

Supporting Information

J. Chem. Metrol. 17:1 (2023) 79-92

Development of a stability-indicating HPLC method for Lasmiditan and its process related impurities with characterization of degradation products by LC-MS/MS

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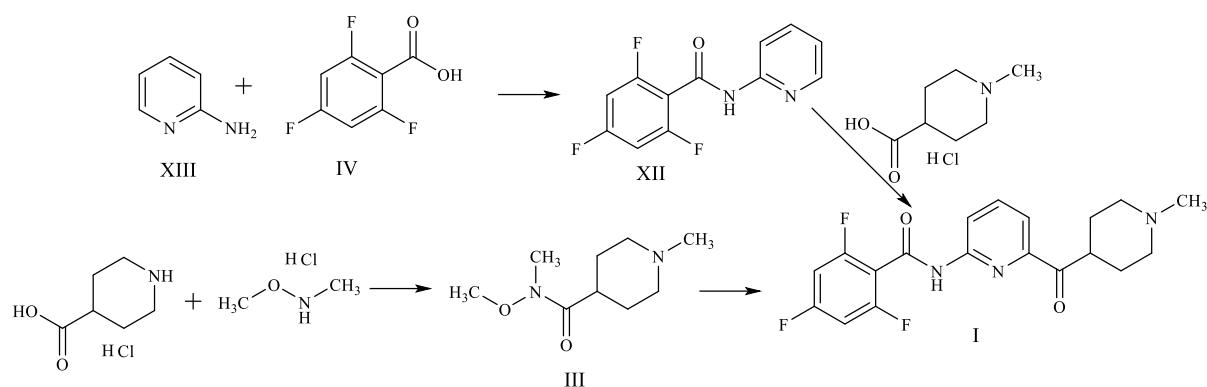


