ABSTRACT

Ramirez, Juan Carlos. Ph.D., Purdue University, August 2005. A Study Of The Charging Characteristics Of Selected Pharmaceutical Dry Powders: Applications To Improve Mixture Formulation And Fugitive Dust Control. Major Professor: Robert B. Jacko.

An instrument for measuring the electrostatic charge of dry pharmaceutical powders has been developed. The instrument quantifies electrostatic charges in the range of -1.25 mV to +1.25 mV with a resolution of 0.61 mV. A 0.5 cc volume of eleven excipients and five active pharmaceutical ingredients (API) conveyed in a 304 stainless steel pipe develops a charge that is measured as the slug of powder passes through an inductive, non-contact sensor ring located in a Faraday cage. Powder charge ranged from +131.2 mV to -598.3 mV, with a standard deviation ranging from non detectable to 31.5 mV and a coefficient of variation ranging from non detectable to 33.7%. We found that binary mixture chargeability standard deviation increased in direct relationship with its chargeability. Considering that chargeability is a physical property of the mixture, this implies both that the chargeability of the mixture can be used as an indicator of the blend uniformity of the mixture and that chargeability needs to be minimized in order to improve blend uniformity. To control the binary mixture chargeability we found that some common excipients can be used also as a charge control agents. Excipients such as colloidal silicon dioxide (Cab-O-Sil®) developed a high negative chargeability, and when mixed with spray-dried lactose, its high negative chargeability controlled the chargeability of the mixture even when their weight percentage was only 5% (w/w). We also found that, for the velocity range studied, chargeability followed a linear relationship with increasing velocity and that the smaller the mean particle size of a compound the greater its chargeability.

The second process studied was the charging of air-entrained particles (fugitive emissions) in order to enhance their particle number decay rate by unipolar ions generated by corona discharge. This portion of the study was completed using a control system called open-path precipitation at the source, in which the source of emissions and the source of ions are in the same space. The analysis of data obtained from the pilot tests

conducted in the 51-liter (1.8 ft^3) chamber under a vertical flow of 424 liter/hour (0.25 CFM) showed that the reduction of the steady-state total number of particles was in the range of 57% to 93%. The percent-reductions on the particle concentration half-life ranged from 8.5% to 91% for the individual particle size ranges, being compound dependent. The analysis of the correlation matrix between the individual half-life values of the particle size ranges and three physical properties (volume-specific chargeability, mass specific chargeability, and true density) indicates that few of the observed relationships were very strong. The strongest relationship was between the half-life of the 0.5 -1 µm size range of all the compounds tested with ions present and their corresponding volume-specific chargeability ($r = 0.815$).The pilot study was followed by a larger scale study, where three compounds were tested in a pharmaceutically relevant conditioned 8.35 m^3 room under zero-net-flow conditions. The average (n=3) percent reduction in the steady state for the total particle concentration was in the range of 20% to 43%. At the individual particle size range level, the percent reduction ranged from 1% for the 10-25 µm (larger particles that settle rapidly) size range of microcrystalline cellulose-Avicel PH®102, to 69% for the 5-10 µm size range of spray- dried lactose. The repeatability of the protocol to conduct these tests in terms of the coefficient of variation presented an average value of 22.3% ±19.5% (S.D).

We concluded that some common excipients can also be used as charge control agents, and that the charge can be adjusted modifying the particle size distribution of the excipient. Also, we verified that the open-path unipolar ion system has the potential to enhance the control at the source of pharmaceutical fugitive emissions.