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应用纪要

Automating the Creation of Chromatographic Methods for Method Validation Using the Empower Sample Set Generator

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This is an Application Brief and does not contain a detailed Experimental section.

Abstract

This application brief demonstrates the use of Waters™ Empower™ Software Sample Set Generator to automate the creation of chromatographic methods and sample set methods, used in the validation of a UPLC™ method for metoclopramide HCl and related substances.

Benefits

The Empower Sample Set Generator simplifies the creation of instrument methods, method sets, and sample set methods by defining ranges of variables needed for testing.

Introduction

The validation process of an analytical method is a complex and demanding activity, consisting of many time-consuming steps. Some of these steps include acquiring, reviewing and processing data, performing calculations, approving, and final reporting of the validation results. One critical task is robustness testing, during which the effects of minor changes in chromatographic parameters on method performance are investigated to establish tolerance limits. Multiple chromatographic methods must be carefully designed and created to acquire data for each validation test. Designing, creating, and verifying these methods manually can be tedious and prone to errors.

The Empower Sample Set Generator simplifies the creation of instrument methods, method sets, and sample set methods by defining ranges of variables needed for testing. By automating these tasks, chromatographic method and the sample sequence generation is streamlined and transcription errors eliminated. As the tedious tasks are minimized, laboratory efficiency and productivity increases.

Here we illustrate the use of the Empower Sample Set Generator to automatically create chromatographic methods for robustness testing in the validation of a UPLC method for metoclopramide HCl and its USP-specified related substances.

Results and Discussion

The UPLC method for metoclopramidee HCl and its USP-specified related substances was validated using the Empower Software’ s Method Validation Manager (MVM).[1] MVM software streamlines the entire validation process in one application, from creating a validation protocol method to acquiring data, reviewing, analyzing, approving, and reporting validation data.

The Empower Sample Set Generator was used to streamline robustness testing for creating chromatographic methods. For robustness, we assessed these parameters:

- Column temp.: 45 ± 2.0 °C
- Flow rate: 0.6 ± 0.05 mL/min

- Wavelength: 270 ± 2 nm

In the Empower MVM project, we opened the Sample Set Generator and loaded the robustness validation test as shown in Figure 1. The MVM experimental design, with a combination of eight different instrument conditions, was imported into the Empower Sample Set Generator.

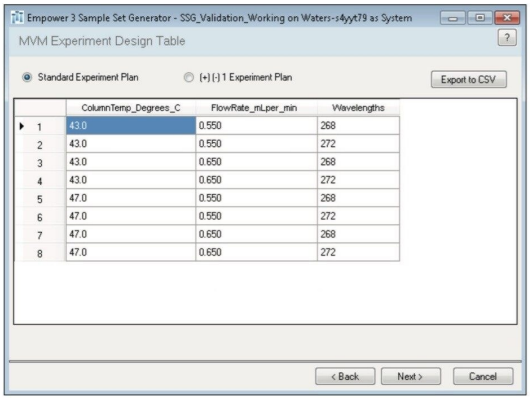


Figure 1. Design of Experiments (DoE) for robustness test loaded into the Empower Sample Set Generator from the Empower MVM protocol.

Next, we used the Sample Set Generator to create instrument methods, method sets, and a sample set method to run the robustness experiments by completing the following steps:

1. Map factors for column temperature, flow rate, and detection wavelength to the desired settings

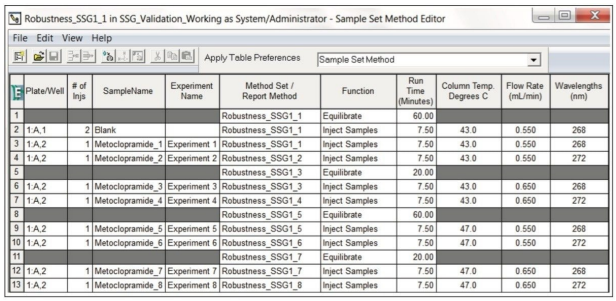
2. Define settings for gradient separation

3. Configure requirements for blanks/standards

solutions and equilibration time

4. Generate sample set method

Using the Empower Sample Set Generator, we were able to automatically create instrument methods with different chromatographic conditions, method sets, and a sample set method for the robustness test. The sample set method for the robustness test (Figure 2) is designed according to the experimental plan for the robustness validation test, with injections of blanks/standard solutions, experiment name, and method sets for each run. The equilibration steps are added between sample lines when there is a change in instrument condition, such as flow rate or column temperature. The instrument methods are automatically built into the methods sets.