Figure S1: Lasmiditan synthesis route

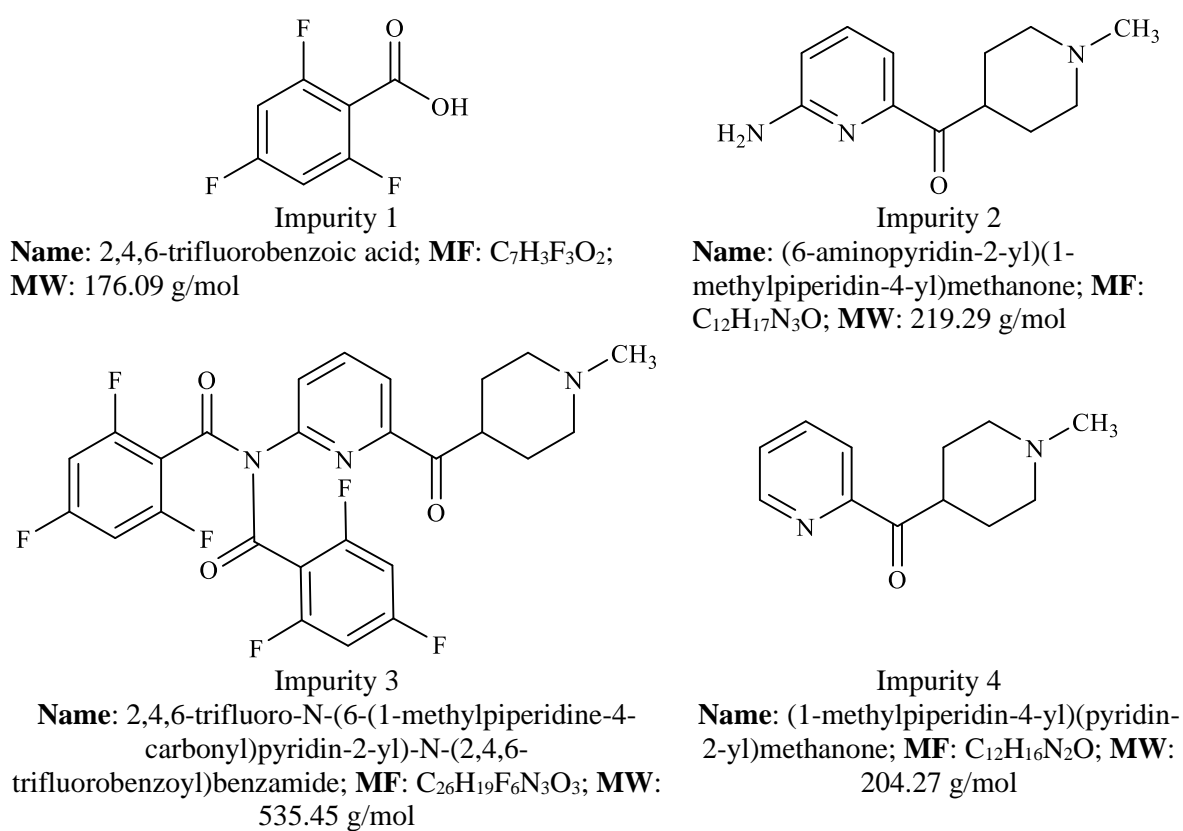


Figure S2: Molecular structure of process related impurities of lasmiditan

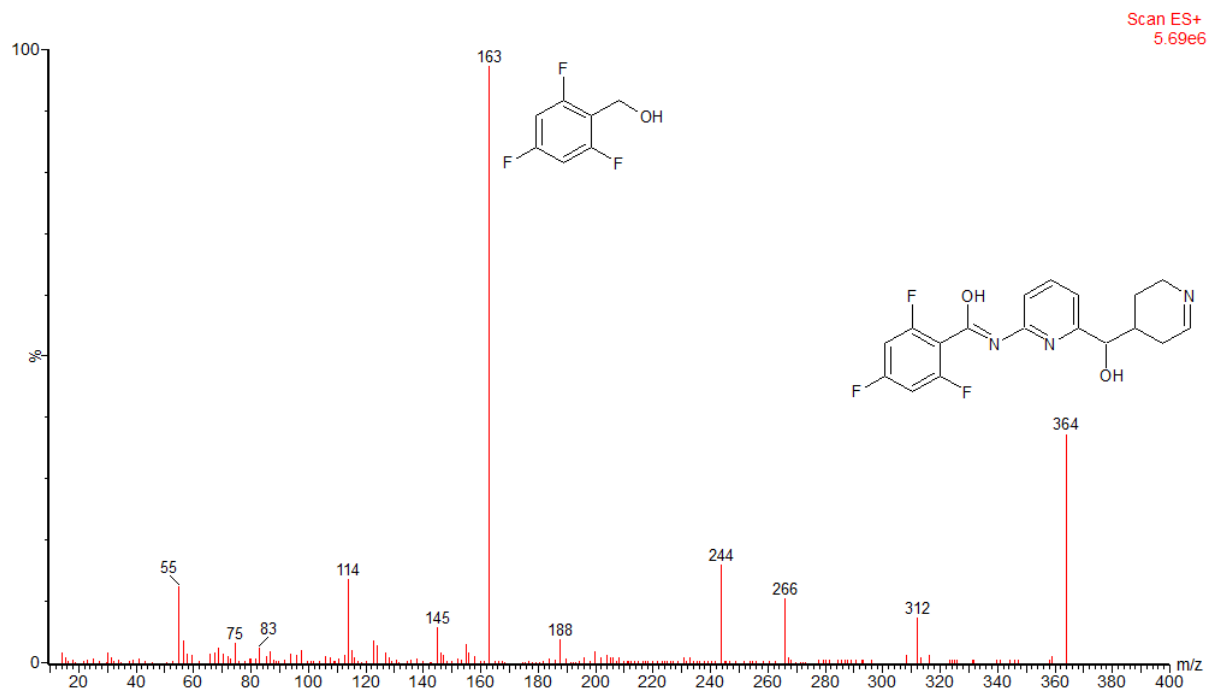


Figure S3: Mass spectrum of DP 1

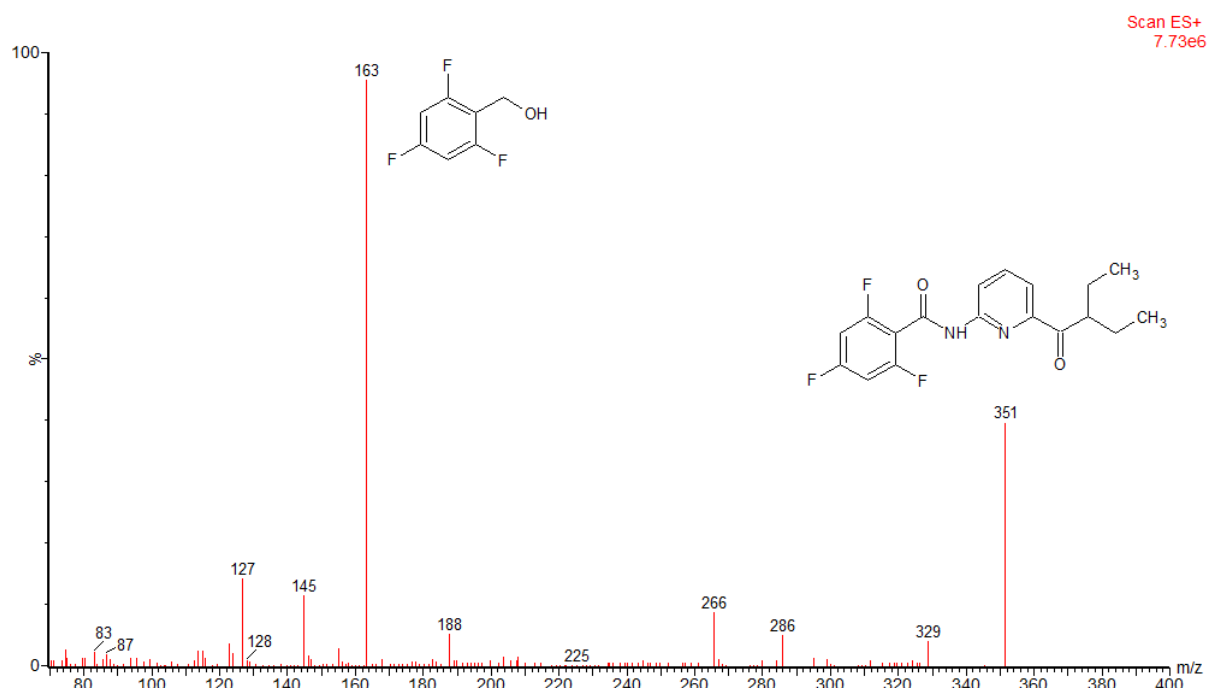


Figure S4: Mass spectrum of DP 2

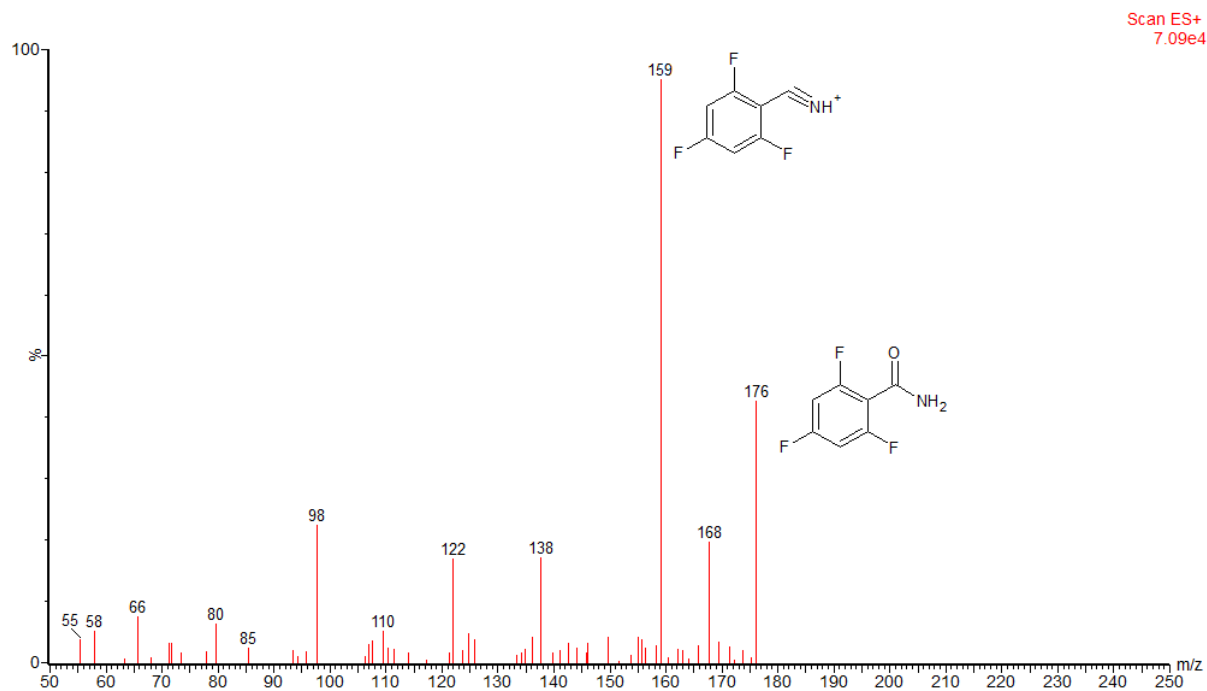


Figure S5: Mass spectrum of DP 3

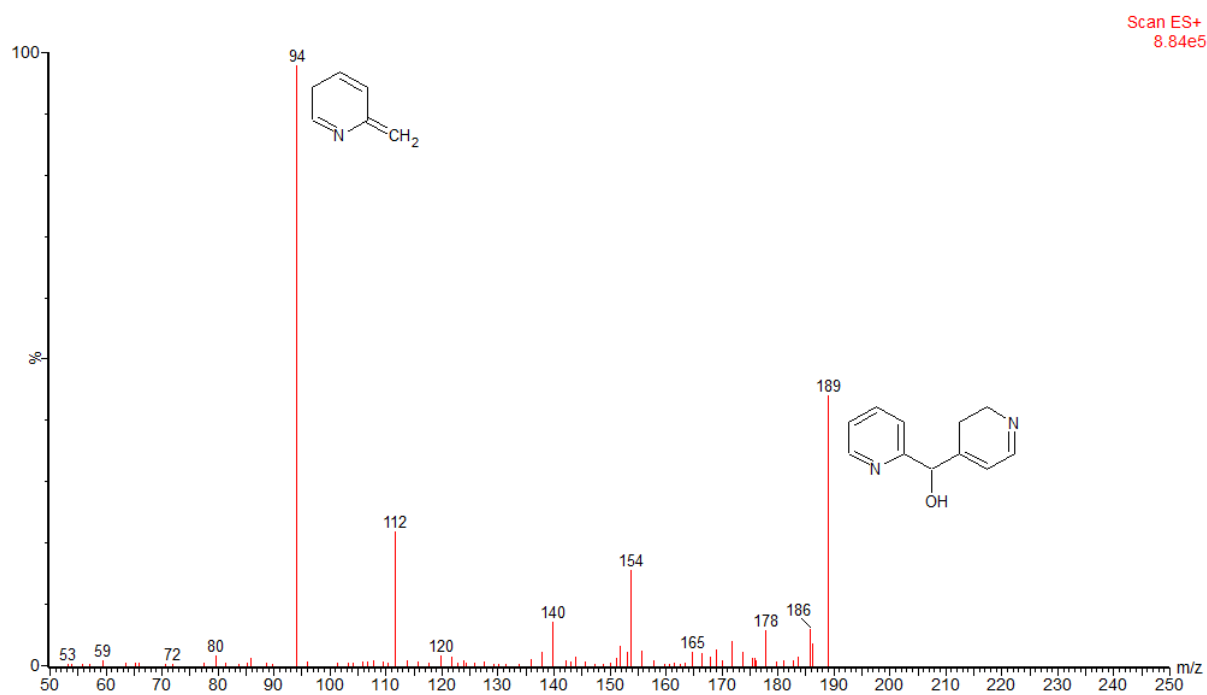


Figure S6: Mass spectrum of DP 4

