



QUALITY BY DESIGN SOFTWARE SYSTEM

$\begin{array}{l} GC \ Method \ Development \ Guide - V \ 4.0 \\ Empower \ CDS \end{array}$



S-Matrix Corporation www.smatrix.com

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GC Method Development in Fusion QbD is done using the Fusion Process Development Module (FPD). Below is a general experiment workflow.



Create the GC Method Development Experiment Design

The Fusion Process Development module is used for creating GC Method Development experiments. In this example, we will describe the process for creating a simple GC experiment using the initial hold time and the temperature programming rate.

1. Launch Fusion QbD. Select the 'Fusion Process Development' module.

Fusion Application Mod	
Method Validation	
Process Development	
O Inhaler Testing	
User Role	
Fusion Super User	
<u> </u>	
OK Can	ce

2. Select the 'Create New File' option.



3. Set the 'No. of Mixture Variables' to zero (0).

Set the 'No. of Process Variables' to your desired number (2 in this example). Enter your variable settings

Initial Hold Time Continuous LB = 0.0 UB = 5.0
Temperature Ramp Rate Continuous LB = 10.0 UB = 30.0

Name Initial Hold Time	Units Minutes	.00 +. 0	Type Continuous	Lower Bound 0.0	Upper Bound 5.0
C Constant					
Name Temperatue Ramp Rate State © Variable © Constant	Units Deg/Min	0 .00	Type Continuous	Lower Bound 10.0	Upper Bound BODE

Note – you can add parameters and set them as 'State=Constant' if you want to document the constant settings used in the experiment.

4. Generate the Design.

Fusion Product Development - GC Study 1	.smae		
ile <u>E</u> dit <u>Activity</u> <u>T</u> ools <u>W</u> indow <u>H</u> elp			
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esign of Experiments • Create a Design • Create a Design Tester Reports ata Entry Analysis • Data Entry • Data Analysis estAnswer Searches • Best Overal Answer • Acceptable Performance Region • Point Predictions isualization Graphics • Single Response Series • Multiple Response Series • Multiple Response Series • Multiple Response Series • Fusion Reporter • Audt Log Reporter	ign Reports beriment Design Name: Administra Company: S-Matr Project: Project 1 Date: 17 FEB 2020 Experiment Design	vtor ix (User Defined) 09:07:40 PST [UTC-08:00] sign	S-Matrix.
		Initial Hold Time	Temperature Ramp Rate
	Run No.	(Minutes)	(Deg/Min)
	1	5.0	10.0
	2	2.0	20.0
	3	2.0	20.0
	5	3.0	30.0
	6	25	30.0
	7	2.5	10.0
	Ľ	0.0	10.0

Create the Companion Testing Design

1. In the Data Entry View, click the '+ Create Testing Design' button on the Menu Bar.

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Design of Experiments								
 Create a Design 		Run No.	Initial Hold Time	Temperature Ramp Rate				
 Design Reports 	1	1	5	10				
Data Entry / Analysis	2	2	2.5	20				
Data Entry	3	3	2.5	20				
 Data Analysis 	4	4	5	30				
BestAnswer Searches	5	5	0	30				
 Best Overall Answer 	6	6	2.5	20				
-	7	7	0	10				
Point Predictions								
Visualization Graphics								

2. Select Standard LC from the 'Testing Design Type' list box.

Use the settings shown in the image below.

Create Testing Design				×
Testing Design Name Testing Design	(1)	Testing Design Type Standard LC	~	1
		Descriptive Statistics Time Series Standard LC Inhaler Testing		
	Replication Scheme No. of Prepa No. of Test Repeats p	ration Repeats 1 • er Preparation 1 •		
The settings are valid.				
		Ba	ick Finish	Cancel

