Laser diffraction: Safe migration from Malvern Mastersizer 2000 to Mastersizer 3000

By

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Laser diffraction: How to handle differences between instruments Mastersizer 2000 versus Mastersizer 3000

One of the most widely used instruments for determination of particle sizes are Malvern's *Mastersizer*. For many years, Mastersizer 2000 has been the preferred instrument. However, in recent years, a newer equipment, with improved performance, is taking over: Mastersizer 3000. In a few years it will no longer be possible to support Mastersizer 2000, so companies must replace the old instruments!

At Particle Analytical we can perform method transfer (and if required, additional method validation), to secure that the exchange of instruments takes place smoothly.

The pharmaceutical industry has very strict requirements for securing, that the quality of the products are not affected when any change is implemented – including when instruments are replaced.

When exchanging instruments into the “same type”, it should be straight forward: A comparison of results on the old equipment should be compared to results on the new equipment – and if agreement exist, everything is in fine order. However, due to some of the advanced possibilities on the Mastersizer 3000, you cannot consider it as same type – and you will not obtain exactly the same results. Thus, care should be taken when transferring methods between the equipments.

Method transfer between Mastersizer 2000 and 3000 can be regarded as a *robustness test* of the method: If the validation of your method on Mastersizer 2000 has been “perfect”, you *will* get very similar results on both instruments. However, if not all parameters have been tested sufficiently, you will observe differences in the results. Thus, the difference in results is not due to “malfunction” of the old or new equipment, but rather to the fact that some parameters have not been sufficiently under control. Some examples of things to consider are given here:

- For accurate method transfer, it is important to make sure that the optical properties (refractive index) are correct. If incorrect optical properties are used then, due to the difference in detector designs, the results obtained on each system may be different. This implies that you should use the correct refractive index of both particles and solvent – and you should never use default instrument values!!!

- One potential source of differences in results may occur when samples are at the extremes of the instruments dynamic range (which corresponds to very small and very large particles): On Mastersizer 3000, large particles, that were not detected on Mastersizer 2000, might suddenly be seen. Samples containing particles greater than 2000 µm will therefore show larger results on the Mastersizer 3000 and may show a cut off on the Mastersizer 2000 results.

- If the obscuration (concentration of particles) is too high then the measurement becomes affected by multiple scattering, causing a reduction in the measured particle size. Due to improvements in the optical design, the Mastersizer 3000 is less susceptible to multiple scattering. Thus, the "false" low result on particle sizes observed on Mastersizer 2000 at higher obscurations, might no longer be observed, thus are more correct picture of particle size is obtained.

- If you are using dry dispersion, special caution should be taken: The pressures applied using the old dispersion unit "Scirocco" does not correspond to the new "Aero" dispersion unit, as an optimised mechanism is used. Due to this change in dispersion mechanisms, it is recommended that a pressure titration is carried out in order to determine which disperser and what pressure is appropriate for the sample.

Remember, that replacement of the instrument requires documentation – and you should either be able to show that the validation on the old equipment also apply to the new equipment – or you should make a full method validation. Please contact Particle Analytical if you would like advice or support on securing smooth transition between Mastersizer 2000 and 3000.

At Particle Analytical we can perform all tests related to particles properties – and furthemore, we are able to help you set the optimal specification limts for controlling the drug product. Do not hesitate to contact us at info@particle.dk for questions or a quote.