## New in-vitro bioequivalence approaches for generic nasal suspension products

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Since early 2016 there has been significant focus from the generic pharmaceutical industry in pursuing an in-vitro only approach to bioequivalence for ANDA submissions to the FDA for nasal spray products. This new approach has been triggered by the successful approval of a generic Nasonex® by Apotex Corp, demonstrating Q1/Q2/Q3 equivalence and thus provided a weight of evidence approach that bypassed the traditional in-vivo clinical endpoint study requirement. Subsequently, the FDA have issued several sets of product specific guidance for nasal products, including the suggestion of an alternative approach to comparative clinical endpoint study.

The principle new technique used was the inclusion of a novel in-vitro method that utilised Morphologically- Directed Raman Spectroscopy (MDRS) technology developed by Malvern Panalytical to chemically identify and characterise the particle size distribution of the API particles within the nasal spray formulation. This technique has opened the possibility to assess and characterise API particle sizes not only from the formulation excipients but also in the size range of <3µm enabling more detailed comparison of the key particle size metrics for test and reference products.

There are limitations to this technique once the size is less than 0.5um which is typically the case for some of the API material present. To address this, orthogonal techniques can be incorporated such as laser diffraction. While it lacks specificity to API particles, using the MDRS data to inform the laser diffraction data interpretation, allows a detailed characterisation of the API within complex formulation types.