

# Robustness of the 6490 Triple Quad LC/MS with iFunnel Technology for the Analysis of Verapamil in Human Plasma



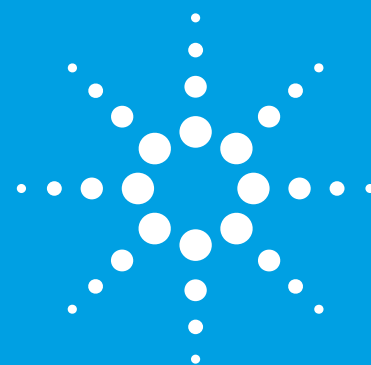
## Objective

To provide rugged and robust performance analysis of verapamil in human plasma for extended periods of operation (>2000 injections over 4 days of continuous operation) using the Agilent 6490 Triple Quadrupole LC/MS System with iFunnel technology.

## Background

Matrix contamination in an LC/MS system becomes a concern for the analysis of samples in complex matrices. Plasma is a well known complex and heterogeneous matrix that challenges the ability of an LC/MS to prevent residual proteins, peptides, lipids, and salts from contaminating the ion optics and degrading analyte response.

This note describes the robustness of the 6490 Triple Quadrupole LC/MS System with iFunnel technology for the analysis of over 2000 samples of low concentrations of verapamil in human plasma over a period of four days.



## Compound

- Verapamil

## Key Benefits

- Robust performance and operation – no contamination effects observed for the analysis of >2000 samples
- 10 X increase in sensitivity
- Up to six orders of linear dynamic range
- Zeptomole sensitivity for the most challenging applications



## The Approach

To test for any decrease in signal intensity, 20 femtograms of verapamil in protein precipitated plasma was injected on-column. This amount is below the limit of detection for many tandem LC/MS systems.

We have evaluated the performance of the 6490 for the analysis of over 2000 verapamil samples in human plasma. The HPLC method used an Agilent 1200 Series LC system with an Eclipse C18 column and water/acetonitrile gradient. The LC/MS run time was three minutes per sample resulting in a total analysis time of over 100 hours. Samples were prepared with a verapamil concentration of 309 pg/mL (1 nM) in human plasma. Following protein precipitation with acetonitrile, samples were centrifuged at 13,200 rpm. The supernatant (200  $\mu$ L) was diluted with 3 parts of water (e.g. 600  $\mu$ L) and 1  $\mu$ L injected for LC/MS analysis. This corresponded to a total of 20 femtograms of verapamil injected on-column.

Figure 1 shows the peak area response for replicate injections of 20 femtograms of verapamil.

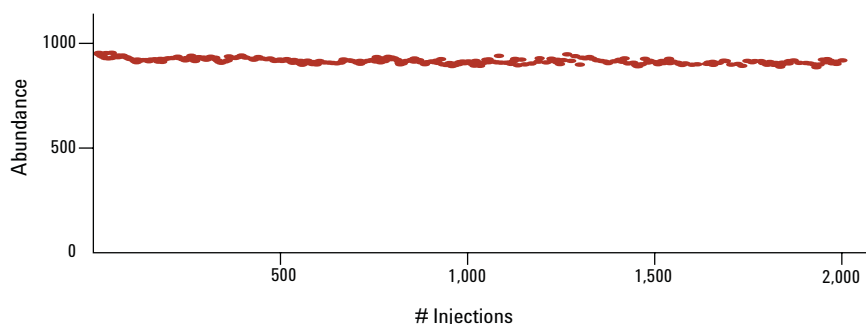


Figure 1. Absolute Area Response (2,000 injections over a period of 4 days). Area RSD = 5.3%

## Summary

- Robustness has been demonstrated for the analysis of target analyte (with internal standard) in human plasma
- Extended continuous sensitivity performance was shown for the analysis of over more than 2000 samples - over four days of continuous sample analysis
- Measured RSDs were < 6% and well within assay acceptance criteria of 15% to 20%
- Analyte response remained essentially constant throughout the four days
- No contamination effects were observed

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Published in the U.S.A. September 24, 2010  
5990-6403EN

## Ion Funnel Maintenance

As with all LC/MS instruments, periodic routine maintenance is necessary. The ion funnel should be cleaned periodically after extended periods of LC/MS analysis. The dual ion funnel is easily removed and cleaning is performed by sonicating the ion funnel assembly in a bath of 100% isopropanol for 15 minutes.



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