Fusion QbD® Software Platform

Fusion Method Development

Robust LC Method Development Software

The Only Software That Has It All!

- 100% aligned with FDA/ICH Quality by Design (QbD) guidances!

- Fully automates QbD method development experiments on multiple instruments and CDS systems!

- Gives you knowledge – and statistical assurance – that you have the best performing and most robust method – not just incremental improvement!

- Can shorten LC method development time by at least 75%!
Automated ● QbD Aligned ● LC Method Development

Key Benefits of the Fusion QbD Software

- Quality by Design (QbD) Principles and Guidelines – **Built In!**
  - **Formal Experimental Design – Built In**
    - ICH-Q8(R2) – Formal Experimental Design – A structured, organized method for determining the relationship between factors affecting a process and the output of that process. Also known as “Design of Experiments”
  - **Interaction Effects Characterization – Built In**
    - ICH Q8(R2) – Information from formal experimental designs can be useful in identifying critical or interacting variables...
  - **Integrated Monte Carlo Simulation for Robustness – Built In**
    - FDA Reviewer Guidance – Validation of Chromatographic Methods – ... methods should be validated and also designed by the developer or user to ensure ruggedness or robustness
    - ICH Q2(R1) – The evaluation of robustness should be considered during the development phase...

- **Automated QbD-aligned Experimentation – Built In!**
  - **Experimental Design Wizard** – examines your stage of work (screening or optimizing) and study parameters, then instantly generates the most efficient and defensible statistical experiment design
  - **Experiment Automation Wizards**
    - **Export Wizard** automatically builds your experimental design in the CDS as ready-to-run methods and sequence
    - **Import Wizard** automatically imports all chromatogram results data from the CDS as analysis-ready data sets
  - **Data Analysis & Modeling Wizard** – automatically performs multiple integrated analyses, including experimental error, outlier, nonlinearity, and instantly builds statistically defensible models for all included method performance characteristics

- **QbD Design and Operating Space Visualization — Built In!**
  - **Best Answer Search** – instantly identify the best performing method overall in terms of simultaneously meeting all your studied method performance goals
  - **Design Space** – graphically visualize the QbD Robust Design Space (also called Method Operable Design Region – MODR) exactly as described in ICH Q8(R2)
  - **Proven Acceptable Ranges** – add the study parameter operating ranges which meet all your method performance requirements directly onto your design space graph

- **21 CFR Part 11 Compliance Support – Built In!**
  - Automated and fully audited bi-directional data exchanges with the CDS
  - E-record and E-signature controls with full work auditing
  - Workflow Management System with E-review and E-approve Capabilities
Automated LC Method Development Experimentation – Five Step Workflow

1. You complete a simple experiment setup template.
2. Fusion QbD generates the experimental design and exports the design to the CDS.
3. The CDS runs the experiment on the target LC system.
4. Fusion QbD imports the chromatogram results from the CDS and analyzes the data.
5. Fusion QbD automatically creates final reports with QbD visualization graphics.

Step 1 – You Complete the Template

Fusion LC Method Development Software (FMD) has simple experiment setup templates for method development experiments. FMD automatically adjusts the LC-centric template to the stage of the study – Screening or Optimization, the type of LC (e.g. Binary or Quaternary pump), and the type of chemistry (e.g. Reversed Phase, Ion Exchange, etc.).

Select Your Experiment Type

FMD supports Screening and Optimization studies for:

- Isocratic Methods
- Reversed Phase
- Chiral
- HILIC
- Gradient Methods
- Normal Phase
- Ion Exchange
- Size Exclusion

FMD provides visual displays to simplify setup for complex settings such as required pump program conditions and key settings for each included column such as pH upper limit and conditioning time.

Select Your Study Parameters

Simply select the instrument and chemistry parameters to study. FMD adds settings controls for each parameter to the setup template so that you can define the range or levels you want to explore.

Online Preparation (OLP)

OLP automates mobile phase preparation for pH (shown at right), Buffer Strength, Additive Concentration, or Salt Concentration. OLP configures the display for simple experiment setup, and (2) builds the proportioning required for each experiment run into the instrument methods it automatically constructs.

Maintain target level in each run: the software can maintain the target OLP variable in a given run (injection) as an absolute constant within the mobile phase independent of the change in the Strong/Weak solvent ratio across the gradient.
**Step 2 – Fusion QbD Generates the Experiment and Exports it to your CDS**

FMD automatically constructs the experiment designs within the CDS as ready-to-run methods and sequences. It also automatically orders the design for fast, efficient execution and adds column conditioning for chemistry system changes between injections (e.g. strong solvent type and/or pH).

**Step 3 – CDS runs the Validation Experiment**

FMV sequences run automatically on the CDS. FMV even enables you to include a Shutdown method as the last method run so that you can execute FMV sequences overnight while you sleep!

**Step 4 – Fusion QbD Imports and Analyzes the Chromatogram Results**

FMD automatically imports the required peak result data from the CDS, and re-maps the results to the design for automated analysis, graphing, and reporting.

