MODEL 3321 AERODYNAMIC PARTICLE SIZER® SPECTROMETER 3D-CORRELATED DATA ANALYSIS FOR PHARMACEUTICAL APPLICATIONS

APPLICATION NOTE APS-005

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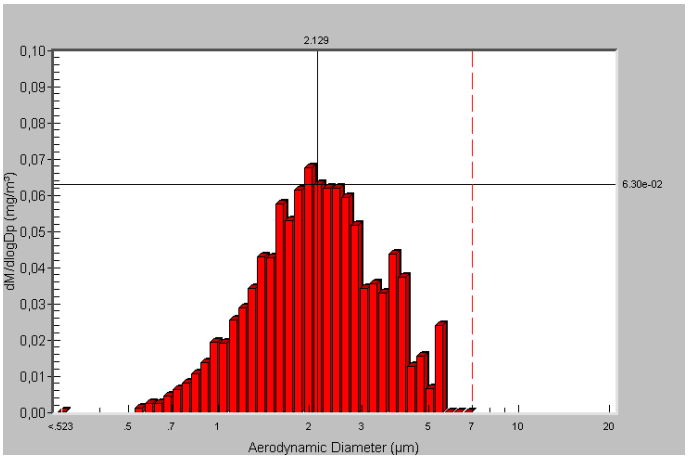
Introduction

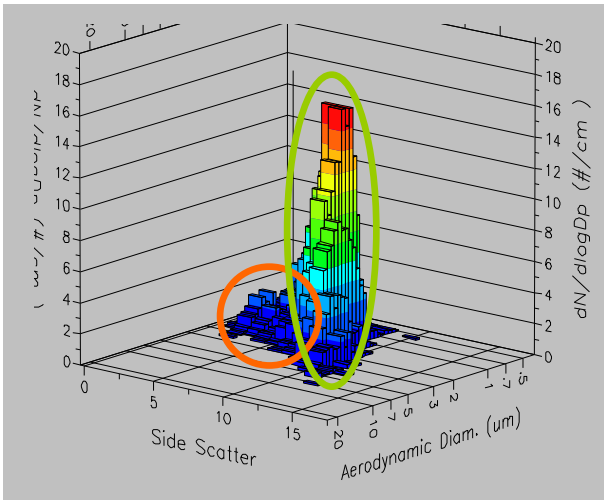
Data from an APS spectrometer as provided by a pharmaceutical customer from measurements of an inhalable drug formulation were analyzed. The data were good quality for number distributions as can be seen from the instrument's "event data" (80 to 90% event 2s, very little coincidence event 3s) but somewhat too low concentration for accurate mass conversion. Higher concentrations are recommended for future measurements to improve the statistics for coarse particles. Nevertheless mass based size distribution and MMAD could be determined rapidly.

DPI A (one active drug + one excipient)

MMAD: 2.10 µm



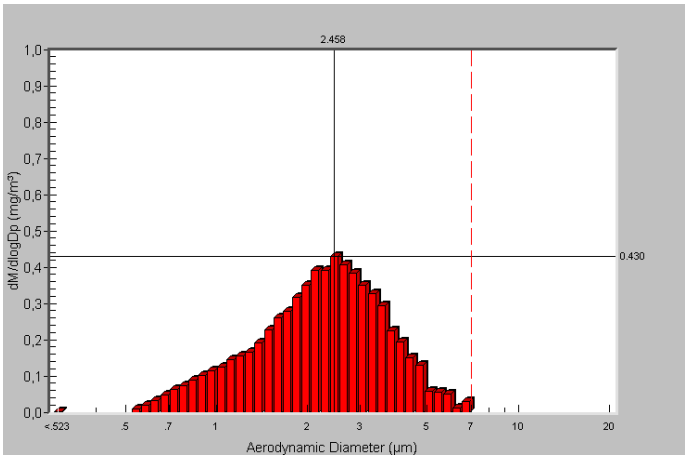
In correlated measurement mode, the 3D-plot of the number size distribution of DPI A indicates two modes. The smaller mode at low side scatter is hidden in the aerodynamic size distribution of the larger mode. These two modes indicate two particle types, one representing the active drug, the other one the excipient.



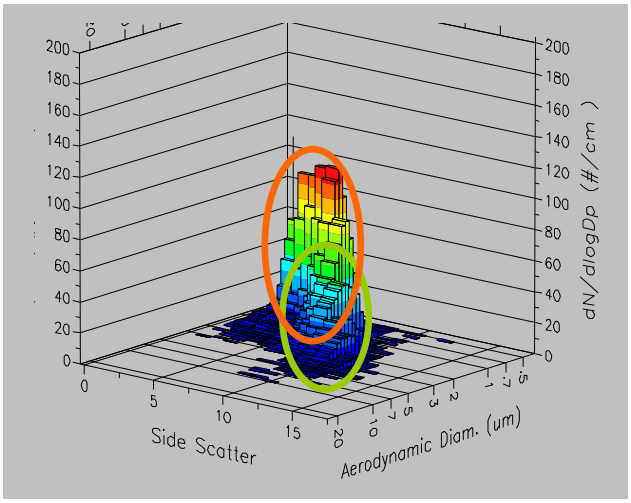
DPI B (one active drug + one excipient)

Two samples for DPI B representing the same DPI gave very similar results. The data show a very stable concentration between the two samples, so the measurement was repeated well. Already the aerodynamic size distribution shows a larger share of smaller particles as the shape of the distribution is not ideally Gaussian.

