

Dry Method Development for Laser Diffraction Particle Size Measurement

Developing an appropriate method for measuring particle size distribution of powders dispersed in air using laser diffraction requires a structured approach. The basic goals for developing a dry method include: place a representative sample into the analyzer, disperse the sample using a pressure that breaks up agglomerates but not individual particles, choose appropriate system settings for measurement, and test for reproducibility.

Introduction

Developing an appropriate method for measuring particle size distribution using laser diffraction requires a structured approach. Samples analyzed as a dry powder have a few unique considerations compared to wet analysis, but the majority of the content in this document will be applicable to all methods.

In all cases the basic goals remain the same; decide what the purpose of the measurement is, place a representative sample into the analyzer, select an appropriate dispersion setting, choose appropriate system settings for the measurement, and test for repeatability and reproducibility.

Sampling

It is rare that the entire sample brought into the lab is measured in the instrument. More typically a sub-sample of the total is analyzed, creating the need to consider the sampling technique.

Several references (1,2) can provide both background information and practical suggestions on proper sampling techniques. Too many scientists simply tumble a powder sample and then remove a portion for analysis. Ignoring the sampling component of the method is inappropriate for several reasons:

- Accepted standards stress the importance of sampling. ISO 13320 (3) and USP <429> (4) both advise that a representative sample be prepared using a sample splitting technique. (5)
- One of the goals of proper method development is to minimize the total error. If sampling is ignored the developer doesn't know which portion of the total error comes from the sampling.

Even once a representative sample has been placed in the instrument a non-optimized method may lead to segregation and bias within the dry powder feeder.

Determine the Refractive Index

Although this document will not address this subject in detail, it is important to enter an appropriate refractive index (RI) value for the sample. Methods to obtain the sample RI include literature and internet searches, use of an Abbe refractometer, and RI matching liquid and Becke line testing.

Choosing an imaginary RI value can be facilitated by varying the imaginary component until the residual R value calculated in the LA-960 software is minimized. It is better to determine the RI early in the method development process in order to understand the general shape of the distribution before conducting other tests.



LA-960 Partica with PowderJet Feeder

Choosing the Dispersion Pressure

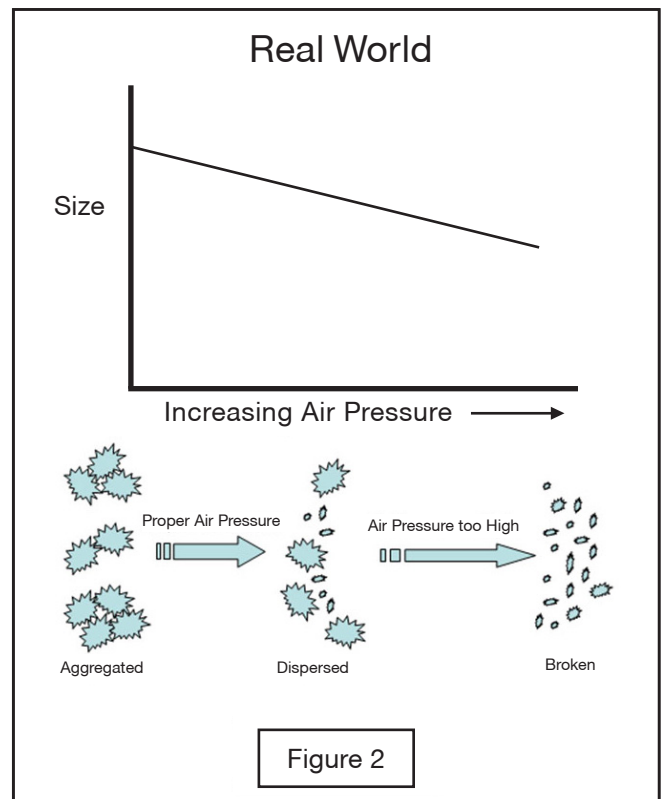
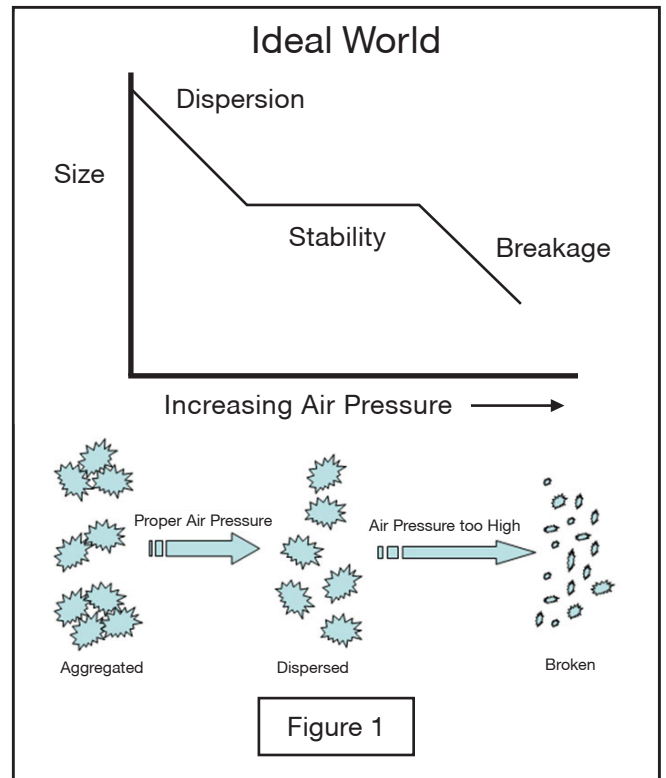
Air pressure in the dry powder feeder is used to create a shear force on the particle system, dispersing agglomerates. The dispersion pressure is adjustable depending on the needs of the sample.

