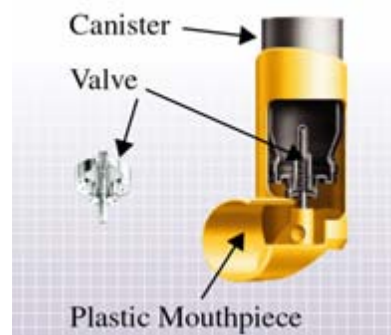


Aerodynamic Particle Sizer[®] (APS[™]) Spectrometer Model 3321 Pharmaceutical Applications

Application Note APS-003

Pharmaceutical aerosols produced by metered dose inhalers (MDIs) or dry powder inhalers (DPIs) are widely used for the treatment of lung diseases, such as asthma and chronic obstructive pulmonary disease (COPD). Inhalers are also being developed for the treatment of other diseases, such as diabetes, for their ability to rapidly deliver drugs into the systemic circulation. The aerodynamic size distribution of the spray delivered from an inhaler is a key parameter controlling the effectiveness of these devices. As a result, aerodynamic size distribution tests are widely used during the development of inhalation devices and are a required test by regulatory agencies evaluating inhalation devices.

Historically, these particle size measurements were made using cascade impactors with subsequent chemical analysis of the collected material. Unfortunately, these tests are extremely labor intensive (approximately 2 to 4 hours for the preparation and analysis of a test). Furthermore, due to the nature of the chemical analysis, results are usually not available until at least a day after the test is conducted. Recently, Stephen Stein and researchers at 3M[™] Drug Delivery Systems, have been using the Model 3321 Aerodynamic Particle Sizer[®] (APS[™]) spectrometer to characterize these aerosols. Tests that used to take hours can now be completed in about five minutes. When desired, the Model 3306 Impactor Inlet can be used in conjunction with the APS spectrometer to provide a chemically-specific estimate of the dose that has a high probability of reaching the patient's lungs. ("Respirable dose" is typically defined as those particles with aerodynamic diameters less than about 5 micrometers.)



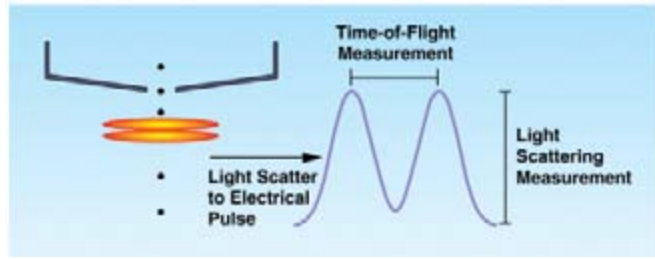
MDI illustration courtesy of Stephen Stein, 3M[™] Drug Delivery systems



3321 APS[™] Spectrometer shown with Model 3306 Impactor Inlet

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Previous time-of-flight particle sizers, such as APS™ Models 3300 and 3310 or the Aerosizer® analyzer, were not suitable for MDI measurements due to coincidence problems caused by the very high particle concentration of an MDI aerosol. (When an MDI is actuated, many millions of particles are generated in a fraction of a second.) Even with an aerosol diluter, coincidence was problematic with older time-of-flight particle sizers. However, the double-crested optics of the Model 3321 APS™ spectrometer allows for characterization of even highly concentrated aerosols such as those from MDIs.

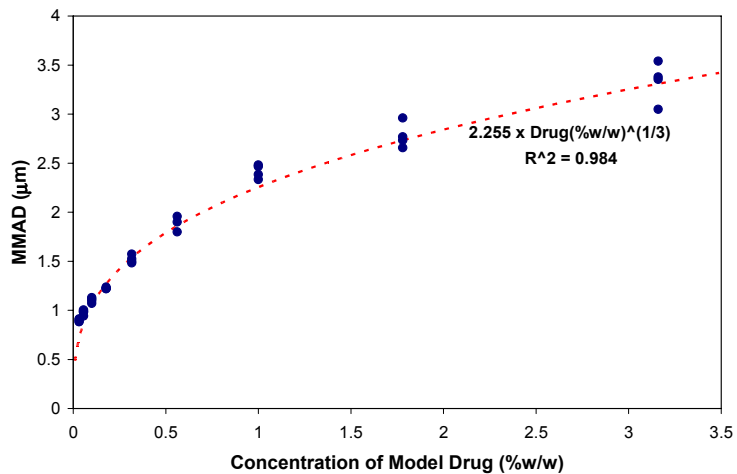


The Model 3321 uses a patented optical system to produce one double-crested signal for each particle, resulting in highly accurate measurements.

The greatly improved productivity when testing with the APS™ spectrometer (as opposed to traditional cascade impactors) allows for improved characterization of these inhalation devices. Experiments that previously would have been prohibitively resource intensive can now be conducted with the APS™ spectrometer. For example, Stein and coworkers, recently completed a study characterizing the particle size distribution of MDIs in which the drug is solubilized in the propellant formulation. The APS™ spectrometer allowed for testing of a large number of configurations with a number of replicates.

This experiment would have been excessively large for a cascade impactor testing protocol. However, the APS™ spectrometer allowed for rapid confirmation of previous theoretical predictions that the mass median aerodynamic diameter (MMAD) from a solution MDI should be approximately proportional to the drug concentration in the inhaler to the one-third power. Researchers are using the 3321 APS™ spectrometer and 3306 Impactor Inlet for many other applications in the development

Assessing the Influence of Drug Concentration on the Size Distribution from Solution MDIs



and characterization of inhalation aerosols. The time savings that these instruments offer over traditional cascade impactors will enable more efficient development of new inhalation therapies. PD

Thanks to Stephen Stein of 3M™ Drug Delivery Systems for contributing this article.

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