3. Save the file with a unique and recognizable file name.

🐺 Fusion Product Development - GC E						-		×
<u>File Edit Activity Tools Window H</u>	<u>H</u> elp							
D 🖻 😂 🖬 🕲 🖡 🎒 📒 +	Create Testing Design 😐 Delete Testing Design	🐺 Create Response	네네 Response Reductions	🛋 Export 🧯 Import Responses	0			
Design of Experiments · Create a Design · Design Reports Data Entry (Analysis	Response Name	Response Units	Lower Limit	<= Response <=	Testing Design Type Standard LC	Vie	w Testing	Desig
bate Entry / Alarysis bate Analysis bate Analysis best Answer Searches estext Searches estext Searches estext Searches estext Searches wisualization Graphics • Single Response Series • Multiple Response Series esporting Toolkit e Fusion Reporter	A 1 1 2 2 3 3 4 4 5 5 6 6 7 7 7							

Construct a Template GC Method in the CDS

- 1. Log on to Empower using your Empower logon credentials.
- 2. Use the 'Browse Projects' option to navigate to the Empower project in which you will export your experiment design.
- 3. Open an existing GC instrument method (or create a new GC method) which correctly operates the GC on which you will run your experiment design and is consistent with your sample compound mix and general experimental approach.
- Edit the method to contain the exact level settings for all GC parameters you did NOT include in your design so that the constant level settings are correct to the study.
 NOTE – you will use this method as the basis of constructing your experiment methods and linking them to your exported sequence. Therefore, constructing this method with the correct constant level settings will reduce the manual editing required to only the experiment design parameters.
- 5. Execute the 'File | Save As...' operation to save the file with a recognizable name. In this example we will use the name "Fusion_GC_Base_Method" for the instrument method and the associated method set method.

Export the Testing Design to the CDS

1. Access the Data Entry View and select the 'Testing Design (1)' tab.

Click the 'Export' button on the main menu bar.

Select on the 'Export to CDS' option on the 'Export Options' dialog.



OK Cancel

2. Click 'Next' on the 1st Export wizard dialog pictured below.

Export			
Selection	1		
	- : 1 - to - : 7 -	Export the testing design by Column	Update
1 to 7			
	Run Label		
1	1		-
2	2		
3	3		
5	5		
6	6		
7	7		
			-
4			•
		<< Back Next >>	Einish Cancel

3. Select a valid LC instrument system in the 2nd Export wizard dialog pictured below, and click Next.

Instrument Name Alliance 1		
Autosampler Configuration Internal Autosampler Tray Name Other First Vial I 9 9	Instrument Data System Waters Empower Instrument Name Alliance 1 Instrument Definition	
Include Blank Injection(s) In each exported sequence Include Suitability Injection(s)		
Maximum number of injections per vial 50 📩		

IMPORTANT

As shown in the image above, you must select an Autosampler Tray with the same Vial Position label designations as your GC instrument autosampler tray.

NOTE – The "**Other**" tray option uses the standard "1, 2, …, 100" vial position designation.

 Select the 'None Selected' option in the Standards Strategy list box within the 3rd Export wizard dialog pictured below, and click 'Finish'.



5. Log on to Empower using your Empower logon credentials.

ile Edit Activity Tools Window H	delp	Crasta Parnonza - Et Parnonza Paductionz	C Empet & Import Personner	0
esign of Experiments - • Create a Design - • Design Reports ata Entry (Analysis	Response Name	Response Units	E Export a Import Responses	Testing Design Type Standard LC View Testing Desig
ula Entry / Artarysis - Data Anaysis EstAnswer Searches - Beat Overall Answer - Acceptable Performance Region - Pour Predictons - Single Response Series eporting Toolkit - Fusion Reporter - Fusion Reporter	A Pan Ho 1 1 2 2 3 3 4 4 5 5 6 6 7 7 7	Empower Login X User Name: Basaword: Database: Local OK Cancel		

6. In Empower, select the Project and Method Set method which will be used to build the Sample Set method, and click 'Next'.

Select Project Select Project Projects Customers Solutributors Solutributors	× Show Methods created by Fusion QbD Method Set Agilent_Infinity_II_1 Altiance1 ✓ Enable Shutdown Method Agilent_Infinity_II_1 Altiance1
Owner	Information
Ready IMPORTANT: Be sure the selected template method has the correct structure ar Refer to the on-line Help for detailed information on these requirements.	nd properties required for the experiment design you are exporting.
	<< Back Next>> Cancel

CRITICAL

Fusion QbD versions prior to Version 9.9.1 require that you select a Method Set method associated with an Instrument method specific to the **LC** instrument system you selected in Step 3 above.

