym for dispersing medium.

4 Symbols

$x_{10,3}$	particle diameter corresponding to the 10th percentile of the cumulative volume undersize distribution (by volume)
$x_{50,3}$	median particle diameter corresponding to the 50th percentile of the cumulative volume undersize distribution (by volume)
$x_{90,3}$	particle diameter corresponding to the 90th percentile of the cumulative volume undersize distribution (by volume)

NOTE The term $D_{y,3}$ is often used instead of the $x_{y,3}$ where y is the 10th, 50th or 90th percentile as defined above.

5 Laser diffraction experiment and measurement

The schematic of the laser diffraction experiment assumed throughout this document is covered in ISO 13320:2020, Figures 1 to 4.

Prior to any measurement, the optical system is normally aligned so that most of the light passes straight through the system where its scatter can be measured on the obscuration monitor. The dispersing medium (gas or liquid) is added via a sample dispersion unit which is often an additional apparatus (or ‘accessory’), separate to the optical instrument itself. The particulate sample is not yet added to the sample dispersion unit in that stage. The system is designed so that any scattered light signals are measured by the light detectors.

Typically, the background scattering of the dispersing medium is then measured, whether gas or liquid, in the absence of the particulate sample to be measured. The particulate sample is then added to the sample dispersion unit and the scattering from both the sample and dispersing medium is measured. The previously recorded dispersing medium background scattering signal is then subtracted in software to yield only the scattering from the particulate fraction. Both single pass dry measurements, where the dispersing medium is a gas, typically air, and recirculating or single pass wet measurements, where the dispersing medium is a liquid, often water, iso-propyl alcohol, hexane or paraffinic oils for example, are in common use. Many measurements are taken and a final average light scattering pattern is then obtained. This is then converted into a volume size distribution using a light scattering theory (normally Mie or Fraunhofer theories). For a more comprehensive outline of the measurement process, see ISO 13320:2020, Clause 4. A risk-based approach to the whole laser diffraction measurement process was conducted as part of the Horizon 2020 project PAT4Nano and this has been summarized in Annex A below as it contains much useful information regarding the laser diffraction measurement process.

6 Information recommended collecting prior to analysis

6.1 Sample information

The customer or submitter of a sample for laser diffraction analysis should provide, as available, all information relevant to the measurement of their sample. Absence of information does not preclude analysis, but availability of information can aid the analyst with respect to sample preparation, measurement design and interpretation of results. In general, the more information known about a sample, the more likely the analysis will be successful and the results meaningful for the customer. This information also reduces uncertainty for the overall measurement process.

The following questions should be answered where possible, some are specific to measurements in a diluent, termed wet measurement and some are specific to measurement in air, termed dry measurement (in order of relative importance):

a) What is the principal mineral or chemical composition or polymorphic form of the sample?

  1) If the particle size is large (over 50 µm) and/or the particles are opaque, optical parameters (refractive index) of the sample are not needed necessarily.

  2) If the particles are small and or transparent, the optical properties of the sample are more relevant. If the refractive index is not known exactly, an estimation of the effective refractive index can be used instead.

  3) If the crystallographic phase is known, this should be noted, as it influences the appropriate refractive index to be used (if Mie theory is employed).

  4) The composition will determine the scattering properties and the refractive index, amongst other properties.

  5) What is the density of the sample? Has a Stokes' Law calculation been carried out to show the settling rate for particles of different sizes? Density is needed if specific surface area estimates need to be calculated.

b) What is the diluent / dispersing medium?

  1) (wet measurements) If the sample requires dilution, the dispersing medium should be compatible with the sample, i.e. it should not react with or dissolve particles in the sample. If needed a technique such as HPLC can be used to check that no dissolution has occurred. The dispersing medium should ideally be compatible with the laser light source(s) used by the instrument i.e. should be non-absorbing at the wavelength(s) used.

  2) (wet measurements) The refractive index of the medium is necessary for analysis (if Mie theory is employed), though what the medium consists of should be noted even if Fraunhofer theory is employed so the measurement can be recreated later.

  3) (wet measurements) Does the medium contain surfactants or additives that are necessary to wet and/or disperse the particles and prevent agglomeration / coalescence over the time frame of the measurement? If so, identify the surfactant or additive and its concentration and be prepared to add this to the dispersing medium prior to measurement to prevent agglomeration / coalescence. This instability can also occur if there was a substantive pH change upon addition to the dispersing medium. This can point to the Zeta Potential of the sample being an issue. ISO/TR 19997 provides advice on how to measure this parameter.

  4) (dry measurements) Is the air supply fitted with moisture / oil / particle traps? Have these been regularly serviced? If the powder is cohesive, is it statically charged, so can the dry feeder unit be earthed?

    5) (dry powder, measured wet) The mechanism of the addition of any surfactant is also important. In many cases, it should be added to the dry powder, lightly stirred to make a paste and then added to the system. A paste also serves as a method of taking a subsample from the paste with a spatula in order to match a target obscuration.

c) (wet measurements) What is the mass concentration of the sample (e.g. 0,01 mg/ml)? This can potentially point to the degree of dilution needed.

d) Is the sample coated? (e.g. is there a polymeric coating, ligand, surfactant, etc. that modifies the surface functionality and stability). This can provide early pointers to the ease of wettability and help suggest stabilizers / means of dilution, or potential difficulty of dry dispersion.

e) Is the sample polydisperse (e.g. does it contain multiple size populations or a very broad size range, is it agglomerated)? The sample's polydispersity will point to the need to obtain a representative sample and the optical configuration that can need to be employed (if there is a choice).