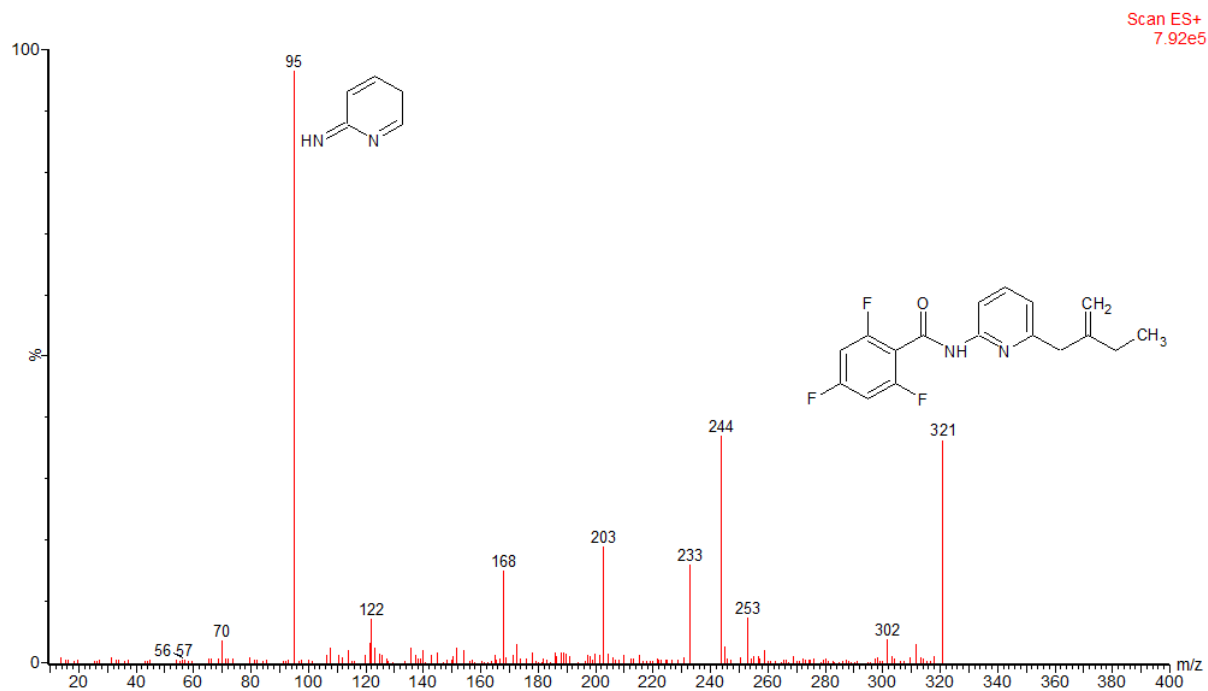


Figure S7: Mass spectrum of DP 5

Table S1: Uncertainty assessment of Lasmiditan

Uncertainty in standard		X	Xi	N	U_{standard} Formula	U_{standard}
		100	99.21	3	$\frac{X - Xi}{\sqrt{n}}$	0.456
Uncertainty in Slope of Calibration Plot		SD	n	Standard Error	$U_{\text{Calibration}}$ Formula	$U_{\text{Calibration}}$
Slope 1	8166.649	40.01	3	23.10	$\frac{\text{Standard Error of Slope} \times 100}{\text{Slope}}$	0.284
Slope 2	8093.501					
Slope 3	8101.989					
Uncertainty in Recovery of Sample		SD	n	Standard Error	U_{Recovery} Formula	U_{Recovery}
Recovery 1	98.69	0.631876	6	0.258	$\frac{\text{Standard Error of Recovery} \times 100}{\text{Recovery}}$	0.261
Recovery 2	98.57					
Recovery 3	98.25					
Recovery 4	98.03					
Recovery 5	99.58					
Recovery 6	99.46					
Uncertainty associated with repeatability		SD	n	Standard Error	$U_{\text{Repeatability}}$ Formula	$U_{\text{Repeatability}}$
Repeatability 1	99.76	0.928061	6	0.378879	$\frac{\text{Standard Error of Repeatability} \times 100}{\text{Repeatability}}$	0.382
Repeatability 2	98.63					
Repeatability 3	98.25					
Repeatability 4	98.15					
Repeatability 5	100.19					
Repeatability 6	100.03					
					U_{Combined} Formula	U_{Combined}
					$\sqrt{(U_{\text{standard}})^2 + (U_{\text{Calibration}})^2 + (U_{\text{Recovery}})^2 + (U_{\text{Repeatability}})^2}$	0.709
					U_{Expanded} Formula	U_{Expanded}
					$U_{\text{Combined}} \times 1.96$	1.390

