The Use of an Integrated Ceramic Micro-Fluidic Separations Device For The High Sensitivity LC/MS/MS Quantification of Drugs in Low Volume Samples from DMPK Studies

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## **Electronic Supplementary Information**

**Figure S1**: Injection of desmopresin standard onto either a 2.1 x 50mm 1.7 $\mu$ m BEH C18 column eluted under gradient conditions at 600 $\mu$ L/min over 3 minutes (lower panel) or a 0.3 x 100mm ceramic microfluidic device packed with 1.7 $\mu$ m BEH C18 material and eluted a 5-95% formic acid (aq) acetonitrile gradient over 3 minutes at 12 $\mu$ L/min (upper panel) with detection by positive ion MRM.



**Figure S2**: Injection of aqueous alprazolam with increasing injection volumes from 0.1 to  $2\mu L$  onto a 0.3 x 100mm ceramic microfluidic device packed with 1.7µm BEH C18 material and eluted a 5-95% formic acid (aq) acetonitrile gradient over 3 minutes at  $12\mu L/min$  with detection by positive ion MRM.



**Figure S3**: LC/MS Analysis of Alprazolam and the 4-Hydroxylated Metabolite Using Ceramic Micro fluidic Device. Overlaid chromatograms the 1<sup>st</sup> and 1000<sup>th</sup> injection of hydroxylated alprazolam and alprazolam spiked into plasma and prepared by protein precipitation. The samples were analysed on a 0.3 x 100mm ceramic microfluidic device packed with 1.7 $\mu$ m BEH C18 material and eluted a 5-95% formic acid (aq) acetonitrile gradient over 3 minutes at 12 $\mu$ L/min with detection by positive ion MRM.



**Figure S4**: LC/MS/MS analysis of alprazolam, alprazolam d5 internal standard and hydroxyalprazolam metabolite. The separation was performed on a 0.3 x 100mm separation channel packed with 1.7 $\mu$ m C18 BEH material. The column was eluted under gradient conditions (formic acid (aq): acetonitrile) over 2 minutes at a flow rate of 12 $\mu$ L/min. The column effluent was monitored by positive ion MRM mass spectrometry using the transitions 309.2 $\rightarrow$ 281.0, 314.2 $\rightarrow$ 286.0 and 325.0 $\rightarrow$ 297.0