    1) Provide any available information about degree and nature of polydispersity.

    2) Can details on how the sample supplied was taken from the bulk sample be provided?

f) What is the approximate or anticipated mean size of the sample particles, if known?

g) How was the sample prepared (e.g. milled, ultrasonically dispersed, synthesized in situ)?

h) Are special conditions necessary for sample storage and sample preparation before analysis (e.g. refrigerated, in dark). Is there any potential deleterious storage effects such as agglomeration, coalescence or Ostwald ripening that should be considered?

i) Are the principal particles highly asymmetric? (e.g. rod-like). If any images exist, attach them.

j) Is the sample material subject to dissolution? Is it friable? Knowing this information will guide the choice of the dispersing medium and whether to use sonication (wet) and air pressure (dry).

k) Has the safety data sheet for the material been supplied and consulted for the safety information therein? Does the sample have special handling conditions associated with it, such as toxicity or carcinogenicity? Is personal protection equipment needed?

l) Are the particles expected to be homogenous? Proteinaceous samples, for example, are not homogeneous whereas a simple polystyrene latex would be expected to be free from inclusions within each particle.

m) Is the sample material optically active, such as being bi-refringent or fluorescent? If so, then this can mean that laser diffraction is not an appropriate technique, or that the optical properties used in the analysis must be carefully chosen.

n) Is the material cohesive? Its cohesiveness impacts the difficulty of dispersal by dry means and also points to the need to wet and to potentially sonicate the sample for wet analysis. Of course, if the primary size is not of interest, the sample can be measured as is (see 6.2).

6.2 Desired outcome of analysis

In addition to providing the analyst with basic information about the sample, it is equally important for the customer or submitter to indicate the purpose of the analysis. This information will determine the level of effort expended and aids the analyst in experimental design. The following questions should be answered.

a) The results obtained for the sample vary depending on the needs of the analyst. If information related to the state of agglomeration is desired, care should be taken to disperse the sample as gently as possible to preserve the agglomerated state (enough pump and stir in the tank to suspend the material but not to disperse it, or low air pressure for dry measurement). If the primary particle size is needed, then care should be taken to disperse the material [but not dissolve or damage (fracturing by ultrasound, too high an air pressure) in any way]: a titration over pump-stirrer or ultrasound settings looking for a stable sample can be necessary, with final, selected settings that have an appropriate factor of safety over and above values where setting-dependent effects are seen in the reported particle size distribution of the sample. This avoids measuring the sample too close to a ‘performance edge’ and reduces overall systematic and random uncertainty in the final particle size distribution.

b) Is this analysis related to quality control, research and development, or product characterization?

   1) Quality control (QC) applications typically require less stringent analysis; relative changes compared to a control, for instance, can require only a mean size determination. “Is this the same as yesterday”.

   2) Research and development (R&D) or product characterization can require higher levels of data quality depending on the application need.

   3) Analysis in a regulated environment (normally the pharmaceutical industry) strictly adheres to a prescribed method, and any retesting is strictly controlled.

   4) In all of these cases, care should be taken to ensure the sampling is consistent. Inconsistent sampling can lead to poor conclusions about the process. The more polydisperse a sample is, the more important that care is taken in obtaining a representative sample (see 6.4).

c) How many repeat measurements are needed? Will more than one sample be tested?

   NOTE Many pharmaceutical regulations can require the measurements of up to six independent samples.

d) What type of dispersion is needed? If the sample is to be used dry or has been dry milled, then dry analysis is likely to be most appropriate (especially true, if the state of agglomeration or the powder flow properties of the sample are of interest). If the sample is to be used wet or has been wet milled, then wet analysis is likely to be most appropriate (especially true if the primary particle size is of interest). Finer samples, especially where the distribution is predominantly sub-micrometres, are often best measured wet due to their cohesive nature of the product. For example, if the level of fines needs to be examined, the $x_{50,3}$ or the percentage below a size in the low micrometres area can be of interest. If tight control is needed, specifications should be tighter than when a broad indicative value is needed.

6.3 Other sample considerations

There are many relevant properties of powders which affect the preparation of the sample for laser diffraction analysis, such as powder flow properties and powder cohesion, particle segregation, particle density, particle fragility, the electrostatic charge on the particle, particle surface wettability, swelling and solubility in liquids.

Powders can be free-flowing or cohesive. Typically, dry powders containing near-spherical particles greater than about 20 µm are reasonably free flowing or slightly cohesive. Powders with smaller sizes or damp powders are cohesive. Particle shape also can have a significant influence on powder flow properties. For example, highly acicular particles, like fibres or flakes, hamper flow properties. Free-flowing powder properties lead in case of increasing PSD widths to greater possibilities for particle segregation, which in turn leads to greater challenges for obtaining representative test samples. Cohesive powders do not show a tendency for segregation, so that adequate blending can minimize any heterogeneity that is caused by fluctuating PSDs coming from the production process. Thus, well-blended cohesive powders that can be split and dispersed easily show optimum precision in tests of particle sizing instruments.

If the powder samples are toxic or highly reactive in air, then wet dispersion may be preferable on the grounds of safety considerations. This is especially true if the sample is toxic and fine / potentially inhalable (less than 10 µm).

Materials containing acicular particles (having small aspect ratios) can be more suited to image analysis based sizing techniques than light scattering based techniques especially if there is any flow alignment occurring.

For emulsions and suspensions, knowledge on stability, stabilizing agents and behaviour of particle sedimentation and creaming is important. The samples are likely to require dilution for laser diffraction measurement, and knowledge of this will influence the diluent. If the diluent has the same pH, ionic strength, stabilizer concentration as the bulk liquid, dilution is more likely to proceed without aggregation.

