ABSTRACT:

Measurements for OINDP Quality – I: Delivered Dose Uniformity (DDU)

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There are two principal metrics associated with OINDP quality assessments: (1) **delivered dose uniformity** (DDU), in which the total mass of active pharmaceutical ingredient(s) in the airborne particulate from the inhaler is quantified using the **Dose Uniformity Sampling Apparatus** (DUSA), and (2) **aerosol aerodynamic particle size distribution** (APSD) that is determined by **multi-stage cascade impactor** (CI). Both DDU and APSD are critical quality attributes for determining inhaler performance and their determination is described in the pharmacopeial compendia. DDU addresses the quantification of the stability of dose delivery across several inhalers of the same lot, examining performance at beginning and end of the life of the inhaler. As with all types of dosage form, DDU is important as the means to assure reproducible dose delivery.

The presentation begins by identifying the focusing on the attributes that make a method for inhaler quality control robust, introducing the concepts of accuracy, precision and traceability. Next the two types of Dose Uniformity Sampling Apparatus (DUSA) for pressurized aerosols and dry powder inhalers respectively are introduced. DDU determination, looking at specification setting and data assessment using parametric tolerance interval testing. Key aspects of the harmonized methodologies for DDU contained in both the European and United States pharmacopeias are described. The talk continues by introducing DDU for the two major categories of nasal inhalation systems, pressurized nasal metered-dose inhalers and aqueous nasal spray pumps, and continues by showing how the compendial methods address each nasal product category. DDU accuracy, precision and method limitations are next described. The section on product quality control concludes with a summary of batch acceptance from DDU measurements using parametric tolerance interval testing (PTIT), which has a sound statistical basis. The focus of the presentation then transitions to look briefly at more clinically relevant aspects of DDU for orally inhaled products, by introducing breathing simulation, rather than sampling at a constant flow rate and the use of anatomic and idealized inlets to determine the fine particle/droplet portion of the dose capable of penetrating the oropharynx. In conclusion, a summary of the key aspects of DDU is provided for product quality control purposes.

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