

A Brief History of Fusion QbD[®]

Experiment Automation

Fusion QbD

Quality by Design Software System

WINDOWS[®]



S-Matrix[®]

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LC Method Development and Validation

Over the Last 17 Years S-Matrix has Worked Continuously to Advance and Extend **Fusion QbD[®]** Experiment Automation to the HPLC and UHPLC Systems and Software Used by our Customers.

This is why S-Matrix is the World Leader in QbD Experiment Automation for Liquid Chromatography Method Development and Validation.

S-Matrix developed specific work-tailored user interfaces and LC instrument automation under a project sponsored by Pfizer.



Phase 1 Goals:

1. Experiment Setup Interfaces and Designs for All Validation Studies Required for a Complete Validation Set, Including Robustness.
2. Automated Construction of the Experiments as Ready-to-Run Sequences within the CDS, including:
 - Flexible Setup of Standard Injections for a Variety of Strategies (e.g. Bracketing Overlap, Bracketing Non-overlap, and Grand Average)
 - Automated Integration of Standard Injections into the CDS Sequences.
3. Automated Retrieval of the Chromatogram Results from the CDS for Analysis, Graphing, and Reporting.

Proof-of-Concept HPLC Platform

- TotalChrom CDS
- PE Series 200 LC



S-Matrix extends its prototype Automated Experimentation platform and adapts it to target production CDS Systems.

Phase 2 Goals:

1. Adapt Automated Data Exchange to Waters Millennium³² and Empower.
2. Develop an Integrated Workflow Management System.



1. Extended Automated Experimentation Support to all Empower **Classic-driver** controlled LCs.
2. Adapted Automated Experimentation to Waters Empower 2.
3. Developed Full Support for 21 CFR 11 Compliance.

Waters Alliance



File-less
Data
Exchanges



Agilent 1100



Extended Full Experiment Automation Support to Waters Acquity Binary UPLC Systems and Waters H-Class UPLC Systems, including External Column Compartments/Valves and Solvent Valves.

Acquity Binary



Acquity H-Class



Adapted the Full QbD Automated Experimentation Capability for LC Method Development and Method Validation to:

1. Agilent ChemStation CDS.
2. Waters Empower 3
3. Agilent Instrument Control Framework (ICF) and ICF-LC Drivers for Agilent LCs Controlled via Empower.



Adapted the Full QbD Automated Experimentation Capability for LC Method Development and Method Validation to:

1. The Waters Acquity Arc System.
2. The Waters UPC² CC System.

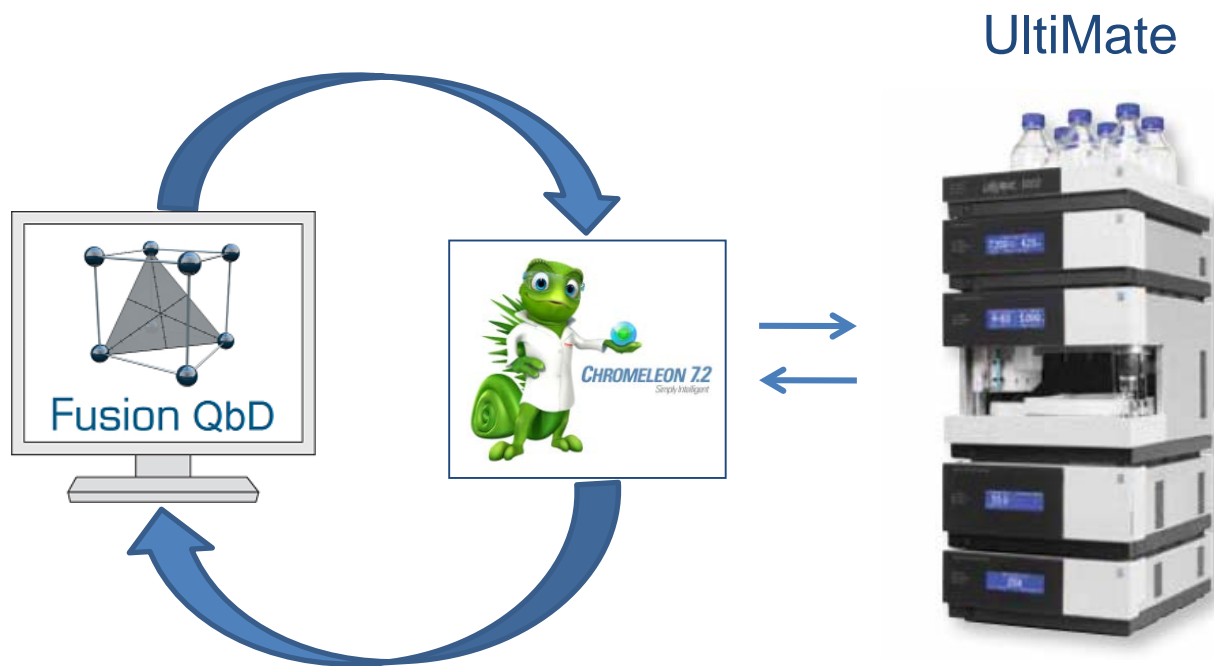
Acquity Arc



Acquity UPC²



Adapted the Full QbD Automated Experimentation Capability for LC Method Development and Method Validation, including the Full Experiment Suite and all Supported Standard Injection Strategies to all UltiMate LC Systems Controlled by Chromeleon 7.2.