IMPORTANT

If you build your Sample Set method manually, or using the New Sample Set Method Wizard, make sure that the "Dual Tower" option is UNchecked, as shown below.

Select Sample Set Method Type - Untitled	×
Select the type of sample set method to create. LC or PDA/MS GC GC BF Internal Standards Betch Tower Betch Tower <td></td>	
< <u>B</u> ack <u>N</u> ext > Cancel Help	

7. Enter a recognizable name which will be used to name the Sample Set method, Instrument methods, and Method Set methods built as part of the export operation, then click 'Finish'.

Enter the Sample Set Name					×
	Sample Set Name GC Testing Experiment 1		-		
	Set Equilibration Time Run Time 20 Injection Volume 1	minutes minutes uL			
			<< <u>B</u> ack	Einish	<u>C</u> ancel

IMPORTANT

Equilibration Time, **Run Time** and **Injection Volume** – the level settings you enter here will be automatically written to the Sample Set method. You should review and edit these settings as needed in Empower for your experiment run conditions.

Construct the Required GC Methods in the CDS

- 1. Log on to Empower using your Empower logon credentials.
- 2. Use the 'Browse Projects' option to navigate to the Empower project in which you exported your experiment design.
- 3. With Empower open, launch Fusion QbD, open your GC experiment design file, navigate to the 'Design Reports' View, and select the 'Experiment Design' report from the 'Design Reports list box, as pictured below.

Fusion Product Development - GC Study 1.sm	ae					
Eile Edit Activity Jools Window Help						
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Design of Experiments Octate a Design Design Design Design Design Design Design Experi Data Entry /Analysis Deta Entry Design De	Reports ment Design					
- • Data Analysis						
estAnswer/Searches	Name: Administrator Company: SMatrix Project: Project 1 (User Defined) Date: 17 FEB 2020 09:07:40 PST [UTC-08:00] Experiment Design					
	Due No.	Initial Hold Time	Temperature Ramp Rate			
	1	(windles)	(begiwin)			
	2	25	20.0			
	3	2.0	20.0			
	4	2.0	20.0			
	6	5.0	30.0			
	6	25	30.0			
	7	2.0	20.0			
	Ľ	0.0	10.0			

- Open the template (base) GC instrument method you created according to the steps in the earlier section titled "Construct a Template (Base) GC Methods within the CDS".
- Edit the GC method to reflect the level settings of the variables in Experiment Run No. 1 (refer to the Fusion QbD experiment design for the required run settings).

6. Execute the 'File | Save with Method Set...' operation to save the GC Instrument method, and its associated Method Set method, with a recognizable name and a Run 1 extension. In this example we will use the name "Fusion_GC_Study_001".

			Inbox - Josep
n	GC Method 001 in SMD20	19 as Syster	m/Administrator - Instrument Method Editor
	File Edit View Help		
-	New	Ctrl+N	
2	Open	Ctrl+O	2
fE	Save	Ctrl+S	16
ea	Save As		
SI V	Save with Method Set		ature Solvents Channel
ita	Exit		
	deneral cystem a annot		

Repeat Steps 4 – 6 above to generate the Instrument methods and associated Method Set methods required for 1) all experiment design runs, and 2) all Column Conditioning runs required for correct experiment execution (e.g. to support column baking required prior to executing the next experiment run or runs). It is best to do this in the sequential order of the experiment design – for example:

Fusion_GC_Study_Conditioning_1 (Initial Conditioning) Fusion_GC_Study_001 Fusion_GC_Study_002 ... Fusion_GC_Study_007

Note – doing this in sequential order minimizes mistakes, and supports ease of association of the methods into the associated Sample Set method constructed at the time of export from Fusion QbD.

 Select the Sample Set method which Fusion QbD constructed within your target Empower project, and open it for editing.

