Technical Note – TN0105
Plume Front Velocity

The recent FDA draft guidance on Beclomethasone Dipropionate has included spray velocity as a valuable addition to traditional *in vitro* BE studies (spray pattern, plume geometry, single actuation content, and aerodynamic particle size distribution). This metric will help quantify the aerodynamic performance of the drug-device combination product and has significant discriminatory power for bioequivalence comparison.

Proveris has extended basics of the well-established SprayVIEW® technique (which produces calibrated, time-synchronized image sequences of the entire aerosol plume) with a proprietary measurement algorithm to study and quantify the emitted aerosol spray velocity called Plume Front Velocity (PFV). The PFV methodology presented here is a novel approach based on the well-established SprayVIEW technique for plume geometry measurements, with full validation capability for use under cGMP conditions, including tools to achieve 21 CFR Part 11 compliance.

The method involves identifying the leading edge of the aerosol (i.e., the plume front) from the time at which the aerosol emerges from the actuator mouthpiece (start of emission), tracking the plume front's position until the time that the emission finishes or the plume front moves out of the camera's field of view. This approach utilizes a significant amount of pointwise data for each spray event (i.e., the collected images) to arrive at the PFV value. This PFV measurement describes the velocity of the bulk aerosol in the emission direction and allows for direct comparison of test and reference products while avoiding some of the challenges of vector mapping associated with traditional methodologies that involve tracking individual particles.

The PFV analysis involves leveraging the capabilities of the benchmark SprayVIEW technology (that incorporates laser illumination and a camera) and your existing validated plume geometry method to capture a time sequence of images of the emitted aerosol from a sideward view along the actuator mouthpiece centerline (also known as plume geometry measurement). The location of the plume front is then determined from the image intensity profiles provided in the system software, tracking the plume front's position vs. time in the image sequence until the plume front leaves the field of view as shown below:

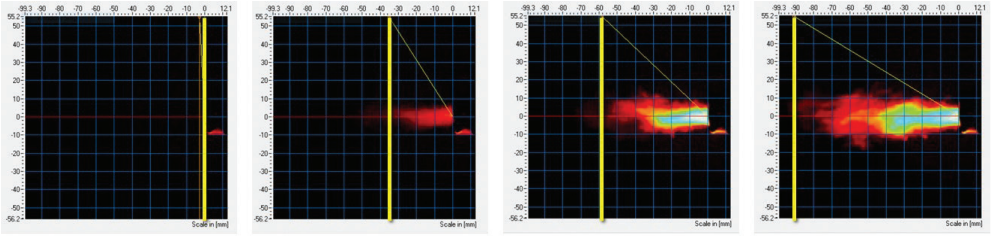

Figure 1: Time sequence of images of the emitted aerosol from a sideward view

Based on the collected data, a relative distance vs. time graph is plotted of the leading edge plume, and velocity is calculated based on a curve fit (e.g., linear least-squares) of the data. The slope of the linear fit (4.445) is reported as the PFV in units of m/s, exemplified in Figure 2 below.

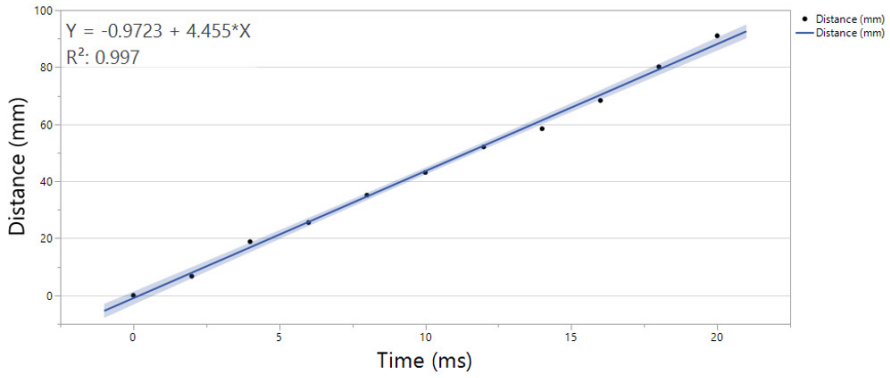

Figure 2: Relative distance vs. time graph of the leading edge plume. Velocity is calculated from the slope of the linear fit.

This approach is more discriminatory as the velocity of the spray can be traced and segmented into near-field and far-field regions from the mouthpiece edge. This compares at a macro level how the entire spray travels in the intended direction with a straightforward output – the PFV (and its rate of change).

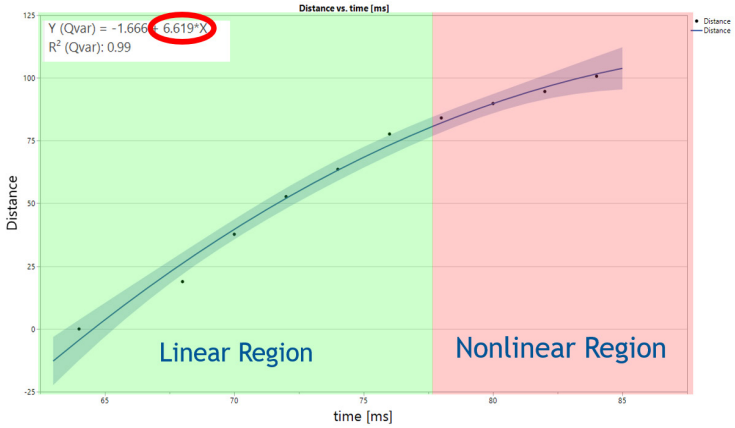

Figure 3: An example of the distance vs. time graph for PFV analysis discriminating between near field (linear region) and far field (non-linear region) regions from the mouthpiece edge.

PFV is directly related to the aerodynamic performance of the emitted aerosol from the drug-device combination product and can lead to a powerful, yet simple, way of characterizing the bulk structure of these aerosols while forming a common basis for comparison between T and R product versions.

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