Table S2: Uncertainty assessment of Impurity 1

Uncertainty in standard		X	Xi	N	U_{standard} Formula	U_{standard}
		100	98.76	3	$\frac{X - Xi}{\sqrt{n}}$	0.716
Uncertainty in Slope of Calibration Plot		SD	n	Standard Error	$U_{\text{Calibration}}$ Formula	$U_{\text{Calibration}}$
Slope 1	8166.649	4303.52	3	2484.64	$\frac{\text{Standard Error of Slope} \times 100}{\text{Slope}}$	0.358
Slope 2	8093.501					
Slope 3	8101.989					
Uncertainty in Recovery of Sample		SD	n	Standard Error	U_{Recovery} Formula	U_{Recovery}
Recovery 1	98.16	1.060	6	0.433	$\frac{\text{Standard Error of Recovery} \times 100}{\text{Recovery}}$	0.434
Recovery 2	99.76					
Recovery 3	98.54					
Recovery 4	99.89					
Recovery 5	100.91					
Recovery 6	100.37					
Uncertainty associated with repeatability		SD	n	Standard Error	$U_{\text{Repeatability}}$ Formula	$U_{\text{Repeatability}}$
Repeatability 1	0.1029	0.0009	6	0.00035	$\frac{\text{Standard Error of Repeatability} \times 100}{\text{Repeatability}}$	0.351
Repeatability 2	0.1016					
Repeatability 3	0.1006					
Repeatability 4	0.1027					
Repeatability 5	0.1014					
Repeatability 6	0.1023					
					U_{Combined} Formula	U_{Combined}
					$\sqrt{(U_{\text{standard}})^2 + (U_{\text{Calibration}})^2 + (U_{\text{Recovery}})^2 + (U_{\text{Repeatability}})^2}$	0.898
					U_{Expanded} Formula	U_{Expanded}
					$U_{\text{Combined}} \times 1.96$	1.759

Table S3: Uncertainty assessment of Impurity 2

Uncertainty in standard		X	Xi	N	U_{standard} Formula	U_{standard}
		100	98.94	3	$\frac{X - Xi}{\sqrt{n}}$	0.612
Uncertainty in Slope of Calibration Plot		SD	n	Standard Error	$U_{\text{Calibration}}$ Formula	$U_{\text{Calibration}}$
Slope 1	348072.93	1491.603	3	861.18	$\frac{\text{Standard Error of Slope} \times 100}{\text{Slope}}$	0.249
Slope 2	346228.14					
Slope 3	345120.21					
Uncertainty in Recovery of Sample		SD	n	Standard Error	U_{Recovery} Formula	U_{Recovery}
Recovery 1	98.69	1.031	6	0.421	$\frac{\text{Standard Error of Recovery} \times 100}{\text{Recovery}}$	0.442
Recovery 2	99.32					
Recovery 3	98.46					
Recovery 4	100.85					
Recovery 5	100.13					
Recovery 6	100.75					
Uncertainty associated with repeatability		SD	n	Standard Error	$U_{\text{Repeatability}}$ Formula	$U_{\text{Repeatability}}$
Repeatability 1	0.0995	0.0006	6	0.00023	$\frac{\text{Standard Error of Repeatability} \times 100}{\text{Repeatability}}$	0.229
Repeatability 2	0.0991					
Repeatability 3	0.0994					
Repeatability 4	0.1005					
Repeatability 5	0.1003					
Repeatability 6	0.0996					
					U_{Combined} Formula	U_{Combined}
					$\sqrt{(U_{\text{standard}})^2 + (U_{\text{Calibration}})^2 + (U_{\text{Recovery}})^2 + (U_{\text{Repeatability}})^2}$	0.817
					U_{Expanded} Formula	U_{Expanded}
					$U_{\text{Combined}} \times 1.96$	1.601

