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Determination of particle size distribution — Single particle light interaction methods —

Part 3:
Light extinction liquid-borne particle counter

Détermination de la distribution granulométrique — Méthodes d'interaction lumineuse de particules uniques —

Partie 3: Compteur de particules en suspension dans un liquide par extinction de la lumière

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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 documents 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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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*.

This second edition cancels and replaces the first edition (ISO 21501-3:2007), which has been technically revised. The main changes from the previous edition are as follows:

— Clause 4 for "Principle" and Clause 5 for "Basic configuration" have been added;

— "size calibration" and "verification of size setting" have been combined as "size setting error" in the requirements (Clause 6);

— "Test report" (3.10 in the previous edition) has been changed to 6.9 on "Reporting of test and calibration results";

— information about uncertainties has been enriched and is now the subject of Annex B.

A list of all parts in the ISO 21501 series can be found on the ISO website.

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

Monitoring particle contamination levels is required in various fields, e.g. in the electronic industry, in the pharmaceutical industry, in the manufacturing of precision machines and in medical operations. Particle counters are useful instruments for monitoring particle contamination in liquid. The purpose of this document is to provide a calibration procedure and verification method for particle counters, so as to minimize the inaccuracy in the measurement result by a counter, as well as the differences in the results measured by different instruments.

Determination of particle size distribution — Single particle light interaction methods —

Part 3: Light extinction liquid-borne particle counter

1 Scope

This document describes a calibration and verification method for a light extinction liquid-borne particle counter (LELPC), which is used to measure the size and particle number concentration of particles suspended in liquid. The light extinction method described in this document is based on single particle measurements. The typical size range of particles measured by this method is between 1 µm and 100 µm in particle size.

The method is applicable to instruments used for the evaluation of the cleanliness of pharmaceutical products (e.g. injections, water for injections, infusions), as well as the measurement of number and size distribution of particles in various liquids.

The following are within the scope of this document:

— size setting error;

— counting efficiency;

— size resolution;

— maximum particle number concentration;

— sampling flow rate error;

— sampling time error;

— sampling volume error;

— calibration interval;

— reporting results from test and calibration.

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 terminological databases for use in standardization at the following addresses:

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

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

3.1
calibration particles
monodisperse spherical particles with a known mean particle size, e.g. polystyrene latex (PSL) particles, where the certified size is traceable to the International System of Units (SI), a relative standard uncertainty of the certified size is equal to or less than 2,5 %, a refractive index that is approximately 1,59 at the wavelength of 589 nm (sodium D line)

Note 1 to entry: For spherical particles, the particle size is equal to the diameter.

3.2
counting efficiency
ratio of the particle number concentration measured by a *light extinction liquid-borne particle counter* (3.3) of a *certified reference material* (3.7) for particle number concentration to the certified value of the CRM

3.3
LELPC
light extinction liquid-borne particle counter
instrument that measures liquid-borne particle numbers by counting the pulses as the particles pass through the sensing volume, as well as particle size by the attenuation of light

Note 1 to entry: The optical particle size measured by the LELPC is the light extinction equivalent particle size and not the geometrical size.

3.4
PHA
pulse height analyser
instrument that analyses the distribution of pulse heights

3.5
size resolution
measure of the ability of an instrument to distinguish between particles of different sizes

3.6
coincidence loss
reduction of particle count caused by multiple particles passing simultaneously through the sensing volume and/or by the finite processing time of the electronic system

3.7
CRM
certified reference material
<particle number concentration> particle suspension, typically polystyrene latex particles suspended in pure water, sufficiently homogeneous and stable, characterized for the mean particle size and number concentration by a metrologically valid procedure, accompanied by a reference material certificate that provides the associated uncertainties for the traceable values, and a statement of metrological traceability

Note 1 to entry: If no CRM standards are available, the use of a particle suspension characterised with corresponding uncertainties for particle size and concentration is sufficient.

3.8
MPE
maximum permissible error
limit of error
extreme value of measurement error, with respect to a known reference quantity value, permitted by specifications for a given measurement, measuring instrument, or measuring system

Note 1 to entry: This document uses decimal numbers for the requirements to MPEs to avoid confusions that may arise when relative uncertainties of test results are reported in percent figures.

4 Principle

The measurement principle of the LELPC is based on detection of light extinction by a particle when the particle passes through an incident light beam.

The particle size is determined from the attenuation of light, and the number of particles from the number of light extinction pulses by individual particles.

More specifically, a sample liquid is drawn from the inlet of the LELPC at a constant flow rate, and introduced to the sensing volume of the LELPC where a light beam is irradiated. When a particle suspended in the sample liquid passes through the light beam, it attenuates the light, occurring a light extinction pulse. The light extinction pulse is detected by a photo detector, and converted to an electrical pulse. The electrical pulse height is proportional to the attenuation of light, and depends on the optical system design, the electronic components used, and the light source. The attenuation of light is dependent on the size, refractive index, and shape of the particle. In order to establish a relationship between the electrical pulse height and the particle size, calibration of each LELPC with use of particles having a well-defined size, refractive index, and shape is required.

5 Basic configuration

An LELPC is composed typically of a light source, a sample liquid supply/suction system, a sensing volume, a photoelectric conversion device, a pulse height analyser, and a display (see Figure 1). Some LELPCs do not contain a sample liquid supply/suction system and/or a display.

To make the particle size calibration possible, the LELPC should be constructed so that pulse height distributions for calibration particles can be measured.