1. Adapted External Solvent Selection Valve Support to the Acquity Binary Solvent Manager (BSM) module.
2. Extended ICF Support to All Agilent LCs.



- ✓ Solvent Selection Valves
- ✓ Column Switching Valves

Agilent 1100s
And 1200s



Agilent 1260
Infinity Series



Agilent 1260
Infinity II Series



Agilent 1290
Infinity Series



Agilent 1290
Infinity II Series

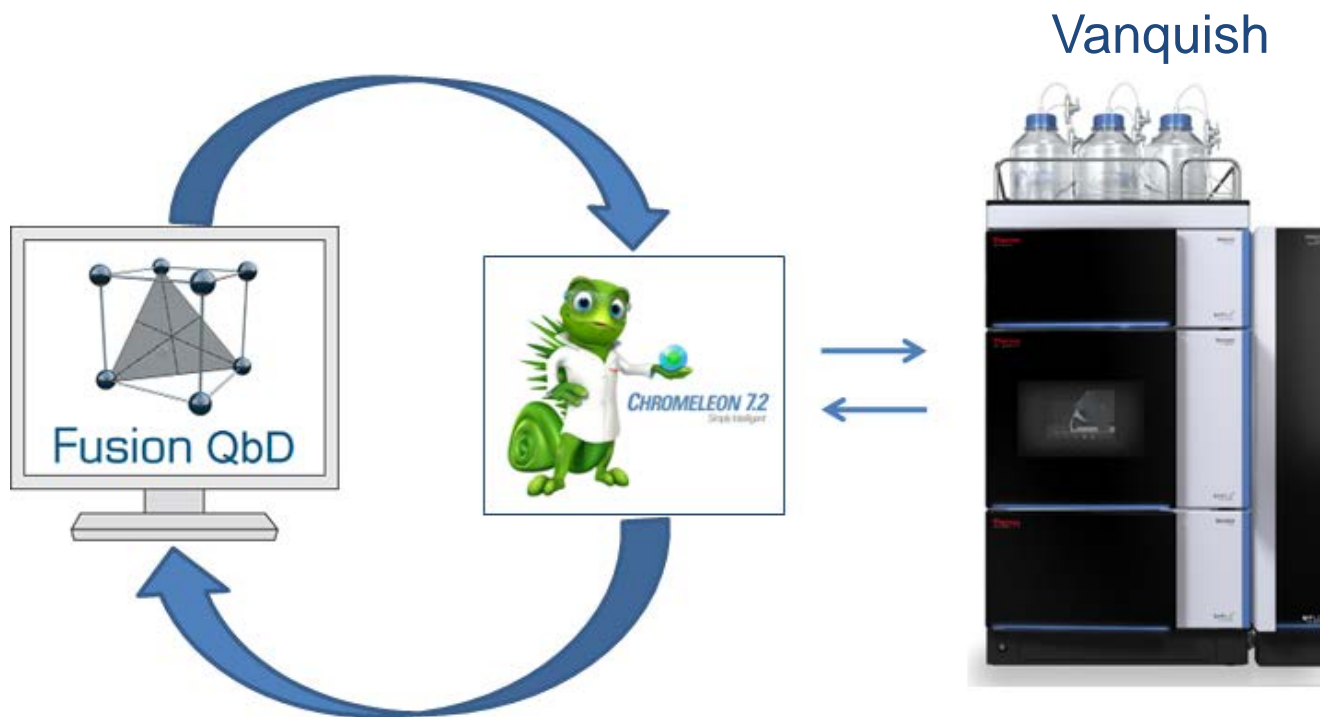


1. Extended ICF Support to OpenLab 1.x.



OpenLab 1.x –
ChemStation Edition

2. Adapted Method Development and Method Validation Experiment Automation to Vanquish LC Systems Controlled by Chromeleon 7.2.



Adapted the Full Method Development and Method Validation Experiment Automation Capabilities to All Agilent LC Systems Controlled by Chromeleon 7.2 via the Agilent ICF.



- ✓ Solvent Selection Valves
- ✓ Column Switching Valves

Agilent 1100s
And 1200s



Agilent 1260
Infinity Series



Agilent 1260
Infinity II Series



Agilent 1290
Infinity Series



Agilent 1290
Infinity II Series



Developed Online Preparation (OLP) within Fusion QbD for LCs with quaternary pump modules:

- Automated pH Screening – with built-in buffer titration curves.
- Buffer Strength Optimization.



