Method Validation for a Low Level Stability Indicating Assay Method of Multiple Glucocorticoids in Nasal Spray Products Using UPLC

T. Heiser
Next Breath, LLC

Purpose
To validate a rapid and comprehensive stability indicating analytical method which utilizes Ultra High Pressure Liquid Chromatography (UPLC) technology to separate, identify, and quantify five of the most commonly used glucocorticoid steroids found in nasal spray products.

Methods
This assay was validated for five active pharmaceutical ingredients found in nasal sprays such as Triamcinolone Acetonide (Nasacort®, Budesonide (Rhinocort®), Fluticasone Propionate (Flonase®), Mometasone Furoate (Nasonex®) and Beclomethasone Dipropionate (Beconase®). Chromatographic separation was achieved using a column: Kinetex C18, (50 x 2.1mm ID, 1.7μm) and Ultra HPLC in line filter (0.5μ depth x 0.004in ID). The mobile phase consisted of Acetonitrile / H2O (73:27), addition of 0.5mL of Acetic Acid per liter (adjusted to pH 3.9 NaOH). Waters Acquity UPLC with PDA detection was employed for the rapid separation of the glucocorticoids.

Results
Linearity was consistently demonstrated with R-Squared of >0.99 with a range from LOQ to 150% (0.5ppm – 25ppm). The analytes show matrix stability demonstrated by 24 hours at ambient and refrigerated conditions. ICH and FDA guidelines were adhered to during the validation process including; Precision, Intermediate Precision, Linearity, Accuracy, Robustness, Range, Specificity, Mobile Phase and Diluent stability, and LOD/LOQ determination. Related substance Compound D was identified and separated from Fluticasone Propionate with resolution ≥1.5. Epimers B & A were separated and easily resolved from Rhinocort.

Conclusion
A stability indicating UPLC method was developed and validated which allows for the concomitant quantification of Triamcinolone Acetonide, Budesonide, Fluticasone Propionate (including Compound D), Mometasone Furoate, and Beclomethasone Dipropionate. The method was shown to be accurate and robust and will not only allow for a quicker and more cost effective analysis but can be utilized as a screening for cleaning validation purposes.