The best diluent however is spun off or filtered bulk liquid that is particle free. Solid particles greater than about 10 µm and having a high density settle fast in media having a low viscosity, like water, so the sample presentation conditions (pump/stir) need to be carefully selected to avoid bias. Dispersions of small air bubbles in water can be very stable, especially in the presence of surfactants.

6.4 Best sampling practice prior to laser diffraction measurements

6.4.1 General

Typically, small portions of powder are applied to characterize the quality of much larger material batches. This requires that the test samples are representative for the batch of material within stated limits. ISO 14488 sets the standards for and gives background and advice on the sampling procedures. Typically, the sampling comprises different steps: the primary samples taken from large batches are usually too large for measurement and, thus, must be split to form test samples. The primary sampling step from large batches is often a major error source in the final PSD result, especially for segregated batches of material that have a wide size distribution. The degree of segregation should be investigated through analysing test samples coming from primary samples taken at different locations in the batch. Having established the degree of segregation, test samples should be prepared from a gross sample composed from an appropriate number of sample increments having about equal masses.

For statistical reasons, test samples should contain enough particles to reach a stated precision for the PSD. Poisson statistics show that small particle numbers cause low precision for the PSD characteristics. This may, for example, be the case at the upper end of broad volume-based PSDs, because particle volume relates to the particle size cubed. It is especially true at large $x_{90,3}/x_{10,3}$ ratios.

6.4.2 Sampling of powders

The 'golden rules' for sampling are as follows.

- The material should be sampled when it is well-mixed.
- The material should be sampled when it is in motion.
- Care should be given during sampling to avoid fluctuations that adversely influence the collection of a representative particle size. Sample the whole cross-section of particulate flow; do not stop the flow.
- The sampling container should be designed large enough and without constraints.
- The sampling container should not be overfilled.
- A rotary sample splitter should be used for optimum precision, wherever possible.
- Validated procedures should be used for all sampling steps.
- Representative test samples should be used for material characterization.
- Sampling errors should be quantified through the analysis of multiple samples and then minimized through the analysis of a test sample coming from a bulk sample.
- A specific and well-documented sampling protocol should be made for each product.

Produced materials are usually stored in e.g. heaps, silos or bags. Therefore, primary samples are often collected from those stored batches, despite the recommendation of sampling material when it is in motion. Large batches of material can be brought into motion in e.g. blender silos, followed by transport belts or pipelines and then sampled. For fairly small batches, the best way is to apply spinning rifflers that are available for different amounts of material, from about 1 g to 1 kg. Such rifflers cause – for reasonably flowing materials – much smaller errors than other sampling means.[10] Alternatively, small quantities of dry powders may be divided following the addition of a few drops of surfactant solution, blending the resulting paste by means of a spatula and then splitting it with the spatula.

Manual means of primary sampling in dry particulate batches – e.g. by means of the widely used sample thief – often lead to significant errors, due to particle segregation and selective access to the sampler. Scoop sampling from the top of a segregated batch is much worse. Sampler errors can be identified through sampling and analysis of small material portions that have a known size distribution. The degree of segregation in a batch can be identified and quantified through analysis of samples coming from different regions of the batch with an appropriate technique. Since the uncertainty in the average result of analysis of N separate sample measurements is reduced by a factor $1/\sqrt{N}$ in comparison to a single analysis, these data also can lead to the number of primary samples that must be taken from the batch to reach a desired maximum uncertainty for the measurement result. It is not necessary to analyse all these primary samples separately all of the time. At a later stage, about equal quantities of them may be combined and then split in the laboratory by means of a spinning riffler into test samples.

Spatulas having a flat surface usually cause large sampling errors in case of wide PSDs, since the largest particles are likely to fall off the edges (large particles are more mobile) and a sampling error will result.

Cohesive powders can cause flow problems in rifflers, which in turn can lead to increased uncertainties. In case of such problems, thief or scoop sampling (following homogenization) can give an alternative, provided that the uncertainties are acceptable. Rounded scoop types are slightly better, but still much worse than rifflers.

There are several methods of subdividing a sample. Methods such as coning and quartering the sample are not as effective as using a rotary sample splitter for example.[10] Selection of the most appropriate available technique is important. If just scoop sampling is available, tumbling the sample prior to sample extraction generally results in a more representative sample being taken than just simply taking a scoop of powder from the top of the material. Gentling tumbling a material is not to be confused with vigorous shaking which can cause breakage of friable material and can potentially increase sample segregation by eventually ending up with large particles at the top of the sample and fine particles at the bottom.

6.4.3 Sampling of emulsions and suspensions

ISO 14488 also advises on the sampling procedures for liquid dispersions.

Emulsions are usually stabilized through the application of optimized complex mixtures of specific dispersing media and stabilizers. They are often stable and fairly homogeneous, since the density of both phases is almost equal. Thus, they can be easily sampled, following gentle mixing by manual methods, e.g. a pipette. If the type of measurement instrument requires dilution of the test sample, this dilution should take due care of the existing mixture of dispersing medium and stabilizers.

Suspensions are typically stabilized by less complex, electrostatic and/or steric aids, like low-foaming surfactants and/or polyelectrolytes. Suspensions containing particles smaller than about 1 µm are usually fairly homogeneous (due to Brownian motion but depending on particle density). Serious particle sedimentation can occur above a particle size of about 1 µm if particle density is high and liquid viscosity low.

