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Laser diffraction measurements — Good practice

Mesures par diffraction laser — Bonnes pratiques

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Foreword

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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 10^{th} percentile of the cumulative volume undersize distribution (by volume)

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

$x_{90,3}$ particle diameter corresponding to the 90^{th} 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 10^{th}, 50^{th} or 90^{th} 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?