The Investigation of Factors Contributing to Immunosuppressant Drugs Response Variability in LC-MS/MS Analysis

Joseph Herman, Dayana Argoti, Sarah Fair; Thermo Fisher Scientific, Franklin, MA, USA

Overview

Purpose: To investigate the factors that cause variation in response of immunosuppressant drugs to changes in method parameters. The immunosuppressant drugs of interest were Everolimus, Tacrolimus, and Sirolimus, and were investigated in this study.

Methods: A supervised randomly selected sample of the immunosuppressant drugs was performed in a randomized design. The development of the entire set of SDS (including Cyclosporin A, Sirolimus, and Tacrolimus) was extensively validated and evaluated. Several extraction vials were compared for the immunosuppressant drugs. A new Transcend™ system that maximizes efficiency and minimizes assay clean-up time was also evaluated. The coefficient of variability (CV) was used as an ongoing investigation only to the response variability of those compounds when using unit-labeled standards.

Results: The study investigated the factors that cause variation in response of immunosuppressant drugs in matrix. The results show that the type of extraction vial and cross-talk between analytes were investigated in this study. The CV was found to vary significantly with the type of extraction vial used. The results indicate that the type of extraction vial plays a role in the success or failure of the assay for Everolimus and Sirolimus. Both of these analytes prefer silanized glass for preparation and injection suggesting that glass containers are preferable.

Conclusion: The immunosuppressant drugs are often assayed together in matrix. However, this can present issues due to cross-talk and other factors. Figure 10 shows the calibration curves and percent difference for Everolimus (combined prep). The CV was found to vary significantly with the type of extraction vial used. The results indicate that the type of extraction vial plays a role in the success or failure of the assay for Everolimus and Sirolimus. Both of these analytes prefer silanized glass for preparation and injection suggesting that glass containers are preferable.