Emulsions and fairly stable suspensions can be sampled manually, if necessary, after gentle mixing, by means of a pipette. In case of visible sedimentation or creaming, sampling should be done during stirring without introduction of air bubbles. However, care should be taken to ensure the stirrer does not segregate the sample by depositing the largest particles towards the edge of the vessel. The stir speed should be carefully chosen to avoid the creation of a vortex in the vessel which can induce segregation.

Previous stabilization of dispersions should be regarded if their dilution is needed for measurement, so that no destabilization occurs (this can often cause a higher-than-expected size to be recorded as the sample coalesces).

6.4.4 Sampling of sprays, gas bubbles and aerosols

The particle size of droplets is typically not homogeneously spread over the full cross-section of a spray. Moreover, the droplets may evaporate in time at a rate depending on liquid volatility. Therefore, sampling of sprays is impossible and direct in-line analysis needed.

The stability of bubble dispersions in liquids depends on bubble size. Fine bubble dispersions (<100 µm) can be fairly stable (especially if the bubbles are coated with other materials), while dispersions at larger bubble sizes can be unstable.

Aerosol particles typically have a size distribution in the range of 0,01 µm to 100 µm. If the dispersions are stable, they can be sampled for analysis; if not, they must be analysed directly. PSD measurements typically may be performed by suction of the aerosol into the analysis instrument or in some cases by direct measurement through a laser beam (in the case of laser diffraction measurements of sprays).

Stable dispersions of gas/air bubbles in liquid and of aerosols may be sampled by means of a pipette or a sampling tube and then analysed. Attention should be given to potential loss of bubbles or aerosols due to their attachment to the walls of sampler tubes. Loss of bubbles or aerosols due to wall attachment in sampler tubes may be checked through using different lengths and types of tubing. Unstable dispersions should be analysed directly; their development can be followed from the moment of formation to the time that a stable situation is reached.

6.4.5 Improving sampling in the instrument

The sampling by the instrument itself can be improved by increasing the sample size. This can be achieved by increasing the amount of sample measured. For wet measurements, this would be by adding more material to the sample dispersion unit. However, care should be taken to avoid multiple scattering, especially if the sample is fine, see 10.2 for further information. Improved sampling of a material can also be achieved by increasing the measurement time, this is particularly helpful in the measurement of polydisperse material where a short measurement time may not allow significant sampling of larger fractions which are present.

For dry measurements, improving sampling is often just a question of adding more material and increasing the measurement integration time. In this case, it is important to measure all the sample in case there was any sample segregation during measurement (coarse particles tend to be more mobile than fine ones).

7 Samples not appropriate for analysis by laser diffraction

Whilst laser diffraction has a wide applicability, it is not suited for every sample. The list below summarises the samples which pose significant problems for the technique.

a) If the sample median size is substantially smaller than 100 nm, then dynamic light scattering or particle tracking analysis may be a more appropriate solution.

b) If the sample is very optically non-spherical in nature (which may also include nominally spherical particles that have a refractive index distribution internally, such as globular proteins, agglomerated particles, Janus particles, etc.), image analysis can be preferred, particularly if the shape of the material is desired, however laser diffraction results can be used to assess the degree of agglomeration and in some cases (with additional information on the detector used from the vendor) the fractal dimension of the aggregate.

   Very acicular material can produce results that, while interpretable, can lead to modes on the distribution relating to different orientations of the particle (on its side, on its end), so image analysis, if available, can be preferred. However, laser diffraction results can still be used for qualitative analysis or quality control.

c) If a particle count rather than a size is needed, then an appropriate counting technique can be used.

d) If the sample cannot be diluted without changing the particle size distribution, and the concentration of the neat sample exhibits significant multiple scattering, then any result from laser diffraction can be indicative only, so other techniques can be preferred (or measure dry if possible).

e) Extremely inhomogeneous samples with wide polydispersity: In some cases, the range of the particles (especially in geological applications and pharmaceutical applications) is broad to the level that repeatability is very difficult to reach. In those cases, it should be considered if particle size determined by laser diffraction is the critical parameter in the product manufacturing process, if not, maybe it can be based only on other techniques such as sieving.

f) If the particle fluoresces at the laser wavelength used, then image analysis can be preferred.

8 Additional guidance on optical properties of samples

8.1 Coloured samples

For coloured particles, an additional measurement challenge can result depending on the wavelength of the incident light. If this light is strongly absorbed in the particles, Mie theory using a high imaginary refractive index (0,1 or higher) or the Fraunhofer approximation is recommended. If the laser light is reflected or transmitted through the particles for the incident wavelength then measurement of laser diffraction is more complicated and knowledge of the optical properties of the particles for the given wavelength is necessary. Usually, complementary colours of the particles to the incident laser light allow for easier laser diffraction measurements than particles of the same colour.

When measuring a sample that absorbs laser light, it is recommended to measure the sample suspension at the lowest possible concentration that still allows for reproducible results.

8.2 Porous samples

If highly porous samples are being measured in liquid, it must be appreciated that significant intake of dispersing liquid by the particle can occur. This can result in the effective refractive index of the wetted sample being significantly closer to the pure dispersing medium than the dry sample. This effect can be verified under a microscope, as when placed in the dispersing medium, the images of the particles can be of much lower optical contrast than expected. In some cases, the pores themselves can scatter light and be seen as a tail or separate peak of fine material, normally in the sub 10 µm area.

8.3 Mixtures

When measuring a mixture of materials, several approaches are recommended.

If the mixture is a known fraction of different components of known refractive index, a weighted average can be employed.

