

094 Laser Diffraction Particle Size Distribution Analysis Of Hydrophobic Pharmaceutical Powders In Aqueous Media

A.P. Tinke*, R. Govoreanu, L. Lauwerysen, N. Mertens, E. Vander Stichele, K. Vanhoutte and D. Desmaele.

Johnson & Johnson Pharmaceutical Research and Development, Department for Pharmaceutical Development, Pharmaceutical Sciences, Turnhoutseweg 30, B-2340 Beerse (BELGIUM).

* contact address author: Tel. +32 14 607296, Fax +32 14 607083, atinke@prdbe.jnj.com

ABSTRACT

The development of a method meant for the particle size distribution (PSD) determination of a dry powder is related above all to the selection of the dispersion medium and the optimization of the dispersion conditions. In the pharmaceutical industry, due to the brittleness of most coarse- and due to the stickiness of most microfine powders, wet dispersion is generally preferred over dry dispersion. Though the ideal combination of dispersant and surfactant theoretically allows a more gentle dispersion of the sample, some degree of dispersion instability is readily observed thereby leading to a limited accuracy and precision of the method. From the above it should become clear that if ever one would like to facilitate a faster and better PSD method development, a basic knowledge is indispensable on how solid particles interact and what affects their detachment and stability in a liquid medium.

In the pharmaceutical industry one of the current trends is related to the clinical and pharmaceutical development of active pharmaceutical ingredients (API) that are poorly soluble in water. There are various ways to formulate these materials, which typically aim the increase of their surface area (e.g., solid or liquid submicron- or nano-suspensions). In the chemical and pharmaceutical R&D process of the drug product (DP) amongst the various characteristics of the drug substance (DS) that need to be monitored, PSD data are extremely relevant. The hydrophobic nature of the DS has the theoretical advantage that water can be used as a liquid medium for PSD measurement. However, their limited wetting capabilities may readily lead to a variability in size distribution data.

From a particle size distribution analysis perspective the aspects that may affect the wet dispersion of powder typically relate to sample (a) cohesion, (b) wetting, (c) rupture and (d) stabilization. In practise, these aspects are interdependent, and their individual contribution to the overall measurement process is thereby difficult to assess. For this study, the authors developed a laser diffraction (LD) wet dispersion method in water for the PSD measurement of hydrophobic API's. Attempts were made to explain the analytical results from a cohesion, wetting, rupture and stabilization point of view. Thereby, the authors intend to facilitate the user in a faster and better development of wet dispersion particle size distribution methods of poorly soluble pharmaceutical powders.