Robustness_SSG1_1 in SSG_Validation_Working as System/Administrator - Sample Set Method Editor

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Apply Table Preferences | Sample Set Method

	Plate/Well	# of Injs	SampleName	Experiment Name	Method Set / Report Method	Function	Run Time (Minutes)	Column Temp. Degrees C	Flow Rate (mL/min)	Wavelengths (nm)
1					Robustness_SSG1_1	Equilibrate	60.00			
2	1:A,1	2	Blank		Robustness_SSG1_1	Inject Samples	7.50	43.0	0.550	268
3	1:A,2	1	Metoclopramide_1	Experiment 1	Robustness_SSG1_1	Inject Samples	7.50	43.0	0.550	268
4	1:A,2	1	Metoclopramide_2	Experiment 2	Robustness_SSG1_2	Inject Samples	7.50	43.0	0.550	272
5					Robustness_SSG1_3	Equilibrate	20.00			
6	1:A,2	1	Metoclopramide_3	Experiment 3	Robustness_SSG1_3	Inject Samples	7.50	43.0	0.650	268
7	1:A,2	1	Metoclopramide_4	Experiment 4	Robustness_SSG1_4	Inject Samples	7.50	43.0	0.650	272
8					Robustness_SSG1_5	Equilibrate	60.00			
9	1:A,2	1	Metoclopramide_5	Experiment 5	Robustness_SSG1_5	Inject Samples	7.50	47.0	0.550	268
10	1:A,2	1	Metoclopramide_6	Experiment 6	Robustness_SSG1_6	Inject Samples	7.50	47.0	0.550	272
11					Robustness_SSG1_7	Equilibrate	20.00			
12	1:A,2	1	Metoclopramide_7	Experiment 7	Robustness_SSG1_7	Inject Samples	7.50	47.0	0.650	268
13	1:A,2	1	Metoclopramide_8	Experiment 8	Robustness_SSG1_8	Inject Samples	7.50	47.0	0.650	272

Figure 2. Sample set method for robustness test generated using the Empower Sample Set Generator.

This automated generation allowed us to quickly start the chromatographic run with confidence that all the methods are correctly created. In addition, it reduced the time needed to create chromatographic methods

by about 95% compared to a manual process. The chromatographic data acquired for the robustness test is shown in Figure 3.

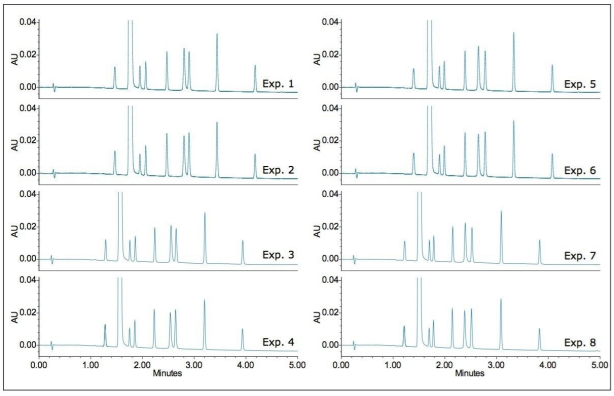

Figure 3. Separation of metoclopramide and USP-specified related substances according to the experimental design for robustness.

Conclusion

By using the Empower Sample Set Generator, users are able to simultaneously and automatically create instrument methods, method sets, and sample set methods to perform chromatographic runs. As a result of automation, transcription errors that may arise during the manual process are eliminated and the time associated with generation of chromatographic methods is reduced. This improves laboratory efficiency, hence enabling an increase in productivity.

The Empower Sample Set Generator can be adapted by any analytical laboratory to automate creation of

chromatographic methods for a wide range of applications performed on Waters ACQUITY UPLC Systems, ACQUITY Premier, ACQUITY Arc™, Arc Premier, and Arc HPLC including method development and validation.

References

1. Maziarz M, McCarthy SM, Wrona M. Increasing Efficiency of Method Validation for Metoclopramide HCl and Related Substances with Empower MVM Software. Waters Application Note, 2014: 720005111 .

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ACQUITY Premier System < https://www.waters.com/waters/nav.htm?cid=135077739 >

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