If the material is small (especially less than 10 µm), an acceptable result can often be obtained by using the optical properties of the smallest component (if known).

If the sample is a mix of many materials of unknown fractions (chocolate is a good example), then the Fraunhofer approximation can be used, especially if the result is being used to control a process.

8.4 Mie, Fraunhofer and incorrect use of refractive index

ISO 13320:2020, Clause A.5 has a section on optical model selection which provides advice on when to select Mie and the Fraunhofer approximation. The appropriateness of the optical model used influences the accuracy of the particle size distribution, especially at the bottom end of the distribution, where analysis by incorrect Mie parameters, or the Fraunhofer approximation on fine material can produce fine tails which are not real. However, the purpose of the measurement should also be considered. If the measurement is for more of a rough indicator that a process is behaving in a consistent way, then it can be perfectly acceptable to use an optical model which is not completely correct. Fraunhofer, for example, is used throughout the chocolate industry (chocolate is a complex mix of materials).

The worst case of an incorrect optical model is when there is very little change in observed scattering data on repeat measurements, but the instrument repeatability is poor, there is a feature of the particle size distribution appearing and disappearing. The appropriateness of the optical model should be examined in this case, often small adjustments of the real and especially the imaginary refractive index are needed. Stable scattering data should give stable results. In the development of a method, the selection of a refractive index can be used as a robustness test, do small changes in particle and imaginary refractive index make a large difference in the result.

The occurrence of any tail of fine material should be validated by orthogonal techniques, see Clause 12.

9 Repeatability, intermediate precision and reproducibility

9.1 General

The mathematical comparison of results provides information on many factors such as the stability of a sample, the success of a method transfer between instruments and the sampling regime employed. This clause provides recommendations on acceptable values for different types of result comparison.

— Instrument repeatability quantifies the variation between different readings on a given aliquot. It is influenced by the performance of the instrument itself, but also by effects like sedimentation/flotation of samples and very low particle concentration, both of which result in higher standard deviations.

— Method repeatability includes all the effects of instrument repeatability but, in addition, the effects of sampling and sample preparation.

— Method reproducibility includes all of the above-mentioned effects plus differences between instruments, effects of location and operators.

For the wet dispersion method, the tests for instrument and method repeatability are carried out using one instrument, a single operator, as narrow a time span as can be achieved and the same dispersed sample. For the dry dispersion method only, the method repeatability described in 9.4 can be used for this test. Free flowing dry samples which have been correctly split into subsamples with a very low sample to sample variability should also be able to fulfil the tolerances in this clause.

9.2 Key measurands

Many laser diffraction specifications are based around the 10th, 50th and 90th percentiles of the volume distribution.

These values are commonly used for numerical comparison or process control as they capture the often-complex particle size distributions in simple, physically meaningful measurands. Notable examples include processes that change a particle size distribution from a starting state to a desired final state such as milling or crystallization where specific maxima and minima in the particle size distribution are important for the application. These include inks and toners, where large fractions may block inkjet printer heads or to avoid a gritty feel on the page or to specify a stopping point for industrial scale milling processes, where processing time costs are high. 100 % specifications should be treated with caution, as any number with 100 % of the distribution falling below it, is the 100th percentile. When people state this is needed, they are really requiring the 99,9th percentile, but even then, the use of it is risky due to small variations in sampling, sample preparation and dispersion causing potential large variation in the 100th percentile. If the 100th percentile is needed, the electrical sensing zone method (see ISO 13319-1) or image analysis (ISO 13322-1 and ISO 13322-2) are more appropriate measurement techniques.

9.3 Instrument repeatability

This metric checks whether the instrument itself functions well. Simple samples are selected for this test to avoid mixing the effects of sample preparation/agglomeration etc. with the pure variation coming from the instrument itself.

At least 6 consecutive measurements are performed in a short time period, with the same dispersed test sample at an adequate sample concentration and signal integration period to allow a sufficient number of particles to be analysed.

The results from an instrument fulfilling the specifications of ISO 13320 show the following characteristics.

— The reported cumulative volume distribution from each test at the 10th percentile $x_{10,3}$ does not deviate from the average value of all measured results by more than 2,0 %.

— The reported cumulative volume distribution from each test at the 50th percentile $x_{50,3}$ does not deviate from the average value of all measured results by more than of 1,5 %.

- The reported cumulative volume distribution from each test at the 90th percentile $x_{90,3}$ does not deviate from the average value of all measured results by more than of 3,0 %.

If any of these parameters are less than 5 µm, then the parameters which are less than 5 µm can have their variation doubled.

If the ranges are larger than stated above, the source of the excessive variation has to be identified. This can be a malfunctioning instrument but also an unsuitable sample, i.e. a sample that dissolves/settles/agglomerates/floats.

9.4 Method repeatability (under repeatability conditions)

An important step in the development of a laser diffraction method is to see if the measurement can be repeated. This does not only increase confidence in the measurement method, but also inform which level of control is possible with a given method: it is not possible to detect variations in a process that are smaller than the method repeatability.

This test is usually carried out using one instrument and a single operator, using different aliquots of the same sample using the same prescribed method. It is applicable to both the wet and dry dispersion methods. This type of repeatability includes variability due to sampling and dispersion.

Method repeatability also includes effects of sample preparation, agglomeration, sedimentation etc. which differ from material to material. Method repeatability is therefore determined for the material(s) that are tested in practice.

At least six separate measurements are performed with the samples preferably prepared into separate single shot test samples. Each test is conducted at an adequate sample concentration and signal integration period to allow a sufficient number of particles to be analysed. Each test ideally would be performed three times and the averages for each aliquot are compared.