Both ISO 13320 and USP <429> stress the importance of studying the effects of dispersion pressure on reported particle size: "For the development of a method, it is necessary to check that comminution of the primary particles does not occur, and conversely that a good dispersion of the agglomerates has been achieved." (4). This involves investigating the effect air pressure delivered by the dry powder feeder has on the reported result.

The PowderJet Dry Feeder system for the LA-960 also includes optional dispersion nozzles of different sizes (2 and 4 mm) to optimize the system for different size ranges. This allows the system to impart a greater dispersion force for smaller particles, while the larger nozzle allows larger particles to be measured without clogging.

This selection of nozzle size and air pressure will both have an effect on final results, so they must be studied during method development.

In the ideal world a plot of particle size vs. air pressure would look like Figure 1, with a plateau of stability in the middle. In the real world the plot often looks more like Figure 2, showing a slope without an obvious plateau. The reason for this might be that dispersion and comminution can occur in parallel rather than in series, as seen in the bottom half of the figures.



As an example, magnesium stearate was analyzed on the LA-960 using the PowderJet feeder with the small nozzle at high (3bar), medium (2bar) and low (1bar) pressure settings. Results from these measurements are shown in Figure 3.

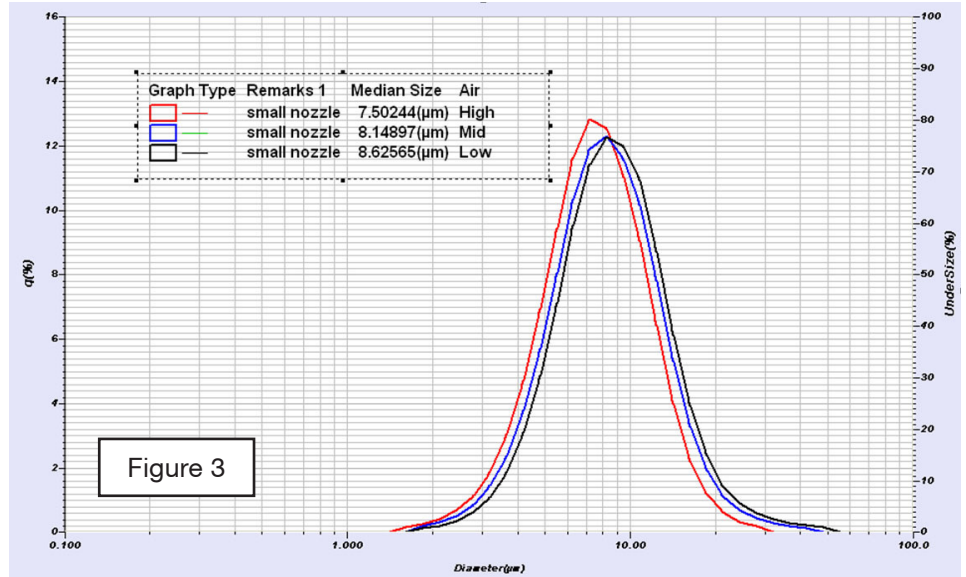


Figure 3

Figure 4 is a plot of size vs. air pressure. In this example, any of the pressures could be justified during method development, so other inputs should be considered including reproducibility data (discussed later in this document) and comparison to wet analysis.

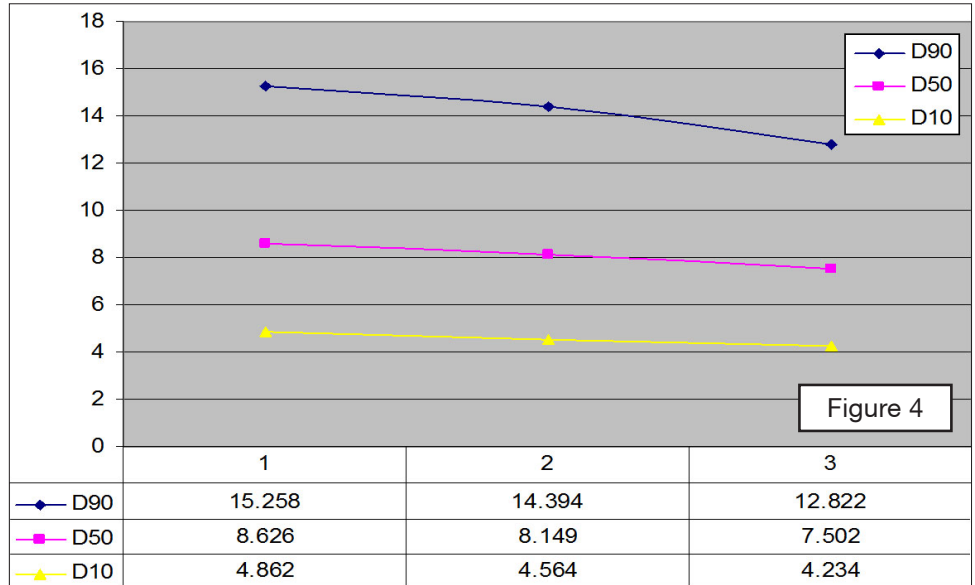


Figure 4

Figure 5 shows wet vs. dry comparison for polylactic acid (PLA) measured on an LA-960 where the median results at optimum conditions varied from 26.85 dry at high pressure (3bar) to 26.65 µm wet. In this example the 3 bar air pressure would be chosen for dry analysis.

