Title: Assay Performance for a Newly Reformulated Immunoassay to Quantify Cyclosporine in Whole Blood

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Background: Recently, Abbott Diagnostics reformulated a new Cyclosporine assay (LN3R30) to eventually replace the current on-market product (LN1L75). Reformulation was necessary following external end-user feedback that the assays imprecision was an opportunity to improve on the existing assay design. During development, numerous analytical studies were completed to confirm the new design change goals were achieved. These data represent internal, external, and additional end-user assessments conducted to confirm performance specifications during design control were maintained for the newly reformulated LN3R30.

Methods: Assay performance studies were conducted using the Abbott ARCHITECT i2000SR, Alinity i, and Liquid Chromatography Tandem Mass Spectrometry (LC-MS/ MS). Abbott assays used in this study include the current on-market Cyclosporine assays for ARCHITECT (LN1L75), ARCHITECT (LN3R30), and Alinity i (LN09P39). Total precision, limits of measurement, metabolite specificity, method comparison, sample and lot-to-lot reproducibility were assessed.

Results: Precision studies using three levels of commercially available whole-blood controls; 80.4, 327.5, 676.6ng/mL resulted in imprecision profiles of 5.3%, 6.6%, and 8.8% respectively. Linear regression models suggest LN3R30 has a concentration dependent bias based on slope (<0.9) and intercept (~10.0 ng/mL) when compared to both comparative methods (LN1L75 and LC-MS/MS). The analytical sensitivity represented at the LoB, LoD, and LoQ were 3.3, 6.7, and 18.0 ng/mL respectively. Results for the reformulated LN3R30 assay displayed an average percent difference between lots of 5.39% (0.0% – 32.1%), compared to LN1L75; 13.75% (0.2% – 58.3%). Sample reproducibility results for LN3R30 indicate a mean percent difference of 5.70% (0.1% - 31.1%), compared to LN1L75; 12.1% (0.0% – 62.1%).

Conclusions: Overall the assay design goals for the reformulated LN3R30 assay were achieved, namely improved precision profiles. As is the case with most immunoassay-based TDM assays, some level of cross-reactivity to the metabolites can occur but is not always predictable when developing the assay. Due to the change in monoclonal antibody, the bias observed for LN3R30 is different than that observed with LN1L75. Based on these differences, it is important to transition the new assay with the appropriate level of physician education and analytical validation prior to patient testing.

Key Words: Cyclosporine, Immunoassay, Immunosuppressants, Solid Organ Transplantation