The acceptable range depends on the application and the material, but typically the performance given below is achieved.

- The reported cumulative volume distribution from each average at the 10th percentile $x_{10,3}$ does not deviate from the average value of all averages by more than 3 %.
- The reported cumulative volume distribution from each average at the 50th percentile $x_{50,3}$ does not deviate from the average value of all averages by more than of 2,5 %.
- The reported cumulative volume distribution from each average at the 90th percentile $x_{90,3}$ does not deviate from the average value of all averages by more than of 4 %.

If any of these parameters are less than 5 µm, then the parameters which are less than 5 µm can have their variation doubled.

The setup of performing multiple measurements on several aliquots also allows evaluation by one-way analysis of variance (ANOVA). In this evaluation, the aliquot is the grouping variable and the standard deviation within groups is calculated as the square root of the mean squares within groups from the ANOVA table (the table used to calculate the variance using the ANOVA method). This is equivalent to the instrument repeatability determined in 9.3.

If the ranges obtained are regarded as being too high, the source of the excessive variation has to be identified. Potential sources are inhomogeneity of the sample (to be resolved by better mixing or taking larger samples), issues with the dispersion – thermal effects or gas bubbles, the effects of sampling and subsampling or problems / inconsistencies in sample preparation.

9.5 Intermediate precision and reproducibility (under intermediate precision/reproducibility conditions)

Intermediate precision and reproducibility assess how much results obtained under different conditions are expected to vary. Note that “different conditions” can relate to a number of factors:

a) the same instrument in one facility operated by various operators;

b) several instruments of the same model in the same facility operated by various operators;

c) different instrument models in the same facility operated by various operators;

d) several instruments of the same model in different facilities operated by various operators (this is termed reproducibility);

e) different instruments models in different facilities operated by various operators.

Strictly speaking, only conditions d) and e) would be reproducibility conditions, whereas conditions a) to c) are conditions of intermediate precision (as described in ISO 13320).

The test for reproducibility includes as much variation as needed for a meaningful interpretation of results. If results are used for process control at a single site where the same instrument is used by several operators, condition a) is sufficient. On the other extreme, when results from different instruments and sites are compared, data obtained under condition e) is used. An example for the application of this test is a typical QA test for a general material and would encompass expected variation for a method and method transfer. An intermediate precision test at a single site [conditions a) to c)] is a good first step, followed by a full method transfer later [conditions d) and e)].

This means that the first step for this test is to determine the degree of variation that is covered by the test. Not less than 6 unique combinations of instrument, operator, instrument model and facility are selected.

As for method repeatability, the observed variation is also influenced by the nature of the sample. This test is therefore performed on a material that closely resembles the actual samples that are measured.

The material is measured using the same prescribed method and including as much variation in operators, instruments, instrument models and facilities as needed. Ideally, for each unique combination of instrument, operator, instrument model and facility, three independent aliquots are measured three times. The average of all results is calculated for each unique combination.

For an example where this has been carried out in practice, see Reference [9].

The acceptable range depends on the application and the material, but typically the performance given below is achieved.

- The reported cumulative volume distribution from each average at the 10th percentile $x_{10,3}$ does not deviate from the average value of all averages by more than 10 %.
- The reported cumulative volume distribution from each average at the 50th percentile $x_{50,3}$ does not deviate from the average value of all averages by more than 7,5 %.
- The reported cumulative volume distribution from each average at the 90th percentile $x_{90,3}$ does not deviate from the average value of all averages by more than 10 %.

If any of these parameters are less than 5 µm, then the parameters which are less than 5 µm can have their variation doubled.

The setup of performing multiple measurements on several aliquots under various conditions also allows evaluation by two-way analysis of variance (ANOVA). In this evaluation, the condition and aliquot are the grouping variables. ANOVA allows estimating average instrument repeatability, average method repeatability, which can be compared to the results obtained in one laboratory as well as the standard deviation between conditions.

9.6 Summary table of experiments detailed in 9.3 through 9.5

Table 1 summarizes the variations advised in 9.3 through 9.5. This has been designed to provide the key information described in these subclauses in a single table that is easy to reference.

Table 1 — Acceptable variations for the three types of experiments

Experiment type	$x_{10,3}$ % variation	$x_{10,3} < 5$ µm % variation	$x_{50,3}$ % variation	$x_{50,3} < 5$ µm % variation	$x_{90,3}$ % variation	$x_{90,3} < 5$ µm % variation
Instrument repeatability	2	4	1,5	3	3	6
Method repeatability	3	6	2,5	5	4	8
Intermediate precision and reproducibility	10	20	7,5	15	10	20

9.7 When is tighter or wider control needed?

The variations described in 9.6 should be considered maximum acceptable variations. If pass / fail specifications are being set, then most instruments with a good method are capable of tighter limits being used. However, it is recommended that method transfer / intermediate precision experiments are conducted before any tight specification is finalised, as the specification need to be robust enough to cope with different machines, users and laboratory environments.

9.8 What are the most appropriate control parameters?

Particle size distribution parameters are often chosen as primary characteristics for the behaviour of particulate materials, because of easy measurement, relation to fundamental properties and transferability to other material types. The critical parameters are selected following careful investigations by experienced analysts to relate these parameters to the behavioural aspects, e.g. material grittiness or its sedimentation behaviour to the amount of 'coarse' material or the $x_{90,3}$, or its filterability or dusting behaviour to the amount of 'fine' material or the $x_{10,3}$.

