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TRANSFER OF A COMPENDIAL LC METHOD FOR IMPURITY ANALYSIS OF CHLORHEXIDINE FROM A WATERS ALLIANCE HPLC SYSTEM TO A VANQUISH CORE HPLC SYSTEM

Instrument-to-instrument transfer of liquid chromatographic (LC) methods is a challenging task most analytical laboratories face frequently under several scenarios. For example, an established application needs to be run by several instruments within one laboratory to distribute major workload. Another scenario is inter-laboratory transfers from research and development (R&D) labs to quality control (QC) labs, or when specific tasks are outsourced, for example, to contract labs.[1] A third scenario is the replacement of legacy instrumentation by modern technology.

In either instance, a transfer is only considered effective if equivalent results are obtained. The success and the required effort of such a transfer depend on multiple factors. The robustness of the method to be transferred as well as instrumentational deviations of the involved systems play an important role.[1] Some technical characteristics of a system, like its gradient delay volume (GDV), pump mixing mode, hydrodynamic behavior, column and eluent thermostatting options, may affect critical results like peak resolution or retention times.[2-4] The requirements of the chromatographer to the analytical outcome and the defined limits of acceptable deviations from the originating system determine the complexity of the transfer job. In addition, only very limited modifications of method parameters are usually accepted during a transfer to prevent the need of a time-consuming revalidation.

This article gives an overview of the seamless transfer of the European Pharmacopoeia (EP) monograph[5] method for chlorhexidine digluconate impurity analysis from a Waters™ Alliance™ HPLC system to a Thermo Scientific™ Vanquish™ Core HPLC system. Chlorhexidine is a common antiseptic and disinfectant, listed on the World Health Organization's (WHO) Model List of Essential Medicines[6] and is available as an over-the-counter drug. It is widely used in dental medicine and hygiene, for example, in mouthwashes and for skin disinfection purposes.

For best comparability, seven consecutive injections were executed on an Alliance HPLC system and a Vanquish Core HPLC system using the same conditions. For reasons of clarity, the focus is on all peaks that exceeded a minimum peak area of 0.3 mAU·min. Figure 1 illustrates that similar chromatograms were generated and for all peaks, the absolute retention times differed less than 4% between the systems. A summary of relative retention times, experimentally obtained and provided by the EP monograph, is given in the Table. Good agreement on relative peak areas related to the main peak is seen in Figure 2. Vanquish Core HPLC system has a lower system dispersion volume generating narrower peaks which resulted in higher resolution values as compared to the Alliance HPLC system.

The repeatability of retention times and peak areas, expressed as relative standard deviations (RSD) over the seven injections, was massively improved with the Vanquish Core HPLC system as displayed in Figure 3. The system suitability criteria given by the EP monograph, which requires a resolution of the impurity pair L and G of minimum 3 and a peak-to-valley ratio of impurity B of minimum 2, were easily met by either LC system with a resolution ~8 and a peak-to-valley ratio >5 (Alliance) and >7 (Vanquish Core).

The discussion in this article in general is also valid for the United States Pharmacopoeia (USP) method[7], as the analytical method, i.e. column and gradient, are identical.

References

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5. European Directorate for the Quality of Medicines & HealthCare; European Pharmacopoeia (Ph. Eur.) Online, 10th edition 2018 (10.0), monograph 0658: Chlorhexidine digluconate solution.
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8. Information Leaflet Ph. Eur. Reference Standard: Chlorhexidine for system suitability CRS batch 2; European Directorate for the Quality of Medicines & HealthCare; European Pharmacopoeia (Ph. Eur.); 7, Allée Kastner CS 30026, F-67081 Strasbourg (France).

Table. Relative retention times related to the main peak as stated in the EP monograph and averaged from Alliance and Vanquish Core chromatograms (Figure 1)

Peak #	Compound	EP monograph	Alliance	Vanquish Core
1	Unknown 1		0.20	0.20
2	Impurity L	0.23	0.22	0.21
3	Impurity Q	0.24	0.23	0.22
4	Impurity G	0.25	0.27	0.26
5	Unknown 2		0.30	0.29
6	Impurity N	0.35	0.36	0.36
7	Impurity B	0.36	0.38	0.37
8	Impurity F	0.50	0.42	0.41
9	Unknown 3		0.45	0.44
10	Impurity A	0.60	0.57	0.56
11	Unknown 4		0.78	0.78
12	Impurity H	0.85	0.87	0.87
13	Impurity O	0.90	0.90	0.90
14	Impurity I	0.91	0.91	0.91
15	Impurity J	0.96	0.97	0.98
16	Chlorhexidine	1.00	1.00	1.00
17	Unknown 5		1.08	1.08
18	Unknown 6		1.30	1.31
19	Impurity K	1.40	1.39	1.39
20	Unknown 7		1.47	1.47
21	Unknown 8		1.51	1.52