💽 S-	Matrix\ADL\ADL Template Proje	ect as System/Admini	strator - Project				-		×					
Eile Edit View Jools Database Help														
Filter B	9: Default	▼ E	dit Vie <u>w</u> Update Max Rov	/s: 1000										
٩Þ	Sample Sets Injections Char	nels Methods Res	ult Sets Results Peaks Fra	actions Sign	Offs Curv	s View Filters Custom Fields Audit Trails								
Ĕ-	Method Name	Method Type	Method Date	Method Id	Old Id				^					
1	1 GC Testing Experiment 1_1 Samp		2/16/2020 7:54:19 PM PST	1040										
2	Acquity H Class QDa 1 Base Method Set		8/15/2019 3:31:00 PM EDT	1019										
3 Alliance 1 Method Set		Method Set	8/15/2019 3:36:46 PM EDT	1031										
4 Acquity 1 Base Method Method Set		Method Set	8/15/2019 3:31:00 PM EDT	1022										
5	Acquity H Class QDa 1 Base	Instrument	8/15/2019 3:31:00 PM EDT	1000										
6	Alliance 1	Instrument	8/15/2019 3:36:31 PM EDT	1030										
7	Acquiby 1 Race Method	Instrument	8/15/2010 3-31-00 PM EDT	1004					~					

Manually insert conditioning rows as needed. For each column conditioning run (row) in the Sample Set method, use the Instrument method list boxes within the 'Method Set / Report or Export Method' column to select the GC conditioning method you constructed in the previous section for the conditioning run.

2	GC	Test O	01_1 in	SMD2019 as	System/Admi	nistrator -	Sample Set Metho	d Editor								- 0	×
E	e Ec		ew H ≫	elp <u>'참고'</u> '''	3.16.18. Ap	oply Table F	Preferences Sem	ple Set Method		•							
E	Vial	Inj Vol (uL)	# of Injs	Label	SampleName	Level	Function	Method Set / Report or Export Method	Label Reference	Processing	Run Time (Minutes)	Data Start (Minutes)	Next Inj. Delay (Minutes)	MS Tune Method	MS Calibration Method	Column Position	Auto Addition
1	1	10.0	1	Unk-001-001	1		Inject Samples	GC Method 001 💌		Normal	20.00	0.00	0.00				
2	2	10.0	1	Unk-001-002	2		Inject Samples	Alliance 1 Base Method		Normal	20.00	0.00	0.00				
3	3	10.0	1	Unk-001-003	3		Inject Samples	Alliance 1 Base Method		Normal	20.00	0.00	0.00				
4	4	10.0	1	Unk-001-004	4		Inject Samples	Alliance 1 Base Method		Normal	20.00	0.00	0.00				
6	5	10.0	1	Unk-001-005	5		Inject Samples	Alliance 1 Base Method		Normal	20.00	0.00	0.00				
6	6	10.0	1	Unk-002-001	6		Inject Samples	Alliance 1 Base Method		Normal	20.00	0.00	0.00				
7	7	10.0	1	Unk-002-002	7		Inject Samples	Aliance 1 Base Method		Normal	20.00	0.00	0.00				
Г																	
Г																	
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- 3. Modify the Vial positions in the 'Vial' column of the sequence so that all experiment run injections point to the vial position containing your sample compound mix.
- 4. Perform a column conditioning run to bake your column either prior to running the experiment or by adding a new first row to the sequence for the baking method.

- 5. Confirm that the equilibration times, run times, and injection volumes match the experiment method requirements, and your method times.
- 6. Save the edited Sample Set method when the exchanges and edits are complete.

Run your Experiment in the CDS and Import Your Results

- 1. Prepare your GC system. Load and execute the Sample Set in Empower.
- After running the experiment on the GC, process the completed Sample Set into a Results Set using an appropriate processing method. Review the processed results to correct any integration issues.
- 3. Launch Fusion QbD and access the Fusion Product Development module.
- 4. Open your experiment file, and access the Data Entry View.
- 5. Select the 'Testing Design (1)' tab, and import your experiment chromatogram results for analysis and visualization.



Note – refer to the Empower Data Exchange module under the Help menu in Fusion QbD for tips with integration and the Fusion QbD import operation.