LC-MS/MS Software Data Processing and Review Workflow
Improvements for Clinical Research

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Background: In the field of quantitative LC-MS/MS, the need for efficient, accurate and user-friendly data review software is paramount, with the data generated in the clinical laboratory meeting local guidelines, as well as rigorous method performance characteristics defined by the FDA Bioanalytical Method Validation and CLSI C62-Ed2 guidelines.

The quantitative LC-MS/MS workflow is dependent on interfacing to LMS/LIMS for sample traceability, batch analysis using matrix-matched external calibrators and quality controls for quantification and acceptance, and stable-isotope labeled internal standards to compensate for sample extraction, recovery, matrix effects and analytical variability. The demands on the laboratory to run multiplexed analyte panels and analyze a greater number of samples produces large amounts of analytical data which must still go through batch and quality review before release from the laboratory to the clinicians. The Waters Data Review Software significantly reduces the burdensome aspects of batch quality control by introducing a series of innovative features. These include improvements in workflow, a modernized interface, and the ability to flag exceptions based on acceptance criteria.

Methods: Samples for three multiplexed LC-MS/MS panels with previously defined analytical method performance characteristics were acquired using Waters IVD Systems controlled by MassLynx software. The data was processed, quantified, and reviewed using both the existing TargetLynx XS IVD Application Manager and the new Data Review software. Three quantitative LC-MS/MS methods selected to demonstrate the capabilities of the new Data Review software were the analysis of four immunosuppressants drugs in whole blood using protein precipitation, a twelve steroid panel in plasma following SPE clean-up and a urine dilute and shoot method for a drugs of abuse panel containing greater than 80 analytes. Each method used matrix matched calibrators and QCs for quantification and batch control with performance characteristics including calibration linearity, carryover, precision and accuracy.
Results: The analytical performance data generated using the new Data Review software compared to the TargetLynx XS data met the same method performance criteria of the analytical laboratory. For example, a summary of the immunosuppressants precision and accuracy is given. The mean repeatability and total precision (%Coefficient of Variation) respectively for the individual QCs processed using TargetLynx XS were for cyclosporine ≤2.2% and ≤5.9% CV, everolimus ≤7.8% and ≤7.8% CV, sirolimus ≤10.3% and ≤10.8% CV and tacrolimus ≤5.2% and ≤8.0% CV. The mean repeatability and total precision (%CV) respectively for the immunosuppressant individual QCs processed using Data Review were for cyclosporine ≤2.2% and ≤5.9% CV, everolimus ≤7.9% and ≤7.9% CV, sirolimus ≤10.4% and ≤11.3% CV and tacrolimus ≤5.2% and ≤8.0% CV. The mean % bias of External Quality Assurance Sample (n=40) for each analyte processed using TargetLynx XS were cyclosporine 7.94%, everolimus -4.04%, sirolimus -0.70% and tacrolimus 4.35% respectively whilst the mean % bias calculated using Data Review were cyclosporine 7.94%, everolimus -4.15%, sirolimus -0.97% and tacrolimus 4.59% respectively.

Many benefits of the software including a user friendly interface, batch level review, simplified task-oriented accelerated workflows and focused review by exception help to reduce time reviewing software particularly of large multiplexed panels by up to 50% as demonstrated by the urine definitive drug panel. The software is simple to use with batch level review giving an immediate view as to whether the batch has passed and the task-oriented workflow decouples complicated data review into several simple tasks.

Conclusions: The new Data Review software generated results equivalent to the existing TargetLynx XS Application Manager. The software’s enhanced workflow capabilities streamlined the review process in a new user-friendly interface which reduced the training burden enabling scientists to generate high-quality data quickly and easily. The exception focused review functionality allowed tailored rule sets which reduced the time spent reviewing data by up to 50%. Whilst the batch-level review and task-oriented workflow improved batch acceptance and simplified the review of complicated datasets into easy tasks.

By integrating these features, Data Review software offers a comprehensive solution that not only improves the efficiency and accuracy of batch quality control but also contributes to the overall reliability and integrity of quantitative LC-MS/MS analysis.

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