LE400 Sensor Resolution

AccuSizer® SPOS system

The sensor is the most critical component in a liquid particle counter since this is where the actual measurement takes place. The LE400 sensor for the AccuSizer® family of products is the highest performance and specification sensor available with a range of 0.5 – 400 µm. Sensor resolution is another sensor specification less noticed but still an important performance characteristic. This technical note defines sensor resolution and provides example of performance data for the LE400 sensor.

INTRODUCTION

Resolution can be defined many ways. In liquid particle counting, resolution is defined as the measured ability of an instrument to distinguish between particles of different sizes. The same definition is used in both ISO 21501 - 3[1] and USP <1788>.[2] Customers using a liquid particle counter to perform release testing of parenteral drugs following the USP <788>[3] are required to test sensor resolution at the same interval as sensor recalibration. Customers outside of the pharmaceutical industry are not required to test sensor resolution but ISO 21501-3 states that calibration should include at least size calibration, size resolution, counting efficiency, and sampling volume uncertainty at the calibration interval of one year or less.

ISO 21501-3 describes a calibration and verification method for a light extinction liquid-borne particle counter (LELPC). Is the particle sizing systems AccuSizer a "light extinction liquid-borne particle counter"? Yes, absolutely. This question has been asked in the past because the LE400 sensor used in the AccuSizer includes both an extinction and a scattering detector, see Figure 1. There are several reasons why the AccuSizer is considered a "light extinction liquid-borne particle counter". Reason 1: All AccuSizer systems with the LE400 sensor have two operating modes and two calibration curves: extinction and summation. In extinction mode, only the extinction detector is utilized. The scattering detector is not read, and the pulse generated is from extinction only. In this mode the lower size limit is 1.5 µm.

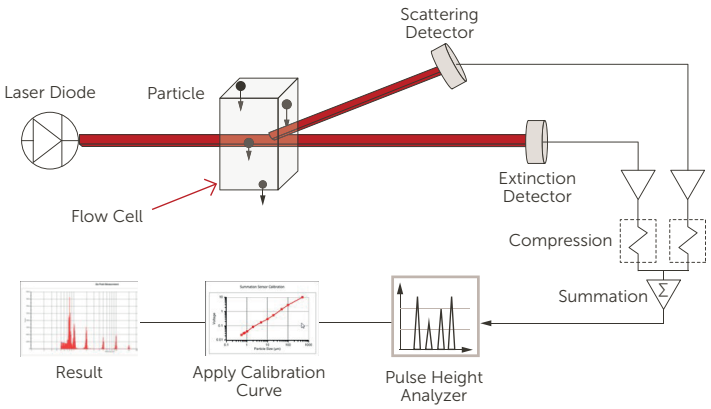

Figure 1. The LE400 sensor

Reason 2: Even when operating in summation mode and utilizing the summation calibration curve, the AccuSizer operates in extinction mode for particles > 2 µm. This is because particles > 2 microns do not scatter enough light to increase the total summation pulse sent to the counter.

At the 10 and 25 µm sizes defined in USP <788> extinction is the only light scattering phenomenon occurring that influences the measurement. The benefit of operating in summation mode is the ability to extend the dynamic range down to 0.5 µm.

TEST METHOD

Sensor resolution is tested by measuring a PSL standard (typically 10 µm) and calculating the broadening of the resultant distribution due to errors contributed by the sensor. This concept is explained in Figure 2. The naturally occurring breadth to the PSL is expressed as a standard deviation (S_{Std}) on the certificate of analysis (C of A) supplied with the PSL, and also directly on the bottle. For example Thermo Fisher catalog number 2010A has a certified mean diameter of 9.7 ± 0.4 µm. The standard deviation of this PSL is 0.4 µm. The value of S_{Std} for this sample is 0.4. The sample is analyzed and the reported standard deviation shown in the result is S_{Obs}. The equation shown below (Equation 1) is then used to calculate the sensor resolution in %. In both ISO 21501-3 and USP <1788> the specification for sensor resolution is less than 10%.

