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CASCADE IMPACTION COMBINED WITH RAMAN SPECTROSCOPY PROVES CHEMICAL HOMOGENEITY OF SPRAY DRIED AEROSOLS FOR PULMONARY DRUG DELIVERY. *JENIFER LOBO, Reinhard Vehring, Nektar Therapeutics, San Carlos, CA.*

Dry powder inhalers are well suited for the pulmonary delivery of active pharmaceutical ingredients both locally and systemically. Key performance parameters that need to be controlled are the efficiency of dose delivery, reproducibility of the dose, and particle size distribution of the inhaled aerosol.

To achieve sufficient powder dispersibility, the first generation of DPI's has used carrier technology, typically powder blends with lactose monohydrate. With this type of powder, the chemical composition of the aerosol varies with particle size, because the carrier particles have a much larger diameter than the drug containing particles. As a result, the particle size distribution of the drug substance within the formulation must be measured by drug specific methods, using labor and time intensive chemical assays of size fractionated powders.

Highly dispersible powders for pulmonary drug delivery are now being efficiently produced by spray-drying. These powders achieve excellent aerosol performance without carrier particles and are typically homogeneous across different particle sizes. Thus, once the homogeneity of the powder is proven, the particle size distribution for these powders can be determined gravimetrically without loss of information. This paper presents a Raman spectroscopic technique that allows rapid verification of the chemical homogeneity of size fractionated aerosols.

Raman measurements were performed with a custom-built dispersive Raman system with excitation in the red spectral region. The system consists of a cryogenically cooled CCD detector, a Czerny-Turner spectrograph outfitted with an additional filter stage, and a diode laser emitting at 670 nm. Aerosols were fractionated using an Anderson cascade impactor. The measurements were performed directly on impaction plates that were transferred from the impactor into a sample chamber with controlled environmental conditions.

Results are presented for a conventional powder based on lactose carriers, and a spray-dried powder. It was feasible to obtain high quality spectra on powder deposited on uncoated stainless steel plates and also on impaction plates that were coated with silicone oil to reduce particle re-entrainement. Typical exposure times ranged from 5 to 90 min analyzing individual impaction spots with sample masses of 1 to 20 μg. The limit of detection was found to be on the order of 0.1 μg. Difference spectra revealed no difference in the drug content of the size-fractionated, spray dried powder. Analysis of the lactose-based powder showed the expected increase in lactose content in the larger size fractions.