10 Interpretation of light scattering and assessment of data quality

10.1 Background stability and alignment quality

Acceptable background levels depend on the instrument being used as every manufacturer have slightly different systems. However, the background should be stable, and not show any signs of misalignment. The refractive index of liquids varies with the temperature; thus, if the dispersing medium changes the temperature as it circulates around the system, the alignment will also change over time. This can result in an initial higher background which will fall over time, resulting in an incorrect background signal subtraction from the subsequent measurement of the particulate sample. See Clause 5 for more information on background measurement.

Manufacturer guidelines to an acceptable background shape should be followed. Any trends over repeat measurements on the shape of the background should be examined, as this is often indicative of sample build-up on the optical surfaces. Cleaning the flow cell windows with alcohol (following manufacturer's recommended procedure) can help, since residual material on the optical surfaces can serve as anchor points for bubbles.

If a warm sample is added to the instrument or if internal sonication on a volatile dispersing medium is performed, the refractive index change described above will reoccur, causing misalignment. This causes scattering on the low angle detectors which can be interpreted as large particles. The manufacturer can have various means of removal of this noise, however as the misalignment is caused by a temperature gradient that is removed when the sample reaches an equilibrium temperature, having a premeasurement delay of some sort is often the most effective way of removing the peak with no risk of removing any really large particles.

10.2 Multiple scattering

As part of method development outlined in ISO 13320:2020, 5.5.4, multiple scattering should be avoided by keeping the concentration sufficiently low so single scattering not multiple scattering is occurring. Multiple scattering can cause the instrument to over-estimate the fine particle fraction which can appear as an enhanced fine tail, a shift in modal size or even the appearance of a spurious fines mode. If this second mode disappears when the sample is diluted, then multiple scattering is the most likely cause. The point at which multiple scattering is likely to occur depends on the primary particle size. Fine material causes multiple scattering at much lower concentrations than larger material. An experiment during method development where the sample is measured at a variety of differing concentrations shows where the particle size starts to deviate downward. Examination of the 10th percentile is a good test.

Incorrect optical properties can also result in tails of fine material on the distribution that are not there. The difference between fines caused by multiple scattering and fines caused by incorrect optical properties (especially the use of an incorrect imaginary refractive index) is a tail induced by multiple scattering is concentration dependent while one induced by an incorrect refractive index is always there (until the results are recalculated with more appropriate optical properties).

Sometimes multiple scattering cannot be avoided. A good example of this is in the measurement of sprays where it is impossible to dilute the sample in any way. In this case, a multiply scattered result is the only result possible, but it is still possible to compare the results for batches of products even if the result is multiply scattered.

10.3 Non-smooth scattering patterns

The scattering pattern (intensity recorded by across multiple detectors) is expected to be smooth. In some situations, the data is not smooth and appears jagged in nature. This scattering is either caused by the sample (and is unavoidable) or by the experiment which is potentially correctable.

An example of this being due to the sample is a material with a very tight distribution where the particles are virtually mono-disperse. These features of the scattering pattern are not observed for polydisperse samples due to the combined scattering patterns of many different particles in the distribution all contributing.

Examples of avoidable non-smooth data, especially at low angle detectors channels, where a high low effect is observed on subsequent channels (often called castellation) are often due to misalignment. A likely cause of this is that the refractive index of the dispersing medium has changed since the background was recorded, so the background should be recorded again, and the experiment repeated. In some cases (often where the transmitter and receiver are separated), non-smooth scattering can be caused by secondary reflections of the laser light. These can often be resolved by careful re-alignment or adjustment of the optics.

11 Interpretation of trends in measurement data

11.1 General

If the repeatability guidelines in Clause 9 cannot be achieved in a series of repeat measurements, possible explanations can be an instability in the sample or poor sampling of the material. This clause considers the most common causes of this problem. This clause contains key advice for users to follow if the particle size results are trending in a certain direction with advice on potential rectification.

It should be noticed that in some circumstances more than one of the deleterious effects described in 11.2 to 11.7 can occur simultaneously.

11.2 Dispersion (wet measurements)

If on a series of repeat measurements (same sample, multiple measurements) there is a decrease in the $x_{10,3}$, $x_{50,3}$ and $x_{90,3}$, particularly $x_{10,3}$, accompanied by a significant increase in the obscuration, it is likely that the sample is dispersing in the diluent. If the raw scattering is observed, then a loss of scattering at smaller angles (larger particles) and an increase of scattering at larger angles (smaller particles) may be observed as well. Ideally, once dispersion conditions have been established for a sample, repeat measurements of the sample should be obtained which provide repeatability in line with Clause 9. If sonication is being used, then breakage can also be occurring, so image analysis can be used in conjunction with the laser diffraction measurements to determine whether dispersion, or fracture is occurring. Sonication can also cause agglomeration (see 11.4).

11.3 Dissolution (wet measurements)

If on a series of repeat measurements (same sample, multiple measurements) there is an increase in the 10th, 50th and 90th percentiles, particularly $x_{10,3}$, accompanied by a significant fall in the obscuration, it is likely that the sample is dissolving in the dispersing medium. If the raw scattering is observed, then a loss of scattering at larger angles (smaller particles) can be observed as well. The maximum observed size of the distribution does not normally increase. If the sample is dissolving, ideally a change in the dispersing medium is recommended. Saturated solutions can sometimes work but require great care to prepare and the degree of saturation can change with temperature, often a change in the dispersing medium or a switch to a dry measurement can be simpler.

