# Effect of physicochemical properties of Q1/Q2 ophthalmic suspensions on ocular bioavailability and bioequivalence

S. Vooturi [1], D. Bourne [2], J. Panda [2], S. Choi [1], H. Kim [1], S. Yandrapu [2], U. Kompella [2]
[1] U.S. Food and Drug Administration, [2] University of Colorado

**Purpose**

To determine the effect of particle size and viscosity on qualitatively (Q1) and quantitatively (Q2) similar ophthalmic suspensions on ocular bioavailability/bioequivalence (BA/BE).

**Methods**

Q1/Q2 budesonide suspensions with varying particle size and viscosity were prepared. Different manufacturing methods such as homogenization and homogenization followed by microfluidization were used to achieve nanosuspensions (~700 nm) and microsuspensions (~2,000 nm), respectively. Viscosity of the suspensions was varied using different grades of hydroxyl propyl methyl cellulose (HPMC). The effect of particle size and viscosity on ocular bioavailability was determined in New Zealand rabbits by placing a 30 μL eye drop in the cul-del-sac of both eyes. At each time point (0.11, 0.5, 1.0, 2.0, 4.0, & 6.0 hours), rabbits were euthanized and aqueous humor was aspirated from the eye and stored frozen until analysis by LC-MS/MS. Pharmacokinetic parameters such as Cmax (mean) and tmax (median) were estimated by observation, whereas AUC (0-6 hr) was estimated using the linear trapezoidal method. Further, a bootstrap method was used to assess bioequivalence.

**Results**

Three Q1/Q2 budesonide suspensions (A, B, & C) differing in particle size and/or viscosity were prepared. Suspensions A and B varied only in particle size (~700 nm vs ~2000 nm), with constant viscosity (4.9 cPs); B and C varied only in viscosity (4.9 cPs vs 53 cPs), with constant particle size (~2000 nm); thus, A and C differed in both size (~700 nm vs ~2000 nm) and viscosity (4.9 cPs vs 53 cPs). For suspensions A, B, and C, the average Cmax was 0.26, 0.22, and 0.35 μg/g and median tmax was 0.50, 0.50, and 1.0 hr, and AUC (0-6 hr) was 0.73, 0.53 and 0.95 μg.hr/g, respectively.. The 90% confidence intervals based on bootstrap analysis for the ratios of AUC (0-6hr) were 0.60-0.97 (C vs A), 1.05-1.75 (B vs A), and 0.46-0.69 (C vs B), respectively.

**Conclusion**

The three Q1/Q2 suspensions varying in particle size and/or viscosity were not bioequivalent to each other. An increase in viscosity from 4.9 cPs to 53 cPs (B vs C) improved the bioavailability of budesonide.