# INTELLIGENT USE OF RETENTION TIME FOR HIGHER ORDER MULTIPLE REACTION MONITORING MULTIPLEXING – *SCHEDULED* MRM™ ALGORITHM

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The utility of Multiple Reaction Monitoring (MRM) on triple quadrupole based MS systems for biomarker verification/validation studies is currently an active area of investigation, driven by the well known sensitivity and selectivity attributes of this type of MS approach. As more extensive protein panels need to be monitored in a targeted way across multiple samples, higher MRM multiplexing is becoming essential for throughput. The challenges of assay development and running these large scale studies are becoming better understood, the need for rapid assay development, the need for higher multiplexing and the need for more robust assays are some of the key challenges.

In this work, the unique combination of triple quadrupole and ion trapping capabilities of the hybrid triple quadrupole – linear ion trap mass spectrometer (QTRAP® System) has been utilized to create 100s of high quality, specific MRM transitions for multiple peptides to many plasma proteins. Iterative analysis provided rapid refinement of MRM parameters without requiring synthetic peptides. Intelligent use of retention time using new acquisition software enables many more MRM transitions to be included in a single acquisition method, while maintaining good peak area reproducibility. The analytical reproducibility of the MRM method developed was found to be extremely high, even in plasma, with the majority of peptides being measured with %CV<10.