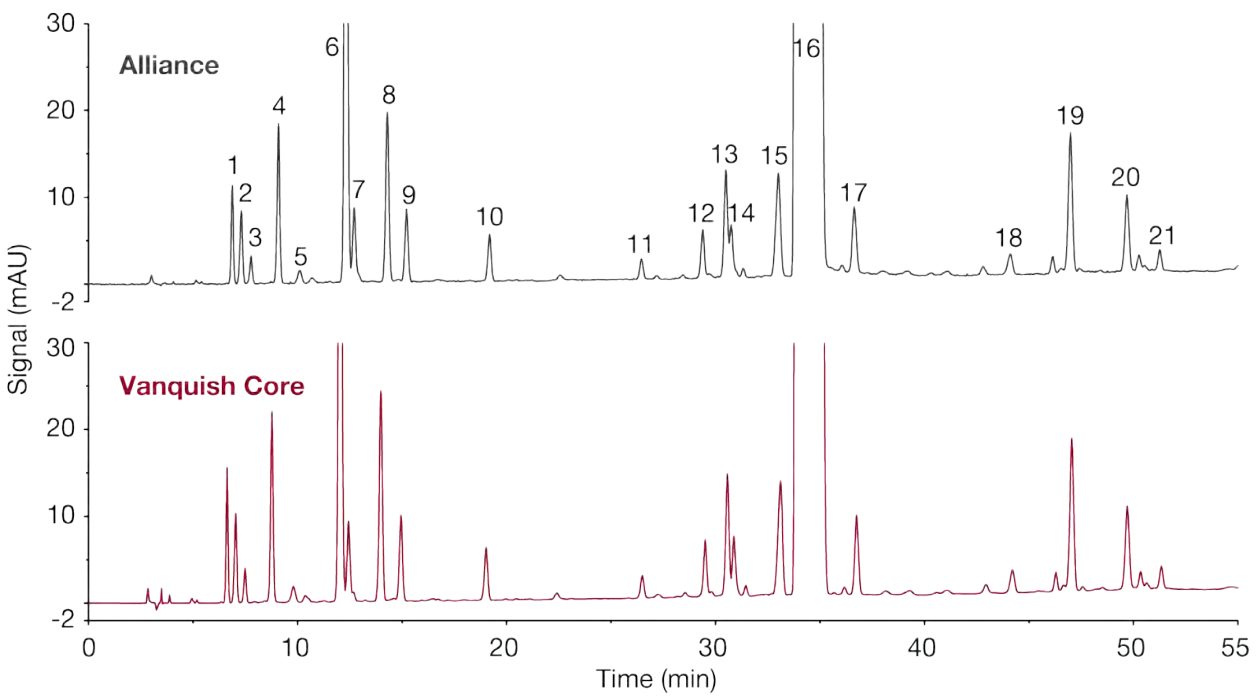

Figure 1. Transfer from Alliance system to Vanquish Core HPLC system according to the EP monograph for chlorhexidine gluconate; peak assignment according to impurity designation in EP monograph and standard leaflet[5, 8]

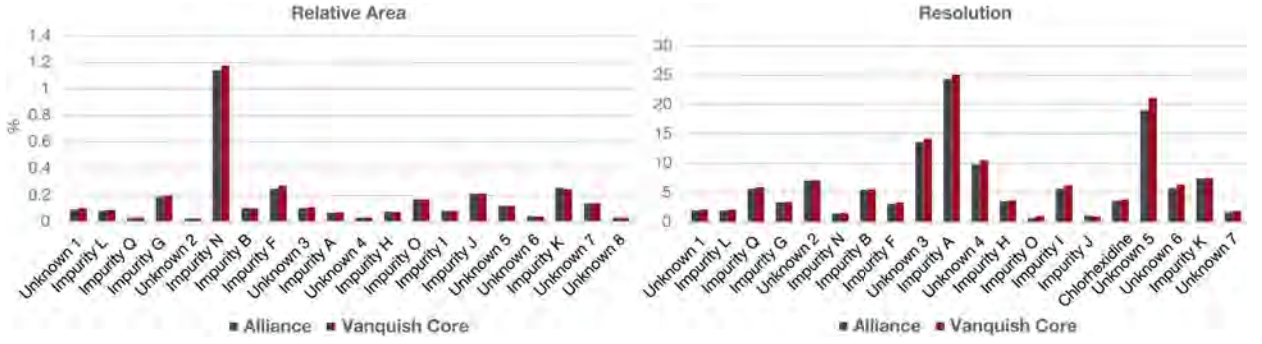

Figure 2. Chromatographic results with Alliance and Vanquish Core HPLC systems under conditions outlined in the EP monograph (Figure 1)

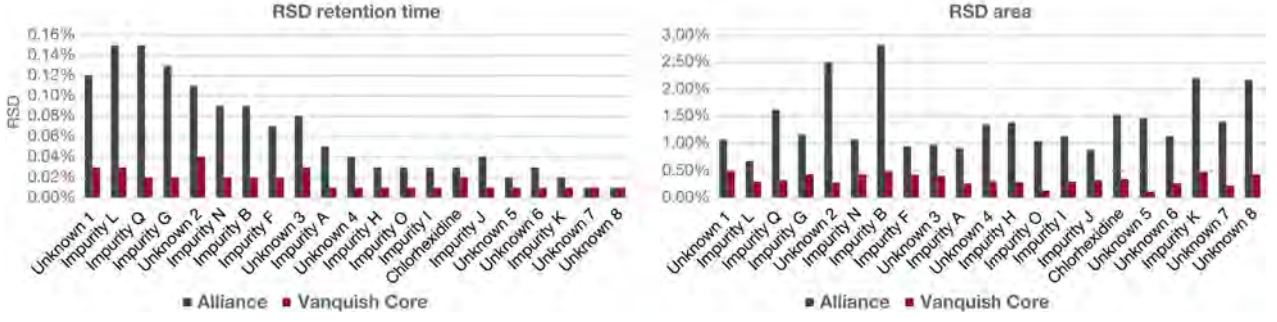

Figure 3. Relative standard deviations (RSD) of retention times and peak areas over seven injections obtained by the Alliance and Vanquish Core HPLC systems

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