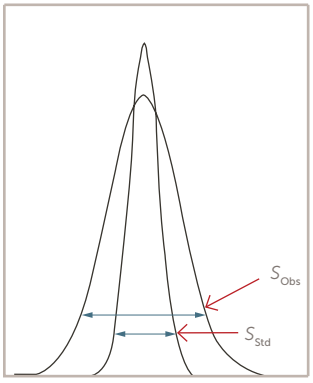

Figure 2. The broadening (S_{Obs}) of a PSL

$$\% \text{ resolution} = (100/D) \times [(S_{Obs})^2 - (S_{Std})^2)]^{½} \quad \text{Equation 1}$$

Testing for sensor resolution is fairly straight forward and is performed in the field on systems installed for USP <788> testing. The calculation of the sensor resolution can be performed manually, or automatically, in the AccuSizer software. Figure 3 shows the tables used to guide the operator to perform the manual calculation.

Sensor resolution test table 1

MANUFACTURER'S (D1) DIAMETER MICRONS	MEASURED DIAMETER	IS 9.5< D< 10.5 MICRONS	(C1) CUM # >DIAM.

Sensor resolution test table 2

(C1) CUM # ≥ DIAM.	C1 * 1.68 # AT MIN DIAM. (C_{MIN})	(D_{MIN}) MIN DIAM. (µm)	C1 * 0.32 # AT MAX DIAM. (C_{MAX})	(D_{MAX}) MAX DIAM. (µm)

Sensor resolution test table 3

MEASURED MEAN DIAMETER D1 (µm)	D_{MIN} (µm)	D1-D_{MIN} (µm)	D_{MAX} (µm)	D_{MAX} - D1 (µm)

Sensor resolution test table 4

MANUFACTURER'S SPECIFIED SIZE D1 TAKEN FROM TABLE 1 (µm)	MAX (µm) OBSERVERED STANDARD DEVIATION	S_s (µm) SUPPLIER STANDARD DEVIATION

Sensor resolution test table 5

RESOLUTION OF THE SENSOR (in %)	(P)ASS OR (F)AIL

Figure 3. Manual calculation tables

The larger value of either (D1-Dmin) or (Dmax-D1) from Table 3 is entered into the second column of Table 4. This is the observed standard deviation, S_{Obs}, used in Equation 1 to calculate the percentage resolution.

Alternatively (and more easily) the 10 µm PSL is measured and the sensor resolution report is used to automatically calculate the value, and a pass or fail result is displayed as seen in Figure 4.

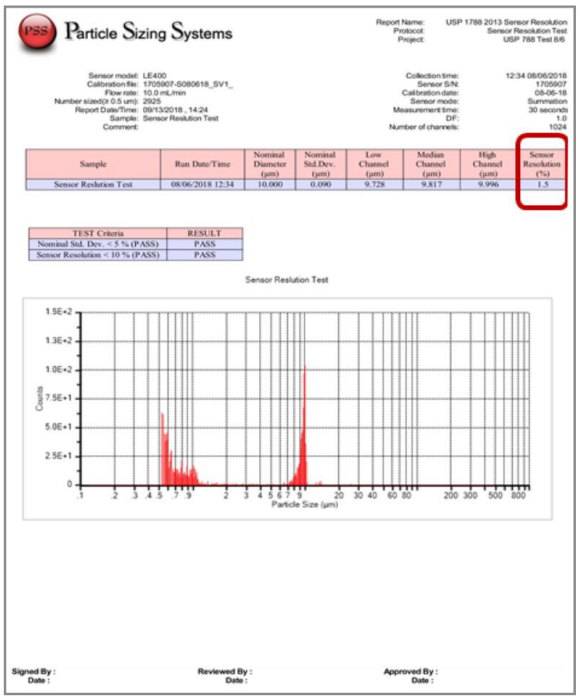

Figure 4. Automated sensor resolution report

CONCLUSIONS

The LE400 sensor easily passes the resolution requirements as defined in both ISO 21501-3 and USP <1788>. Typical values are <4% and all sensors pass the 10% specification. This can be verified in the field using either the manual or automated procedures.

References

[1] ISO 21501-3; Determination of particle size distribution — Single particle light interaction methods — Part 3: Light extinction liquid-borne particle counter

[2] USP <1788>; Methods for the determination of particulate matter in injections and ophthalmic solutions

[3] USP <788>; Particulate matter in injections

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