

Case study: “How Low Can You Go?”

Introduction

Unilabs’ York Bioanalytical Solutions has a reputation of being a leader in high-sensitivity bioanalysis. For this project, we were pushing the limits of the latest technologies and development strategies to achieve an ultra-sensitive method.

Study Requirements

Highly potent basic drug and two metabolites with a C_{max} of 4 pg/mL in plasma. Existing methods had an LLOQ of 1-2 pg/mL and did not adequately describe the absorption and elimination phases. The sponsor asked, “How low can you go?” - Target LLOQ 100 fg/mL.

Approach

A streamlined LC-MS/MS method development process was taken using pre-determined strategies for analysing compounds based on their specific chemistry and required sensitivity with open access robotics.

To achieve 100 fg/mL in human plasma, analyte chemistry was exploited in combination with orthogonal extraction/chromatography approaches and the latest LC-MS/MS technology.

The final method utilized a combination of offline cation exchange mixed mode SPE, online C2 SPE and C18 chromatography.

Outcome

LLOQ of 100 fg/ml achieved for all analytes, tenfold lower than any previous method. The method was validated to current regulatory standards, enabling previously unobtainable PK data to be generated. This ensured rapid progression of the clinical program.



Unilabs was able to meet the sponsor’s expectation and the developed ultra-sensitive method helped to advance the clinical program