Alturas Analytics, Inc.
The LC/MS Experts™

T 208.883.3400
F 208.882.9246
www.alturasanalytics.com

Development of LC-MS/MS methods for the quantitation of commonly co-administered drugs and an assessment of the impact of their presence on the analysis and stability of novel drug candidates in support of a clinical study

Ryan Schmich, Katherine Yahvah, Jennifer Zimmer, Ann Hoffman, Shane Needham

Abstract

Clinical studies involving novel drug candidates are at an all-time high as their use in immunotherapies and other targeted therapies begins to swell. The 2018 FDA Guidance for the Validation of Bioanalytical Methods requires an assessment of the impact of the presence of co-administered drugs on the analytical measurement and stability of novel drug candidates. In support of a clinical study that featured co-administration of Cimetidine, Itraconazole and Paroxetine with a proprietary drug candidate, GLP-compliant methods were developed and validated for each of these commonly co-administered drugs. In accordance with the FDA guidance, the impact of the presence of these co-administered drugs on the sensitivity and selectivity of the measurement of the proprietary drug and its metabolite was assessed. Additionally, the impact of the presence of the co-administered drugs on the freeze/thaw stability, bench top stability and long term storage stability of the proprietary drug and its metabolite were also assessed. Analytical results demonstrated that these co-administered drugs and the proprietary novel drug and metabolite could be measured with acceptable accuracy and precision when analyzed in samples that contained combinations of these analytes. Further, the data indicate that samples containing combinations of the proprietary drug and metabolite along with the co-administered drugs were stable when submitted to conditions similar to the conditions that clinical samples would be subjected to. Subsequent sample analysis in support of the clinical study generated 4031 reportable results for 2783 samples across five analytes. Four HPLC-MS/MS instruments were employed during the study and 93% of analytical runs met acceptance criteria. This work was performed with a 1 month turn-around time for QA reviewed data after the receipt of the final sample shipment.