

QUALITY BY DESIGN SOFTWARE SYSTEM

GC METHOD DEVELOPMENT GUIDE – Empower CDS



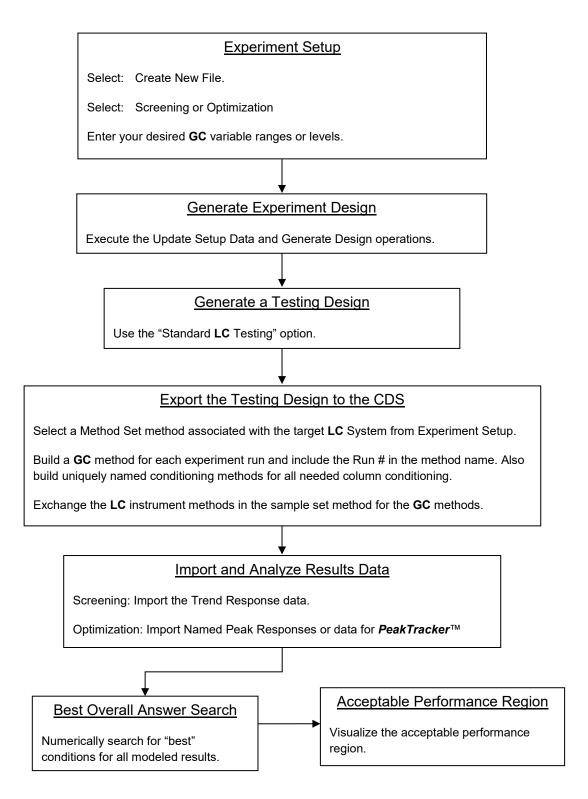
S-Matrix Corporation

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Overview of the Workflow

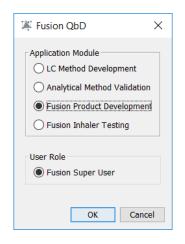
GC Method Development in Fusion QbD is done using the Fusion Product Development Module (FPD). Below is a general workflow.



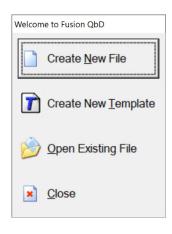
Create the GC Method Development Experiment Design

The Fusion Product 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 Product Development' module.



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



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.

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| n of Experiments | Name: Administrator Company: S.Matrix Project: Project 1 (Us Date: 17 FEB 2020 09: Experiment Design | er Defined) 77:40 PST [UTC-08:00] | S-Matrix. |
| | Experiment Design Ma | | |
| | Run No. | Initial Hold Time (Minutes) | Temperature Ramp Rate (Deg/Min) |
| | 1 | 5.0 | 10.0 |
| I | | | |
| | 2 | 2.5 | 20.0 |
| | 3 | 2.5 | 20.0 |
| | 2 3 4 | | |
| | 2 3 4 5 | 2.5 | 20.0 |
| | 4 | 2.5 | 20.0 30.0 |

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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| 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 | | | | |
| - Acceptable Performance Region | 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.

| Kreate Testing Design | | | | × |
|---------------------------------------|--|---|--------|--------|
| Testing Design Name Testing Design | (1) | Testing Design Type Standard LC | ~ | |
| | | Descriptive Statistics Time Series Standard LC Inhaler Testing | | |
| | Replication Scheme No. of Preparal No. of Test Repeats per | | | |
| The settings are valid. | | | | |
| | | Back | Finish | Cancel |

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

| 🐺 Fusion Product Development - GC E | xport.smae | | | | | - | | × |
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| besign of Experiments | Response Name | Response Units | | | Testing Design Type Standard LC | | fiew Testing | g Desigr |
| Reporting Toolkit | | | | | | | | |

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.