**Patented Trend Responses™ – Screening Experiments**

FMD’s patented Trend Responses eliminate the requirement for laborious and error-prone peak tracking in initial screening experiments. Flexible Trend Response operators enable you to automatically retrieve data for any separation characteristics you want to evaluate. **Example Trend Responses** which FMD can instantly obtain from all experiment chromatograms include:

<table>
<thead>
<tr>
<th>Overall Selectivity Metrics</th>
<th>Auto Peak Tracking Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Integrated Peaks</td>
<td>Main Peaks – all specified results</td>
</tr>
<tr>
<td>No. of Baseline Resolved Peaks</td>
<td>Post Peaks – (elute after main peaks) all specified results</td>
</tr>
<tr>
<td>No. of Peaks with Good Tailing</td>
<td>First Peak – all specified results</td>
</tr>
<tr>
<td>No. of Peaks with Specified S/N Ratio</td>
<td>Last Peak – all specified results</td>
</tr>
</tbody>
</table>
Named Peak Responses – Optimization Experiments

FMD can import and model any results data computed by the CDS for named peaks. You select the results which correspond to your critical method performance characteristics. These are your Critical Quality Attributes (CQA) in QbD terminology!

Best Answer Search

You set the required performance goals for all your modeled CQAs. FMD’s search engine then comprehensively examines the performance of all possible methods that exist within the combined ranges of your experiment variables to identify the method which meets or exceeds your goals.

Patented Robustness Simulator™

All modeling software can only directly predict the mean, or average, performance of a given method. That is why FMD’s Robustness Simulator is so critical to developing your final robust design space.

Robustness Simulator uses a correctly-implemented Monte Carlo simulation engine to:

1. automatically compute accepted method robustness metrics (e.g. $C_p$, $C_{pk}$, $C_{pm}$, $C_{pkm}$) for all CQAs in your optimization experiment.
2. Graphically show all methods which simultaneously meet all your requirements for mean performance and robustness – the unshaded regions in your final robust design space!
Step 5 – Fusion QbD Automatically Creates Final Reports with QbD Visualization Graphics

**FMD** enables you to graphically present your final design space in terms of all your critical method performance attributes (CQAs). A color is assigned to each CQA, and the region of the graph shaded with the color corresponds to methods which do not meet the goal for that CQA.

Here you can select which experiment variables to graph. Slider controls for numeric variables and List Controls for non-numeric variables (e.g., Column Type) allow you to see how the design space shape changes as you change variable settings.

Just move your cursor around the Fusion QbD robust design space graph and see the simulation chromatogram update in real time to visualize the changes in method performance across the graph.

Create any number of Graphical Answer Search reports, with each report containing a unique overlay graph representing the Design Space and Proven Acceptable Ranges at different level setting combinations of critical method parameters. For example, given three study variables you could create three reports with a graph in each to display the continuity of the PAR across the operating range of a non-graphed variable – as shown below for pH.

**FMD** even enables you to integrate images of representative chromatograms into your final reports. You can associate these chromatogram images with any of the individual results reports which **FMD** automatically generates.
Automated QbD Experiments – Supported Platforms

Supported Agilent LC Systems
- Agilent 1100s And 1200s
- Agilent 1260 Infinity Series
- Agilent 1260 Infinity II Series
- Agilent 1290 Infinity Series
- Agilent 1290 Infinity II Series
- ✔ Solvent Selection Valves
- ✔ Column Switching Valves

Supported Thermo LC Systems
- UltiMate LCs
- Vanquish Horizon And Flex LCs
- ✔ Solvent Selection Valves
- ✔ Column Switching Valves

Supported Waters LC Systems
- Alliance HPLC
- Acquity Binary
- Acquity H-Class
- Acquity Arc
- Acquity UPC²
- ✔ Solvent Selection Valves
- ✔ Column Switching Valves
S-Matrix Software Products and Support

S-Matrix Corporation develops advanced software that automates R&D experimental work according to Quality-by-Design principles and methodologies. S-Matrix’s Fusion QbD platform automates and redefines experimentation in Analytical R&D, Chemical and Process R&D, Formulation, and Product R&D.

Fusion QbD Software System Product Suite

- **Fusion LC Method Development**
  Automated QbD experimenting on your LC – automated experimental design, integrated data modeling & robustness simulation. Supports all phases of method development from initial sample/method workup and chemistry scouting through robust method optimization.

- **Fusion Analytical Method Validation**
  Meet regulatory guidelines with a best-practices approach toward LC method validation with comprehensive reporting. Also supports formal validation of Non-LC methods (e.g. GC, CE, Q-NMR).

- **Fusion Inhaler Testing**
  Build simple workflow templates, automate testing and data capture with your CDS via validated and fully audited data exchanges, correctly calculate all particle size distribution results, and generate reports according to USP 601, Ph.Eur. 2.9.18, and ISO 27427.

- **Fusion Product Development**
  The perfect QbD-aligned software for formulation & process development and Non-LC methods development – wizard driven experimental design, automated analysis and modeling, integrated Monte Carlo robustness simulation, elegant effects visualization graphics, and comprehensive reporting.

Sales and Support

Sales: Tel: 800-336-8428 (Outside the USA: 707-441-0406). Email: Sales@smatrix.com
Customer Support: Tel: 707-441-0407. Fax: 707-441-0410. Email: Support@smatrix.com

On-site and Web Training

S-Matrix offers on-site training programs for installed systems. Training includes experiment strategies, experimental design (DOE), data analysis, graphical visualization and ranking of effects, numerical and graphical optimization, and QbD Reporting.

S-Matrix also offers interactive web training which covers software features and operation, along with general principles of DOE and QbD. Web training programs can be tailored to suit your individual focus and information requirements.

To arrange an on-site or web-based training program, call 707-441-0406.

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S-Matrix Corporation
1594 Myrtle Avenue
Eureka, CA 95501 USA

www.smatrix.com