ABSTRACT:

Relationships between Laboratory Measurements, Particle Deposition, Imaging, Pharmacokinetics, and Pharmacodynamics

Prof. Myrna B. Dolovich P.Eng.
Dr. Jolyon P. Mitchell Ph.D., FRSC (UK), C.Chem., C.Sci.

Measurements of inhaler performance in the laboratory are only a small part of the overall picture when it comes to the assessment whether or not an orally inhaled and nasal drug product (OINDP) is approved for sale to patients. The focus of this presentation is primarily on the establishment of bioequivalence, which is important in the development and registration of second-entry (generic) products that are increasingly significant in the marketplace. The presentation begins by examining the significant differences in the way that regulatory agencies in Europe, Canada and the USA currently review orally-inhaled products (OIPs) and these are highlighted in terms of the assessment modalities that have been introduced. Key aspects of laboratory-based *in vitro* testing, pharmacokinetic (PK) and pharmacodynamic (PD) clinical studies are briefly discussed. These components of the complete testing profile of the new OIP, as well as patient use assessments can be thought of as a bridge, with imaging methods to establish the fate of deposited particles in the body, in particular the lungs, as being a key and often missing link in submissions to the regulatory agencies. The question is then addressed: How can lung imaging help clarify the overall understanding of the inhaled drug product in patients? The focus moves on to look at the patient-inhaler interaction, often missed in clinical trials. It continues by examining why an *in vitro*/*in vivo* correlation (IVIVC) for OINDPs is a desirable goal, indicating how recent improvements to laboratory methods is offering the prospect that it might eventually be achieved for at least some drug product classes used with inhalers. The presentation concludes by highlighting how the bridge between laboratory and clinic can be completed by identifying key areas for research that were highlighted in a symposium sponsored by the International Society for Aerosols in Medicine (ISAM) in 2013.

July 2018