

ABSTRACT:

Measurements: Particle Size Measurements for OINDP Quality – I: Cascade Impactor

Dr. Jolyon P. Mitchell Ph.D., FRSC (UK), C.Chem., C.Sci.

Aerosol aerodynamic particle size distribution (APSD) is a critical quality attribute for determining inhaler performance in the quality control environment. This is because likely deposition of inhaled medication in the various regions of the human respiratory tract is highly size dependent. The multi-stage cascade impactor (CI) or liquid impinger are the standard apparatuses in the pharmacopeial compendia for the aerodynamic particle size analysis of aerosols from orally inhaled products. A modification of this technique with reduced number of collection stages may also be useful to quantify the mass of particles larger than about 10 μm aerodynamic diameter that might undesirably penetrate beyond the nasopharynx and enter the lungs, associated with nasal drug delivery products. The presentation begins by examining the purpose, attributes and uses of quality control testing for OINDPs, with the focus on the cascade impactor-based determination of inhaler aerosol APSD. Next, the full resolution CI method is described, looking at the underlying operating principle of inertial size fractionation in the Stokesian regime. The limitation of the CI as a predictive tool for particle deposition location in the respiratory tract and the consequence this restriction places on the interpretation of data are also reviewed. Next, the most frequently encountered CI types are presented before going on to examine the roles of the induction port inlet and pre-separator (if needed). The many factors responsible for introducing measurement variability (precision) are discussed, as are ways to avoid measurement bias (inaccuracy). The presentation continues with an examination of some oral inhaler-specific issues. These are: (1) effect of co-solvents used with some pressurized metered dose inhaler (pMDI) products on APSD determination; (2) the testing of spacer and valved holding chamber add-on devices frequently prescribed for use with pMDIs. The presentation concludes by examining how CI-based methods are being used in the context of evaluating nasal drug delivery products for fine droplets that might penetrate beyond the nasopharynx into the lungs, and thereby affect the safety profile of the drug product.

May 2017