Lot Bridging Considerations for Immunoassay Kits in Biomarker Studies

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Abstract

Purpose
To examine the bioanalytical considerations that are involved in bridging immunoassay kit lots with focus on a case study involving 11 biomarkers for a cutaneous lupus study.

Methods
Three singleplex MSD ECL kits (MCP-2, E-selectin, and VEGF) and one custom 8-plex MSD ECL immunoreactivity assay (TNFα, IFNα, IL-6, MCP-1, I-TAC, MIG-1, IP-10, and TARC) were validated for quantification of these analytes. Lot bridging studies were performed using stability samples and freshly prepared QCs run on old and new lots of kits with old and new lots of calibrators. Ratios of the samples’ mean concentrations between old and new lots of kits or calibrators were examined to determine if a correction factor was needed to bridge measurements from different kit lots.

Results
The three singleplex MSD-ECL kits (MCP-2, E-selectin, and VEGF) and five of the eight analytes (TNFα, IFNα, IL-6, MCP-1, and I-TAC) in the custom 8-plex MSD-ECL kit had similar CV (% ) between old and new lots of kits used in validation and no correction factors were required when measuring these analytes between old and new lots of kits. However, correction factors were required for three of the analytes of the custom kit (IP-10, I-TAC, and MIG) due to a difference in analytical measurement performance between the old lots used during validation and the new lot of kits.

Conclusion
One of the challenges that all bioanalytical labs face today is how to handle the variability in the immunoassay kits that are available in the market today. In particular, this is a challenge when the studies last multiple years requiring bridging between multiple kit lots during the study lifetime. Lot bridging experiments that measure the effect of using different lots of immunoassay kits are critical to ensuring there is consistent measurement of the analyte over the course of the study.

Introduction & Objective
Successful interpretation of a biomarker study in support of both preclinical and clinical studies heavily depends on the quality of the bioanalysis. A hallmark of successful translation is the integration of data and information obtained from multiple sources to create a systems view of disease and one of the key components would be high quality and consistent bioanalytical data throughout the entire project. One of the challenges that all bioanalytical labs face today is how to handle the variability in the immunoassay kits that are available in the market today. In particular, this is a challenge when the studies last multiple years requiring bridging between multiple kit lots during the study lifetime.

This poster presents a case study of bridging three singleplex and one custom multiplex MSD Scaled Discovery electrochemiluminescent (Meso-ESI) immunoreactivity assay kits for 11 biomarkers used in an ongoing cutaneous lupus study.

Methods
Three singleplex MSD-ECL immunoreactivity assay kits for MCP-2, E-selectin, and VEGF, and one custom 8-plex MSD-ECL kit for TNFα, IFNα, IL-6, MCP-1, I-TAC, MIG-1, IP-10, and TARC were validated for quantification of these analytes in human plasma almost a year in advance of sample analysis. Lot bridging studies were performed using stability samples and freshly prepared QCs run on old and new lots of kits with old and new lots of calibrators. Ratios of the samples’ mean concentrations between old and new lots of kits or calibrators were examined to determine if a correction factor was needed to bridge measurements from different kit lots.

Results

Lot Bridging Acceptance criterion: A correction factor was not needed if 90% of the Old/New Lot Ratios comparing the means of the QCs when run on different kit lots fell within 0.75 to 1.25 with CVs for each measurement equal to or less than 25%.

If a correction factor was needed for a particular analyte, the value of the correction factor was determined from the average of the Old/New Lot Ratios.

Conclusions
Lot bridging experiments that measure the effect of using different lots of immunoassay kits are critical to ensuring there is consistent measurement of the analyte over the course of the study.

Reference