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Short communication

Transfer and optimization of methods for particle size distribution from Mastersizer 2000 to Mastersizer 3000

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Introduction

By far the most important physical property of particulate samples is particle size. Measurement of particle size distributions is routinely carried out across a wide range of industries and is often a critical parameter in the manufacture of many products. Measuring particle size distributions and understanding how they affect your products and processes can be critical for the success of many manufacturing businesses.

Particle size analysis is an integral component of the effort to formulate and manufacture many pharmaceutical dosage forms. The link between particle size and product performance is well documented with regards to dissolution, absorption rates, and content uniformity. Particle size specification is very important feature for a poorly soluble drug substance due to the concerns of bioavailability or low dosage drugs due to the concerns of content uniformity. It is important to describe the effectiveness of physical and chemical processes, the quality of raw materials, semi-finished products and final products. Modern techniques cover a size range from nanometers up to millimeters

Materials and methods

The Mastersizer 3000 is the latest generation of the world's most popular particle sizing instrument, which uses the technique of laser diffraction to measure particle size distributions from 10 nm up to 3.5 mm. It has a smaller footprint with lower weight and smaller size dispersers, thereby freeing up space for other key equipment. The Mastersizer 3000 features a smaller detector that allows to measure an upper size limit of 3.5 mm, although its optical bench size is much smaller than that of the Mastersizer 2000. The Hydro MV is an alternative to the Hydro 2000S for smaller sample quantities, facilitating less consumption of high-cost organic dispersants and samples. The Mastersizer 3000 is programmed for direct control of sample pumping/stirring, variable power in-line sonication, dispersant filling and system cleaning. The selection of dispersions is based on the applications for which they are used and it can analyze samples in small quantities. The new Mastersizer 3000 software has all the features of the Mastersizer 2000 software, such as records view, report view, SOPs and data export capabilities, but with easy accessibility and configurability.

Because most of the methods for determination of PSD (Particle Size Distribution) are developed on Mastersizer 2000 instrument, there is a need of transferring and also optimization of those methods on the new version of the instrument (Mastersizer 3000).

Method for determination of PSD of Biperiden hydrochloride

For this method there were applied several modifications and adaptations during the verification process, such as dispersant medium, 1% NaCl solution was replaced with saturated 1% NaCl solution with the examined substance (in this case that is Biperiden hydrochloride). Because the substance is very slightly soluble in water, analysis model was also changed from General purpose (Emulated MS2000/MS2000E) to

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General purpose (MS3000) because the PSD results are not on the detection limit of the instruments, so there is no need to use the MS2000 emulated analysis settings within the MS3000 software.

Method for determination of PSD of Fluoxetine hydrochloride

This method is dry dispersion (it uses dry dispersion unit – Aero S), so there is a need for modification in the air pressure. Because the pressure used for analysis on Mastersizer 2000 is not correspondent with the air pressure value used for Mastersizer 3000, there is a need of increasing of air pressure when transferring methods from Mastersizer 2000 to Mastersizer 3000. According to the method from the manufacturer of the raw material (the method is developed on an Mastersizer 2000 type of instrument and pressure of 4 bar was used), we need to increase the air pressure when we transfer it the method on Mastersizer 3000 type of instrument, but the maximum air pressure on this type of instrument is 4 bar, so there is no possibility to increase the air pressure so that deficiency of air pressure is compensated with high energy venture disperser (instead standard venture disperser). The Hopper gap is set 2 mm higher in order to ensure equal distribution of the sample in the Sample tray.

Method for determination of PSD of Pentoxifylline

In this transfer and optimization of the method, we completely replaced the dispersant, original dispersant in the method is EPF S 20 Fluid with Ref. index 1.43. We chose dispersant with similar properties like the first one and with similar (close) refractive index (Paraffin liquid light which Ref. index is 1.47).

Result and discussion

Tests that were performed in this verifications are Repeatability and Intermediate precision. All samples were prepared just like in the original methods.

Repeatability is determined with six separate samples, with acceptance criteria (RSD) ≤ 10 % for d50 particles and RSD ≤ 15 % for d75 and d90 particles (For particles < 10 µm RSD limit should be doubled).

For Intermediate precision also were prepared six separate samples with same acceptance criteria like for Repeatability (RSD ≤ 10 % for d50 particles and RSD ≤ 15 % for d75 and d90 particles, for particles < 10 µm RSD limit should be doubled). They were measured on different day by the same operator (or on the same day but with another operator) on the same instrument in regards to the Repeatability measurements.

Conclusion

All individual results for particle size distribution are within the specified limits and conform to the acceptance criteria. RSD for repeatability and intermediate precision also conform to the acceptance criteria. From the above data, it can be concluded that the test methods are precise. Hence, it can be concluded that these methods are suitable under actual conditions of use and they are introduced into the routine use for the determination of Particle size distribution of appropriate substances (raw materials). For getting the most relevant results it is recommended to use the same instrument and equipment on which the methods are developed (in this cases Mastersizer 2000), but with small modifications and adaptations of the methods we can get similar (comparative) results on Mastersizer 3000 instrument type.

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Drug Master Files from producers of API

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