

## **Powder Microstructural Analysis for Inhalation Blends**

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**Summary:** Formulation microstructure has emerged as an important topic of consideration for the demonstration of equivalence between different product batches or between branded and generic medicinal products. In the case of dry powder inhalation products, the formulation performance depends on the structuring of the component materials within the powder bed, because it is this structuring which determines the geometries of interparticulate cohesion forces, as well as the permeability of the powder bed to fluidizing airflow. Understanding the link between microstructure, processing, input material properties and product performance is crucial, but a central part of this is the microstructural characterisation. X-ray computed tomography (XCT), a form of x-ray microscopy (XRM), has emerged as invaluable, non-destructive tool for the characterisation in materials science field as diverse as metallurgy to catalysis. XCT is well-known in pharmaceutical sciences for its biological applications, but advances in x-ray optical technologies has resulted in the availability of laboratory instruments with resolution scales suitable for the analysis of inhalation powders. In this lecture, the technology and application of three distinct XRM techniques will be introduced: X-ray attenuation CT; phase-contrast attenuation XCT; and diffraction contrast tomography. Specifically, the ability of XRM to provide microstructural insight at nano- and micro-scales when assessing the distribution of active pharmaceutical ingredients within pharmaceutical blends will be presented. Additionally, the links between powder processing and powder microstructure will be discussed, highlighting the powerful ability of XRM as a non-destructive technology to characterise particle and powder properties, that determine the interactions between formulation components.