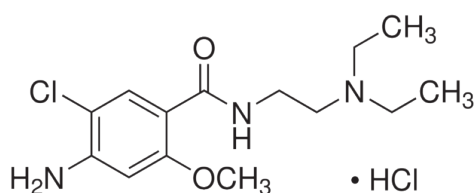


## Analysis of Related Substances of Metoclopramide HCl by an ACQUITY UPLC H-Class PLUS System

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### GOAL

The ACQUITY™ UPLC™ H-Class PLUS System provides comparable results to the ACQUITY UPLC H-Class System with exceptional reproducibility and transferability of validated methods.

### BACKGROUND

Analytical methods used for the testing of drug substances and drug products must be verified to remain in compliance with current Good Manufacturing Practices (cGMP). Method performance is verified by measuring system suitability parameters such as chromatographic resolution, peak tailing, and repeatability of the peak areas and retention times.<sup>1</sup> A verified analytical method is considered acceptable for quality control and will ensure that the system performs correctly at the time of use.

In this work, we assess the performance of an ACQUITY UPLC H-Class PLUS System for related substances analysis of metoclopramide hydrochloride (HCl) by measuring and comparing system suitability parameters and related substances results to the data acquired on an ACQUITY UPLC H-Class System.

The ACQUITY UPLC H-Class PLUS System provides comparable results to the ACQUITY UPLC H-Class System with exceptional reproducibility and transferability of validated methods.

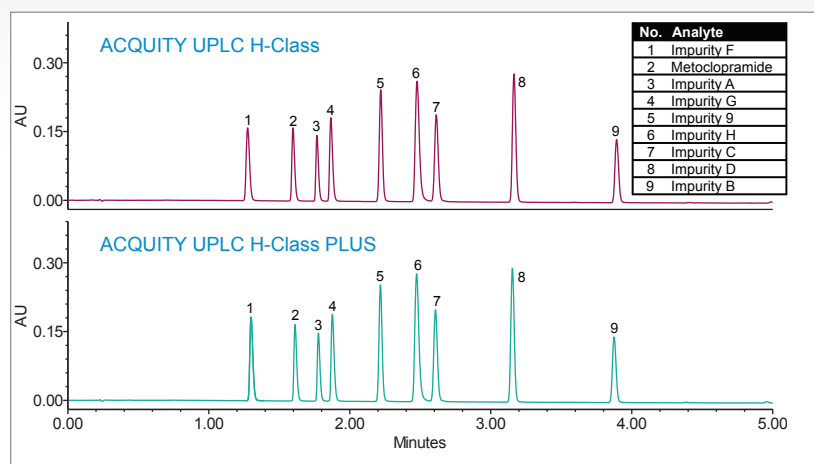


Figure 1. Chromatographic data of 0.06 mg/mL standard solution with metoclopramide API and related substances acquired on the ACQUITY UPLC H-Class and ACQUITY UPLC H-Class PLUS Systems.

### SOLUTION

The LC method for related substances of metoclopramide HCl, previously developed in the application note [720005026EN](#),<sup>2</sup> was run on an ACQUITY UPLC H-Class PLUS System. Comparative studies utilizing the chromatographic data from a 0.06 mg/mL standard solution with metoclopramide API and related substances is demonstrated (Figure 1). The chromatographic separation replicated on an ACQUITY UPLC H-Class PLUS System was comparable with the original results performed on an ACQUITY UPLC H-Class System.

Performance of the method on the ACQUITY UPLC H-Class PLUS System was verified by evaluating system suitability of five replicate injections according to the specifications defined in the USP General Chapter <621> Chromatography<sup>3</sup> and compared to the data acquired on the ACQUITY UPLC H-Class System. As demonstrated in Figure 2, system suitability results acquired on both systems meet the USP success criteria

including repeatability of retention times, peak areas, USP peak tailing, and USP resolution.

A sample solution containing metoclopramide API spiked with 0.05% of related substances was run on both the ACQUITY UPLC H-Class and ACQUITY UPLC H-Class PLUS Systems to evaluate comparability of the related substances results. As shown in Figure 3, the assay results for related substances acquired on the ACQUITY UPLC H-Class PLUS System were comparable to the original method conducted on the ACQUITY UPLC H-Class System. In addition, the relative retention time (RRT) values calculated for each related substance with respect to the API retention time were comparable.