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| Design of Experiments • Create a Design • Design Reports Data Entry / Analysis | Response Name | | Response Units | Lower Limit | <= Respon | Upper Limit | Testing Desi Standard LC |
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| | 4 | | | | | | • |
| | Experiment Design | Testing Design (1) | | | | | |
| Ready | | | | | | | d |
| | | Coptions Select Export Type C Export To Chromat C Export To File | ography Data System | Cancel | | | |

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

| Export | | |
|-------------------------------|------------------------------|--------|
| Selection | | |
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| 167 | testing design by countrie | opuale |
| 1 to 7 | | |
| Run Label | | - |
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| 3 3 | | |
| 4 4 5 5 | | |
| 6 6 7 7 | | |
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| | Tuex >> | Cancel |

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

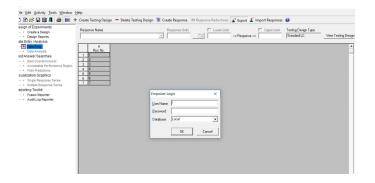
| | Instrument Data System | ^ |
|---|---|---|
| Instrument Name | Waters Empower | |
| Aliance 1 | Instrument Name Alliance 1 | |
| | Alliance 1 | |
| Autosampler Configuration | Waters 2690/2695 Alliance | |
| Internal Autosampler | Waters 2998 PDA Detector | |
| Tray Name | External Switching Valves (contact closure) | |
| 5-Carousel Tray - 120 2-mL vials | | |
| First Vial Last Vial | | |
| 1 120 • | Pump:Quaternary Pump | ~ |
| Include Blank Injection(s) In each exported sequent Include Suitability Injection(s) 5 - In each export | | |
| Maximum number of injections per vial 50 - | a | |

Note – Fusion QbD export automation only works directly with LC instrument systems and methods. Therefore, you must select a licensed LC instrument system. You will match this with the Method Set method you select in Step 6 below, which must be associated with the same LC instrument method and system.

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

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|-------------------------|--|-------|---------------|--|
| Strategy None Selected> | | Cļear | <u>R</u> eset | |
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5. Log on to Empower using your Empower logon credentials.



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

| Find Filter Res Projects Filter Res Projects Constructions Solution Solution Solution Solution | set | Show Methods created by Fusion QbD Method Set Acquity 1 Base Method Acquity 1 Class QD a 1 Base Aliance 1 Information Enable Shutdown Method Acquity H Class QD a 1 Base Aliance 1 |
|---|-----|--|
| er Types (logged in as 'Owner') Owner dy RTANT: Be sure the selected template method has the correct to to the on-line Help for detailed information on these requirement | | nd properties required for the experiment design you are exporting. |

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 minutes | |
| Run Time 20 minutes | |
| Injection Volume 1 uL | |
| | |
| | << Back |

IMPORTANT

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 within 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. Open an existing GC instrument method which correctly operates the GC on which you will run your experiment design.
- Edit the method to contain the correct level settings for all GC parameters you did NOT include in your design in terms of your current sample and this experiment.
- 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".
- 6. 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 | nae | | | |
|--|---|---------------------------------------|--|--|
| ile <u>E</u> dit <u>A</u> ctivity <u>T</u> ools <u>W</u> indow <u>H</u> elp | | | | |
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| - Create a Design | n Reports iment Design | | | |
| Acceptable Performance Region Point Predictions Isualization Graphics Single Response Series Mutiple Response Series teporting Toolkit Fusion Reporter Audé Log Reporter | Name: Administrator Company: S-Matrix Project: Project 1 (User Defin Date: 17 FEB 2020 09:07:40 P Experiment Design Experiment Design Matrix | | S-Matrix. | |
| | | Initial Hold Time | Temperature Ramp Rate | |
| | Run No. | (Minutes) | (Deg/Min) | |
| | Run No. | | | |
| | Run No. 1 2 | (Minutes) | (Deg/Min) | |
| | Run No. 1 2 3 | (Minutes) 5.0 | (Deg/Min) 10.0 | |
| | Run No. 1 2 3 4 | (Minutes) 5.0 2.5 | (Deg/Min) 10.0 20.0 | |
| | Run No. 1 2 3 4 5 | (Minutes) 5.0 2.5 2.5 | (Deg/Min) 10.0 20.0 20.0 | |
| | 1 2 3 4 | (Minutes) 5.0 2.5 2.5 5.0 | (Deg/Min) 100 200 200 300 300 | |