MMAD: 2.28 µm



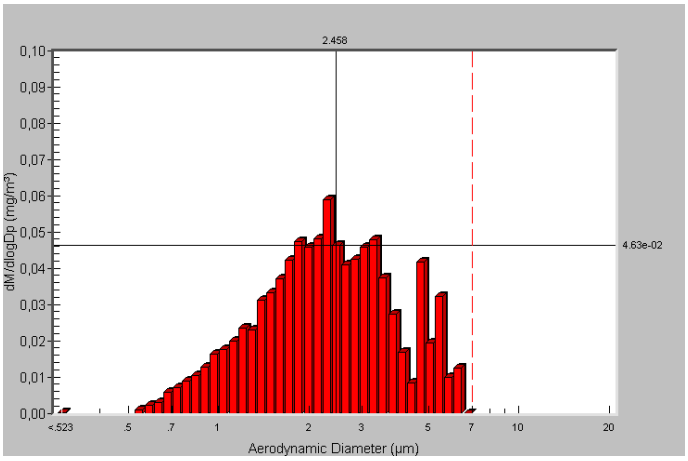
The correlated mode 3D-plot reveals the two modes even more clearly. The small particle mode is in a similar aerodynamic size range to DPI A, but dominating this distribution. Also the small particle mode is over a much wider range of size scatter than in DPI A. The large particle mode starts at about 1 µm aerodynamic size and ends at about 5 µm. This large particle mode is of the highest size scatter, which again shows that two particle types were involved in this sample.



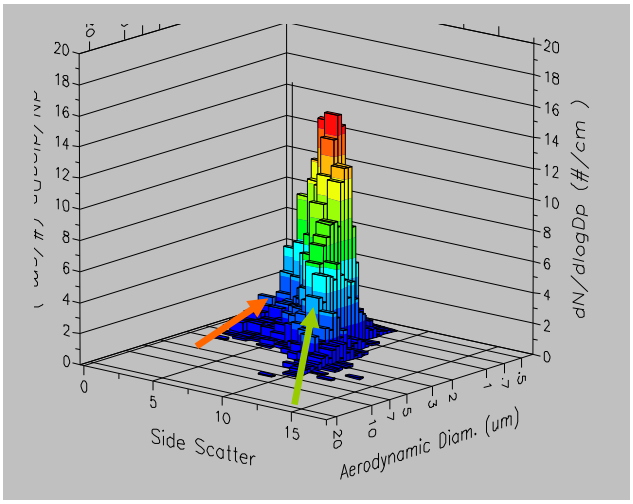
DPI C (one active drug + one excipient)

Two samples for DPI C representing the same DPI were the ones with the poorest statistics for a mass conversion, as can be seen from the scatter for particles larger than about 4 µm.

MMAD: 2.28 µm

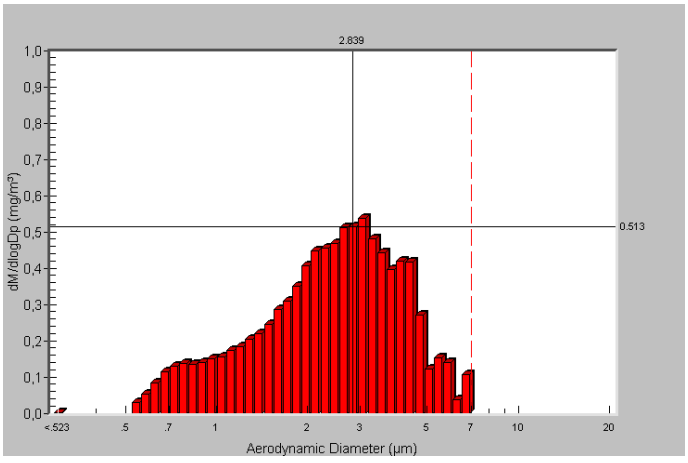


This measurement also presents the biggest difficulty to interpret the correlated data. One could speculate that similar to DPI B there is again one mode at a light scattering intensity of about 5 and one at about 10. One could also speculate that the coarse mode again is from 1 µm to maybe 5 or 6 µm. However, the modes seem merged at a 90° angle which does not allow a clear distinction. This measurement should be repeated at higher concentrations to see if there is any obvious change.

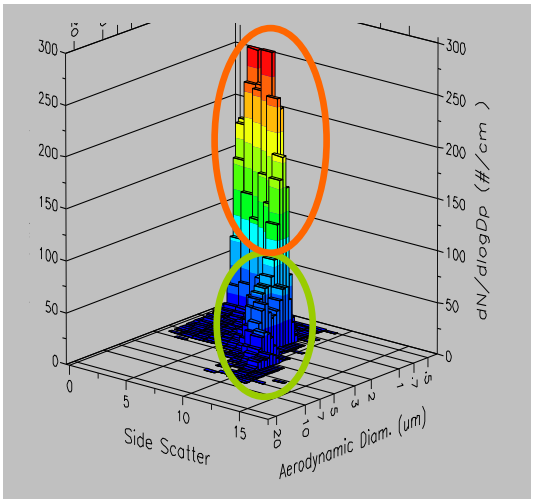


Suspension pMDI (one active drug + one excipient)

MMAD: 2.49 µm



The aerodynamic size distribution of the suspension pMDI again is a non-Gaussian one that indicates two modes. The 3D-plot reveals this even more clearly: one mode is of a very narrow, submicrometer aerodynamic size with a wide light scattering range, while the other mode ranges from 1 to ~6 µm in aerodynamic size but only a small scatter around an intensity of about 10.



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