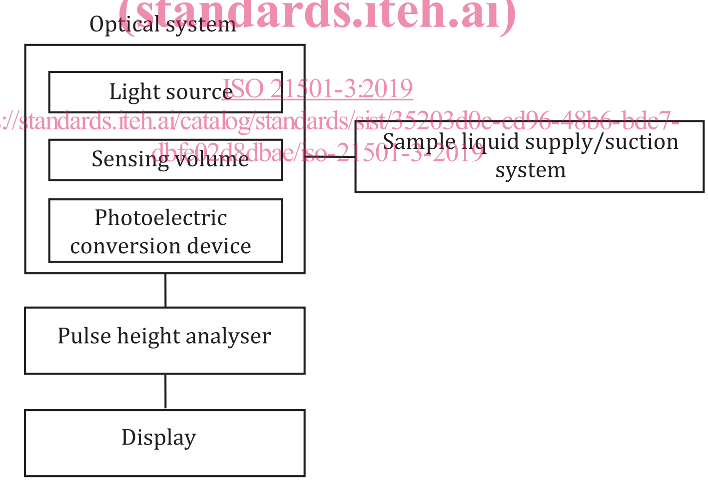

Figure 1 — Example of basic configuration of LELPC

6 Requirements

6.1 Size setting error

The MPE for size setting in the minimum detectable particle size and other sizes specified by the manufacturer of an LELPC is 0,10 (corresponding to 10 % of the specified size).

Size setting shall be conducted before the LELPC is shipped from the manufacturer, and when the size setting error is found not fulfilled in a periodic calibration.

A recommended procedure for size setting is described in 7.1.2. If other methods are used, their uncertainty shall be evaluated and described.

6.2 Counting efficiency

The counting efficiency shall be within 0,80 to 1,20 [corresponding to (100 ± 20) %] when the test is carried out by the method described in 7.2.

6.3 Size resolution

The size resolution shall be less than or equal to 0,10 (corresponding to 10 %) when the test is carried out by the method described in 7.3.

6.4 Maximum particle number concentration

The maximum measurable particle number concentration shall be specified by the manufacturer. The coincidence loss at the maximum particle number concentration of an LELPC shall be less than or equal to 0,1 (corresponding to 10 %).

NOTE The probability of occurrence of coincidence loss increases with increasing particle number concentration.

6.5 Sampling flow rate error

The MPE of the sampling flow rate shall be specified by the manufacturer. The user shall check that the sampling flow rate is within the range specified by the manufacturer.

If the LELPC does not have a flow rate control system this subclause does not apply, however the manufacturer shall specify the allowable flow rate range of the LELPC.

6.6 Sampling time error

The MPE in the duration of sampling time shall be 0,01 (corresponding to 1 %) of the preset value.

This subclause does not apply when the LELPC is not equipped with a sampling system.

This subclause does not apply when the LELPC is equipped with a volumetric sampling system.

6.7 Sampling volume error

The MPE of sampling volume shall be 0,05 (corresponding to 5 %) of the preset value.

This subclause does not apply when the LELPC is not equipped with a volumetric sampling system.

6.8 Calibration interval

The calibration of the LELPC should be conducted at an interval equal to or shorter than one year. The requirements should be met during the calibration interval.

6.9 Reporting of test and calibration results

The report shall contain at least the following information:

a) date of test/calibration;

b) test/calibration particles used;

c) results for the parameters:

   1) size setting error;

   2) counting efficiency;

3) sampling flow rate error;

4) size resolution (with the particle size used);

d) threshold voltage values or channel of the built-in PHA corresponding to the size settings;

e) reference of the test/calibration method used (i.e. ISO 21501-3).

f) report/certificate identification, test/calibration location, title and identification of test/calibration provider including signature and date;

g) identification of customer and device under test, including how output was obtained for counting efficiency (e.g. analogue, display or digital output).

A calibration certificate shall furthermore include:

h) identification and — if possible — statement of metrological traceability of all reference equipment and calibration particles used;

i) relevant environmental conditions (e.g. temperature, air pressure and humidity) under which the calibration was performed;

j) a stated uncertainty for each result for the parameters 1 to 2 with reference to the calculation method (e.g. ISO/IEC Guide 98-3) — Annex B gives a recommended procedure for evaluating the uncertainty of the results of the performance tests.

NOTE Calibration certificates issued by ISO/IEC 17025 accredited laboratories and covering all results for the parameters 1 to 2 are considered to comply with the requirements above.

7 Test and calibration procedures

7.1 Size setting

7.1.1 Evaluation of size setting error

Calculate the size setting error ε according to Formula (1).

$$\varepsilon = \frac{x_s - x_c}{x_c} \tag{1}$$

where

x_c is the certified size of the particles of the suspension of the certified reference material;

x_s is the particle size corresponding to 50 % counts of C_C (see 7.1.2 for the meaning of C_C).

7.1.2 Procedure of size setting

By use of a PHA connected to the output terminal for signal pulses of the LELPC, or by use of a built-in PHA if one is contained as a part of the LELPC, obtain a pulse height distribution for a sample liquid in which calibration particles are suspended. Let V_l and V_u denote the lower and upper voltage limits, respectively, of the range of pulse heights for the calibration particles (see Figure 2). The median voltage V_m of the pulse height distribution in the range from V_l to V_u, shall be calculated, and is assigned to the certified size of the calibration particles, x_c.

When a built-in PHA is used, the abscissa of the pulse height distribution may be given in channel number instead of voltage. In this case, the term “voltage” above and in relevant descriptions below should be interpreted as channel number of the PHA.