 Open the GC instrument method from Step 5 above. Referring to the Fusion QbD experiment design, edit the GC method to reflect the level settings of the variables in Run No. 1. 8. 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 SMD2019 as System/Administrator - Instrument Method Editor | | | | | | | | | | |
| F. | File | Edit View Help | | | | | | | | | | |
| _2 | | New | Ctrl+N | | | | | | | | | |
| 2 | 1 | Open | Ctrl+O | 2 | | | | | | | | |
| f E rea | | Save | Ctrl+S |)6 | | | | | | | | |
| ea | | Save As | | | | | | | | | | |
| esi V | | Save with Method Set | | ature Solvents Channel | | | | | | | | |
| ita | _ | Exit | | | | | | | | | | |

Repeat Steps 7 and 8 above to generate the Instrument Methods and associated
 Method Set methods required for all the experiment design runs. It is best to do this in
 the sequential order of the experiment design – for example:

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.

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| Filter E | By: Default | • E | dit Vie <u>w</u> Update Max Row | vs: 1000 | | | |
| • • | Sample Sets Injections Char | nels Methods Res | ult Sets Results Peaks Fra | actions | Offs Curve | s View Filters Custom Fields Audit Trails | |
| Ē | Method Name | Method Type | Method Date | Method id | Old Id | | |
| 1 | GC Testing Experiment 1_1 | Sample Set | 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 | 8/15/2019 3:36:46 PM EDT | 1031 | | | |
| 4 | Acquity 1 Base Method | 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 | | | |
| - | Acquiby 1 Base Method | lostrument | 8/15/2010 3:31:00 PM EDT | 1004 | | | |

 For each experiment run (row) in the Sample Set method, use the Instrument method list boxes within the 'Method Set / Report or Export Method' column to exchange the LC instrument method for the GC method you constructed in the previous section.

| Filk | e Ec | it Vi | ew H | elp | | | | | | | | | | | | | |
|------|------|---------------------|--------------|-------------|---------------|-------------|------------------|--|--------------------|------------|--------------------------|----------------------------|---------------------------------|-------------------|--------------------------|--------------------|----------|
| R. | 2 | | }=⇒- | 8.375 | <u>美術館</u> Ap | ply Table F | Preferences Serr | ple Set Method | | • | | | | | | | |
| 5 | Vial | lnj 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 | A Add |
| 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 | Aliance 1 Base Method | | Normal | 20.00 | 0.00 | 0.00 | | | | |
| 5 | 6 | 10.0 | 1 | Unk-001-005 | 6 | | Inject Samples | Aliance 1 Base Method | | Normal | 20.00 | 0.00 | 0.00 | | | | Г |
| 6 | 6 | 10.0 | 1 | Unk-002-001 | 6 | | Inject Samples | Alliance 1 Base Method | | Normal | 20.00 | 0.00 | 0.00 | | | | Г |
| 7 | 7 | 10.0 | 1 | Unk-002-002 | 7 | | Inject Samples | Alliance 1 Base Method | | Normal | 20.00 | 0.00 | 0.00 | | | | |
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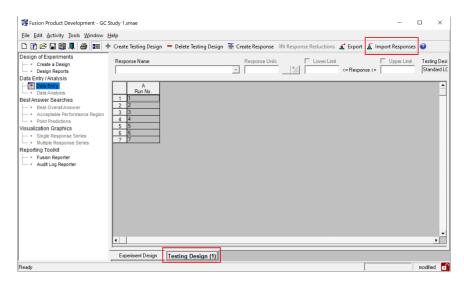
3. Confirm that the run times and injection volumes match the experiment method requirements, and your method times, and save the edited Sample Set method when the exchanges and edits are complete.

IMPORTANT

You should carry out a column conditioning run to bake your column prior to starting your experiment run. You will also need to manually insert rows column conditioning with appropriately constructed conditioning methods as required to support changes between experiment runs.

Run your Experiment within 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.