## SUMMARY

The ACQUITY UPLC H-Class PLUS System produced comparable system suitability and related substances results to that of the ACQUITY UPLC H-Class System. The results of the successful method performance verification demonstrate that the ACQUITY UPLC H-Class PLUS System is a reliable and robust instrument that generates analyses with excellent precision and reproducibility, ensuring that methods validated on the original ACQUITY UPLC H-Class System can be easily replicated on the ACQUITY UPLC PLUS Series Platform.

## References

1. U.S. FDA. Analytical Procedures and Methods Validation for Drugs and Biologics Guidance for Industry. July 2015.
2. Maziarz, M.; McCarthy, S.M.; Wrona, M. Improving Effectiveness of Method Development for Metoclopramide HCl and Related Substances Using a Systematic Screening Protocol. Waters Application Note, [720005026EN](#), April 2014.
3. USP General Chapter <621> Chromatography, USP, United States Pharmacopeia Convention, Official.

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ACQUITY UPLC H-Class							ACQUITY UPLC H-Class PLUS						
<b>System Suitability</b> Sample Set ID: Sample Set Id 1309 Result Set ID: Result Set Id 2023 Channel Name: PDA Ch1 270nm@4.8nm							<b>System Suitability</b> Sample Set ID: Sample Set Id 2161 Result Set ID: Result Set Id 2453 Channel Name: PDA Ch1 270nm@4.8nm						
System Suitability Separation Results							System Suitability Separation Results						
Name	# of Inj.	Ave RT	%R SD RT	%R SD Peak Areas	Ave U SP R s	Ave USP Tailing	Name	# of Inj.	Ave RT	%R SD RT	%R SD Peak Areas	Ave U SP R s	Ave USP Tailing
1 Imp. F	5	1276	0.23	0.19		1.3	1 Imp. F	5	1301	0.08	0.24		1.3
2 API	5	1596	0.11	0.24	7.9	1.4	2 API	5	1613	0.08	0.25	8.0	1.4
3 Imp. A	5	1766	0.09	0.09	4.8	1.4	3 Imp. A	5	1779	0.08	0.23	4.6	1.3
4 Imp. G	5	1864	0.08	0.20	2.7	1.4	4 Imp. G	5	1878	0.07	0.21	2.7	1.4
5 Imp. 9	5	2218	0.06	0.21	8.8	1.1	5 Imp. 9	5	2218	0.05	0.19	8.5	1.1
6 Imp. H	5	2475	0.07	0.17	5.5	1.3	6 Imp. H	5	2475	0.05	0.20	5.5	1.3
7 Imp. C	5	2611	0.07	0.15	2.7	1.2	7 Imp. C	5	2609	0.05	0.20	2.7	1.1
8 Imp. D	5	3161	0.07	0.16	11.8	1.1	8 Imp. D	5	3155	0.05	0.22	11.8	1.1
9 Imp. B	5	3889	0.06	0.21	15.6	1.1	9 Imp. B	5	3876	0.03	0.21	15.5	1.1

Figure 2. System suitability results of five replicate injections acquired on ACQUITY UPLC H-Class and ACQUITY UPLC H-Class PLUS Systems.

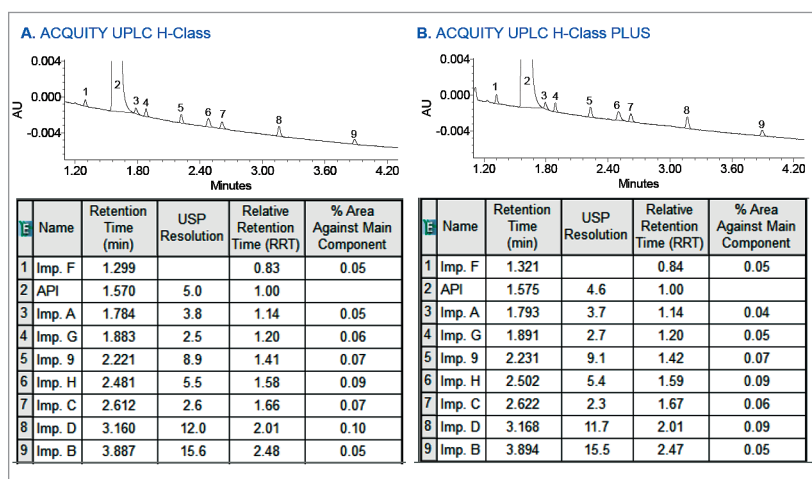


Figure 3. Related substances results for the API sample spiked with related substances at 0.05% level. Results acquired on ACQUITY UPLC H-Class (A) and ACQUITY UPLC H-Class PLUS (B) Systems.

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