Buffer Selector

Select Buffer System

- pH 2.73 - 6.45 [Formate System (20 mM)]
- pH 1.96 - 10.76 [TFA/Ammonium Acetate/Ammonium Hydroxide]
- pH 2.05 - 9.18 [Phosphate System (20mM)]
- pH 2.73 - 6.45 [Formate System (20 mM)]**
- pH 3.25 - 6.73 [Acetate System (20 mM)]
- pH 4.65 - 9.18 [Phosphate System (20 mM)]
- pH 5.67 - 7.90 [Phosphate System (150 mM)]
- pH 6.73 - 10.76 [Ammonium Acetate System]
- pH 2.74 - 10.51 [Formic Acid/Ammonium Hydroxide]

Included	pH	Formic Acid (%)	Ammonium Formate (%)
<input checked="" type="checkbox"/>	2.73	100.00	0.00
<input type="checkbox"/>	2.80	95.00	5.00
<input type="checkbox"/>	2.91	90.00	10.00
<input type="checkbox"/>	3.00	85.00	15.00
<input type="checkbox"/>	3.11	80.00	20.00
<input checked="" type="checkbox"/>	3.20	75.00	25.00
<input type="checkbox"/>	3.29	70.00	30.00
<input type="checkbox"/>	3.37	65.00	35.00
<input type="checkbox"/>	3.45	60.00	40.00
<input type="checkbox"/>	3.53	55.00	45.00
<input type="checkbox"/>	3.61	50.00	50.00
<input checked="" type="checkbox"/>	3.69	45.00	55.00
<input type="checkbox"/>	3.78	40.00	60.00
<input type="checkbox"/>	3.88	35.00	65.00

Select All Select None OK Cancel

Buffer Selector...

pH Online Blending Mode pKa of Primary Compound

pH Buffer Settings: pH 2.73 - 6.45 [Formate System (20 mM)]

No. of Levels:

Buffer	Buffer Name
Acid	Formic Acid (20 mM)
Base	Ammonium Formate (20 mM)

pH Level	Acid %	Base %
2.73	100.0	0.0
3.20	75.0	25.0
3.69	45.0	55.0
4.27	20.0	80.0
4.93	5.0	95.0

Clear Buffer System

1. Adapted Method Development and Method Validation Experiment Automation to the Japanese Language Version of Empower.
2. Adapted Experiment Automation to the following Agilent LC modules:
 - G7104C Agilent Technologies 1260 Infinity II Flexible Pump
 - G7129C Agilent 1260 Infinity II Vialsampler.



G7104C



G7129C



Developed QbD Experiment Automation Support for Setting Wavelength as a Study Parameter in Multiple Agilent Detectors:

- (G1314A) – Agilent 1100/1200 Variable Wavelength Detector
- (G1314B) – Agilent 1260 Infinity Variable Wavelength Detector VL
- (G1314C) – Agilent 1260 Infinity Variable Wavelength Detector VL+
- (G1314D) – Agilent 1200 series Variable Wavelength Detector
- (G1314E) – Agilent 1290 Infinity Variable Wavelength Detector
- (G1314F) – Agilent 1260 Infinity Variable Wavelength Detector
- (G1315A) – Agilent Technologies 1100 Diode Array Detector
- (G1315B) – Agilent 1100/1200 Diode Array Detector
- (G1315C) – Agilent Technologies 1200 Diode Array Detector
- (G1315D) – Agilent 1260 Infinity Diode Array Detector
- (G1365A) – Agilent 1100/1200 Multiple Wavelength Detector
- (G1365B) – Agilent 1200 Multiple Wavelength Detector
- (G1365C) – Agilent 1260 Infinity Multiple Wavelength Detector
- (G1365D) – Agilent 1260 Infinity Multiple Wavelength Detector VL
- (G4212A) – Agilent 1290 Infinity Diode Array Detector
- (G4212B) – Agilent 1290 Infinity Diode Array Detector
- (G7114A) – Agilent 1260 Infinity II Variable Wavelength Detector
- (G7114B) – Agilent 1290 Infinity II Variable Wavelength Detector
- (G7115A) – Agilent 1260 Infinity II Diode Array Detector WR
- (G7117A) – Agilent 1290 Infinity II Diode Array Detector - Fixed Slit
- (G7117B) – Agilent 1290 Infinity II Diode Array Detector - Variable Slit
- (G7117C) – Agilent 1260 Infinity II Diode Array Detector HS
- (G7165A) – Agilent 1260 Infinity II Multiple Wavelength Detector

PeakTracker™ – automatically identifies each peak in each experiment chromatogram using 3D PDA spectral data, and also fully utilizing 3D mass spectral data when the LC system is configured with the Acquity QDa Mass Detector (QDa).

Rs-Map Response – Fusion QbD now uses its hyper-accurate modeling technologies to predict the resolutions of all identified peaks for any given set of experimental conditions using standard USP or EP resolution equations. Fusion QbD then displays the predicted resolution results for all identified peaks in multiple graphics formats: – all of which update in real time as you change chromatographic method conditions.

Forced Degradation Studies – Fusion QbD now has a special mode in which it will design the experiment to run each experiment method on each forced degradation sample, and then combine the chromatogram data to create a composite chromatogram data set for each run which will be used for data analysis, method optimization, and prediction chromatograms.

View the **“Fusion QbD – Amazing New Features in Version 9.9.0”** Slide Deck
to Learn More about These Features and More!