Table S4: Uncertainty assessment of Impurity 3

Uncertainty in standard		X	Xi	N	U_{standard} Formula	U_{standard}
		100	99.71	3	$\frac{X - Xi}{\sqrt{n}}$	0.167
Uncertainty in Slope of Calibration Plot		SD	n	Standard Error	$U_{\text{Calibration}}$ Formula	$U_{\text{Calibration}}$
Slope 1	461147.7	2635.87	3	1521.82	$\frac{\text{Standard Error of Slope} \times 100}{\text{Slope}}$	0.331
Slope 2	460041.0					
Slope 3	456130.6					
Uncertainty in Recovery of Sample		SD	n	Standard Error	U_{Recovery} Formula	U_{Recovery}
Recovery 1	99.68	0.418	6	0.171	$\frac{\text{Standard Error of Recovery} \times 100}{\text{Recovery}}$	0.172
Recovery 2	98.78					
Recovery 3	98.51					
Recovery 4	99.08					
Recovery 5	99.24					
Recovery 6	99.36					
Uncertainty associated with repeatability		SD	n	Standard Error	$U_{\text{Repeatability}}$ Formula	$U_{\text{Repeatability}}$
Repeatability 1	0.0994	0.0007	6	0.0003	$\frac{\text{Standard Error of Repeatability} \times 100}{\text{Repeatability}}$	0.305
Repeatability 2	0.0987					
Repeatability 3	0.0989					
Repeatability 4	0.0993					
Repeatability 5	0.0998					
Repeatability 6	0.1008					
				U_{Combined} Formula		U_{Combined}
				$\sqrt{(U_{\text{standard}})^2 + (U_{\text{Calibration}})^2 + (U_{\text{Recovery}})^2 + (U_{\text{Repeatability}})^2}$		0.511
				U_{Expanded} Formula		U_{Expanded}
				$U_{\text{Combined}} \times 1.96$		1.001

Table S5: Uncertainty assessment of Impurity 4

Uncertainty in standard		X	Xi	N	U_{standard} Formula	U_{standard}
		100	99.67	3	$\frac{X - Xi}{\sqrt{n}}$	0.191
Uncertainty in Slope of Calibration Plot		SD	n	Standard Error	$U_{\text{Calibration}}$ Formula	$U_{\text{Calibration}}$
Slope 1	567104.3	3531.87	3	2039.12	$\frac{\text{Standard Error of Slope} \times 100}{\text{Slope}}$	0.362
Slope 2	561773.5					
Slope 3	560425.3					
Uncertainty in Recovery of Sample		SD	n	Standard Error	U_{Recovery} Formula	U_{Recovery}
Recovery 1	99.63	0.330	6	0.135	$\frac{\text{Standard Error of Recovery} \times 100}{\text{Recovery}}$	0.136
Recovery 2	98.79					
Recovery 3	99.01					
Recovery 4	99.45					
Recovery 5	99.01					
Recovery 6	98.91					
Uncertainty associated with repeatability		SD	n	Standard Error	$U_{\text{Repeatability}}$ Formula	$U_{\text{Repeatability}}$
Repeatability 1	0.0991	0.00036	6	0.00015	$\frac{\text{Standard Error of Repeatability} \times 100}{\text{Repeatability}}$	0.149
Repeatability 2	0.0994					
Repeatability 3	0.0994					
Repeatability 4	0.0997					
Repeatability 5	0.0987					
Repeatability 6	0.0996					
					U_{Combined} Formula	U_{Combined}
					$\sqrt{(U_{\text{standard}})^2 + (U_{\text{Calibration}})^2 + (U_{\text{Recovery}})^2 + (U_{\text{Repeatability}})^2}$	0.456
					U_{Expanded} Formula	U_{Expanded}
					$U_{\text{Combined}} \times 1.96$	0.894