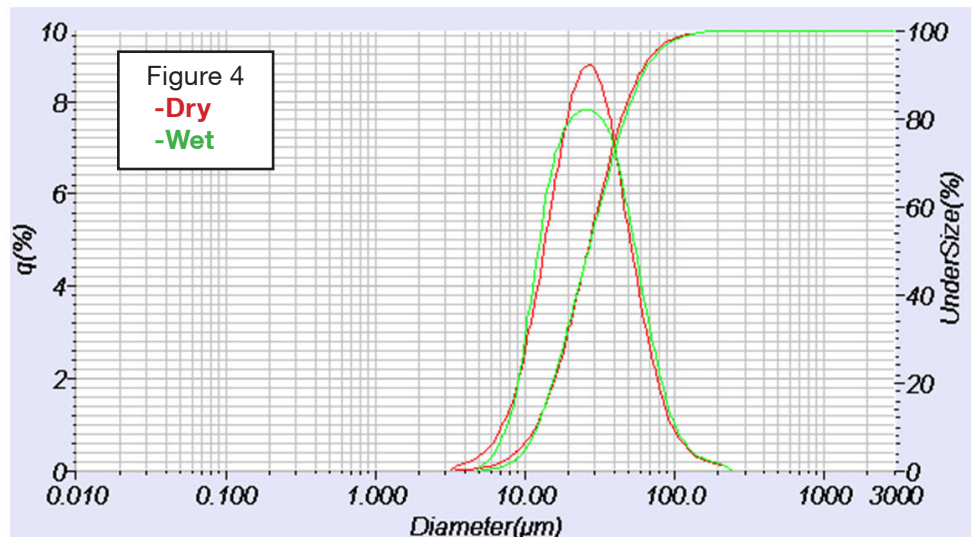


Figure 5

-Dry
-Wet

Sample Concentration and Feed Rate

It is critical to maintain a constant mass flow rate through the instrument during a measurement. Large swings in transmission (concentration) during the measurement will reduce result reproducibility. Constant mass flow rate can be achieved either manually or automatically with the LA-960 PowderJet feeder.

In manual mode the operator specifies a vibration rate and chooses to begin the measurement based on a desired transmission range or an intensity level on a selected detector. In the preferred automatic mode the operator chooses a transmission range and the system automatically adjusts vibration rate to keep the concentration constant during the measurement.

Even with the automatic feedback to control feed rate and concentration, it helps to minimize the flow of large clumps that may not be adequately dispersed by the fixed energy available. There are several available options to mechanically aid in maintaining a consistent feed rate. A roller brush can be placed in the trough to break up clumps and disperse loose agglomerates during feeding while not damaging primary particles. Spatulas or other independent objects can be added to the feed hopper to prevent bridging or clogging.

It is also possible to use feed troughs made of different materials that the sample will not adhere to, such as aluminum or ceramic-coated, or to mix the sample with some kind of flow aid such as fine metal oxide powder like silica (5) or alumina (6).

Check Reproducibility

Once all of the important components of the method have been established it is time to check for reproducibility. Both ISO 13320 (3) and USP <429> (4) establish reproducibility goals at the d10, d50, and d90 based on the coefficient of variation (COV, the (standard deviation/mean)*100) for multiple measurements as described below:

Standard	COV@d50	@d10&d90
ISO13320	<3%	<5%
USP<429>	<10%	<15%

Note: These limits can be doubled if the d50<10 µm

These calculations are now automated in the LA-960 software, facilitating the process of both method development and daily pass/fail determination. Table 1 below shows the results and COV calculations for magnesium stearate measured four times on the LA-960 using 2 bar air pressure for dispersion.

	D50	D10	D90
Mg Stearate	8.254	4.58	14.898
Mg Stearate	8.205	4.568	14.678
Mg Stearate	8.207	4.579	14.583
Mg Stearate	8.236	4.595	14.722
Mean	8.226	4.581	14.720
St dev	0.024	0.011	0.132
COV	0.288	0.242	0.896

Table 1

Conclusions

A systematic and comprehensive approach should result in a reproducible and robust method for dry particle size analysis. Selecting the optimum air pressure to achieve the desired level of dispersion is the major focus of investigation. The automatic feed back control of vibration rate and transmission level facilitates maintaining a constant mass flow rate during the measurement. Following the guidelines presented in this document customers should be able to achieve the reproducibility goals published in international standards.

References

1. T. Allen, Particle Size Measurement Chapman and Hall 4th Edition 1993
2. ISO 14488, Particulate materials -- Sampling and sample splitting for the determination of particulate properties, available at webstore.ansi.org
3. ISO 13320, Particle size analysis -- Laser diffraction methods -- Part 1: General principles
4. USP <429> Light Diffraction Measurement of Particle Size, USP30, NF25
5. For CAB-O-SIL see www.cabot-corp.com
6. For AEROSIL Alu C see www.aerosil.com