11.4 Agglomeration (wet measurements)

If on a series of repeat measurements (same sample, multiple measurements) there is an increase in the key percentiles, of $x_{10,3}$, $x_{50,3}$ and $x_{90,3}$, with only a limited fall in the obscuration, it is likely that the sample is agglomerating in the dispersing medium. The maximum observed size of the distribution will normally increase. If the raw scattering is observed, then an increase of scattering at smaller angles (larger particles) can be observed as well. The use of ultrasound can sometimes cause agglomeration, the energy put into the dispersion increases particle collision and adhesion. Adjustment of the pH or the addition of an emulsifier (such as sodium pyrophosphate) can prevent agglomeration.

11.5 Size decreasing on successive measurements (dry measurements)

If a series of successive measurements on the same tray of material are performed (and the sample has not been exhausted in one single measurement), a trend showing a decrease in particle size can result. This outcome happens because large particles flow more easily along the tray than smaller ones. This effect can be corrected by changing the measurement conditions to longer measurements that exhaust the complete sample in a single measurement. If the pressure is increased between successive measurements, the size decrease can also be due to breakage/comminution of the material.

11.6 Random variation (wet measurements)

If poor repeatability on a series of measurements is observed where there is no obvious trend in the data, and it appears to be random shifts of the measured parameters up and down, then the measurement duration should be considered. If the measurement time is too short, particularly if the sample is polydisperse, this can result in not enough scattering from particles being measured to be representative of the sample. Extending the measurement time so a sufficiently representative sample is obtained will cure this behaviour.

11.7 Other causes of poor repeatability (wet and dry measurements)

If the sample is sedimenting during repeat measurements, then a decrease in particle size (most notably $x_{90,3}$) is observed. An increase in the pump / stir rates of the tank can restore the initial particle size. As noted in 6.2 a), a titration over a range of values to look for a stable region of settings is good practice.

If the material is not thought to be agglomerating, and larger particles than anticipated are observed, the optical surfaces (windows) of the measurement cell should be examined for fouling. If sample is fouling the windows, the addition of a charge stabilizing agent or a change of dispersing medium may help. If bubbles are sticking to the windows, the optical surfaces should be cleaned. If air ingress is a particular issue, care can also be taken in the control of the pump / stir (slow increase up to the desired point) or in the degassing of the dispersing medium. If surfactants are used, they can possibly be at too high a concentration for the stir speed used and the creation of a foam is occurring. Ultrasound can also cause cavitation of the dispersing liquid, and any resultant bubbles is measured as particles.

It must be remembered that a laser diffraction instrument is an optical device with electronic components, so poor repeatability can result from the device being exposed to vibration or electromagnetic disturbances which can affect the instrument. It is recommended that the device be ideally located in an area free from these effects.

For dry measurements, there should be a smooth feed and adequate extraction. Inconsistent flow / temporary blockages in the feed mechanism can also lead to poor results, this tends to give inconsistent loading of the dispersive mechanism which can lead to choking if the flow is too high. These can be visually seen during measurement. The use of a different feed mechanism or a change in vibration can help here. Some powders can carry a large electrostatic charge, so application of an earth to the dry powder feeder can help with powder flow.

If the sample extraction is blocked, then a poor result can also be obtained, so such extraction should be checked and emptied regularly to prevent this, but care must be taken doing this and PPE worn. The degree of risk depends on the nature of the samples recently measured.

Wet or oily dispersive air (dry) can also lead to poor flow and optical contamination.

Some laser diffraction systems are open optical benches, so the optics are exposed to light. Poor repeatability can occur if the ambient light changes significantly during measurement (e.g. background with no protection, measurement with blinds drawn). It is important to keep the light around the instrument as constant as possible. Measurement in the dark or at extremely low light levels is also a potential solution to this issue.

If there is any loss of the scattered light through vignetting — light loss from the measurement (spray, cuvette / cell) occurring outside the working range of the optics, so scattered light occurs beyond the largest measurable angle — a coarser than expected particle size measurement will be obtained. As part of method development, if possible, the distance of the measurement from the lens should be varied to check the intermediate precision is within the limits discussed in Clause 9.

12 Orthogonal techniques for laser diffraction

12.1 Image analysis

Both static and dynamic image analysis are increasingly used to validate / provide additional information on laser diffraction measurements. Imaging can show a needle like particle before ultrasound, and fragments of particle afterwards showing ultrasonic fracture of material, it can identify the difference between agglomerates, bubbles and thermal noise. Regulatory authorities are often asking for imaging results along with laser diffraction results when material methods are submitted as they are used to prove that the diffraction results used in the submission are valid and well understood.

A close agreement between laser diffraction and imaging only occurs for spherical particles. However, imaging provides a unique source of information to test the credibility of the laser diffraction results as effects such as particle breakage, agglomeration and bubbles can be identified easily on the images, which then can be used to inform the laser diffraction method and make it more robust. As the image analysis result is number-based, this should also be considered when making comparisons.

12.2 Dynamic light scattering

If the material in question is substantially sub-micrometres in nature, then it is too small to use imaging as an orthogonal technique. If the upper size range by laser diffraction is <3 µm, then dynamic light scattering can be used as an orthogonal technique, but it should be set to output a volume distribution to compare with the laser diffraction experiment.

If the size range of the sample is appropriate for dynamic light scattering, the size obtained by the technique can be observed to be larger than that obtained by laser diffraction. This is due to dynamic light scattering experiments measuring the size through measurement of the Brownian Motion of the sample giving a hydrodynamic diameter (which is normally larger). This is why, in order to obtain the expected size for materials such as polystyrene latex, the material is measured by dynamic light scattering in 10 mM salt