



2019 EASTERN ANALYTICAL SYMPOSIUM & EXPOSITION

Crowne Plaza Princeton
Conference Center
Plainsboro, NJ
November 18-20, 2019

ENHANCING ANALYTICAL CHEMISTRY
WITH SUSTAINABLE SOLUTIONS

Integrating and Automating the Use of PDA and MS Data in LC and LC/MS Method Development

Fusion QbD

Quality by Design Software System

WINDOWS®



S-Matrix®

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Presentation Outline

1. Introduction to the Fusion QbD[®] Software Platform
 - a. QbD Method Development Experiment Automation
 - b. Cross-platform Data Integrity
- 2. *PeakTracker*** – UV & MS Spectra Based Peak Tracking
 - a. Data Integration for Automated Modeling
 - b. Tracking Automation
3. Forced Degradation Study Automation
 - a. Peak Tracking in Forced Degradation Studies
 - b. Composite Chromatogram Modeling & Visualization

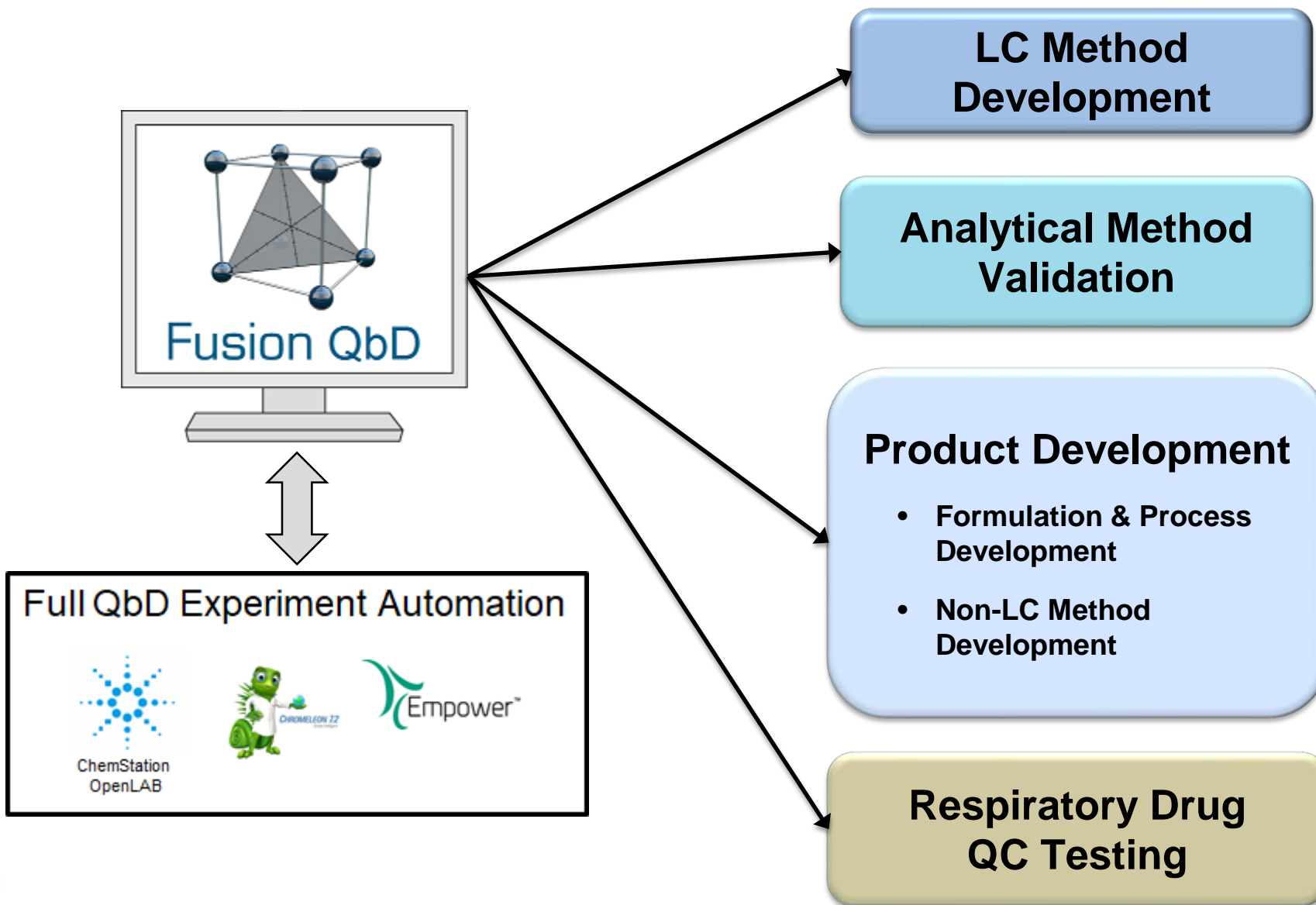
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 - a. QbD Method Development Experiment Automation
 - b. Cross-platform Data Integrity

2. **PeakTracker** – UV & MS Spectra Based Peak Tracking
 - a. Data Integration for Automated Modeling
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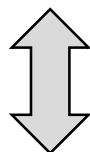
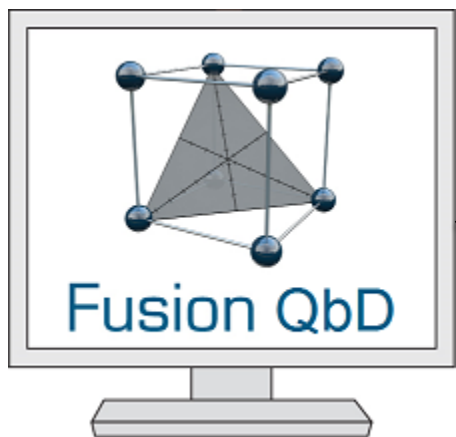
3. Forced Degradation Study Automation
 - a. Peak Tracking in Forced Degradation Studies
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Fusion QbD[®] – Modular Software Platform



Fusion QbD[®] – Modular Software Platform

LC & LC-MS Method
Development



Full QbD Experiment Automation

ChemStation
OpenLAB

CHROMLEON 72

Empower™

A rectangular box containing the text "Full QbD Experiment Automation" at the top. Below the text are three logos: ChemStation OpenLAB (a blue starburst pattern), CHROMLEON 72 (a green cartoon character holding a beaker), and Empower™ (a green stylized wave logo).

Fusion QbD Automation – Supports All Waters LC Systems



- ✓ Solvent Selection Valves
- ✓ Column Switching Valves

Alliance HPLC



Acquity Binary



Acquity H-Class



Acquity Arc



Acquity UPC²



Fusion QbD Automation – Supports All Agilent LC Systems



ChemStation
OpenLab



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





- ✓ Solvent Selection Valves
- ✓ Column Switching Valves

UltiMate LCs



Vanquish Horizon And Flex LCs



Supports all Install Environments

Fusion QbD

Standalone (Workstation)



Network



Citrix Ready Certified

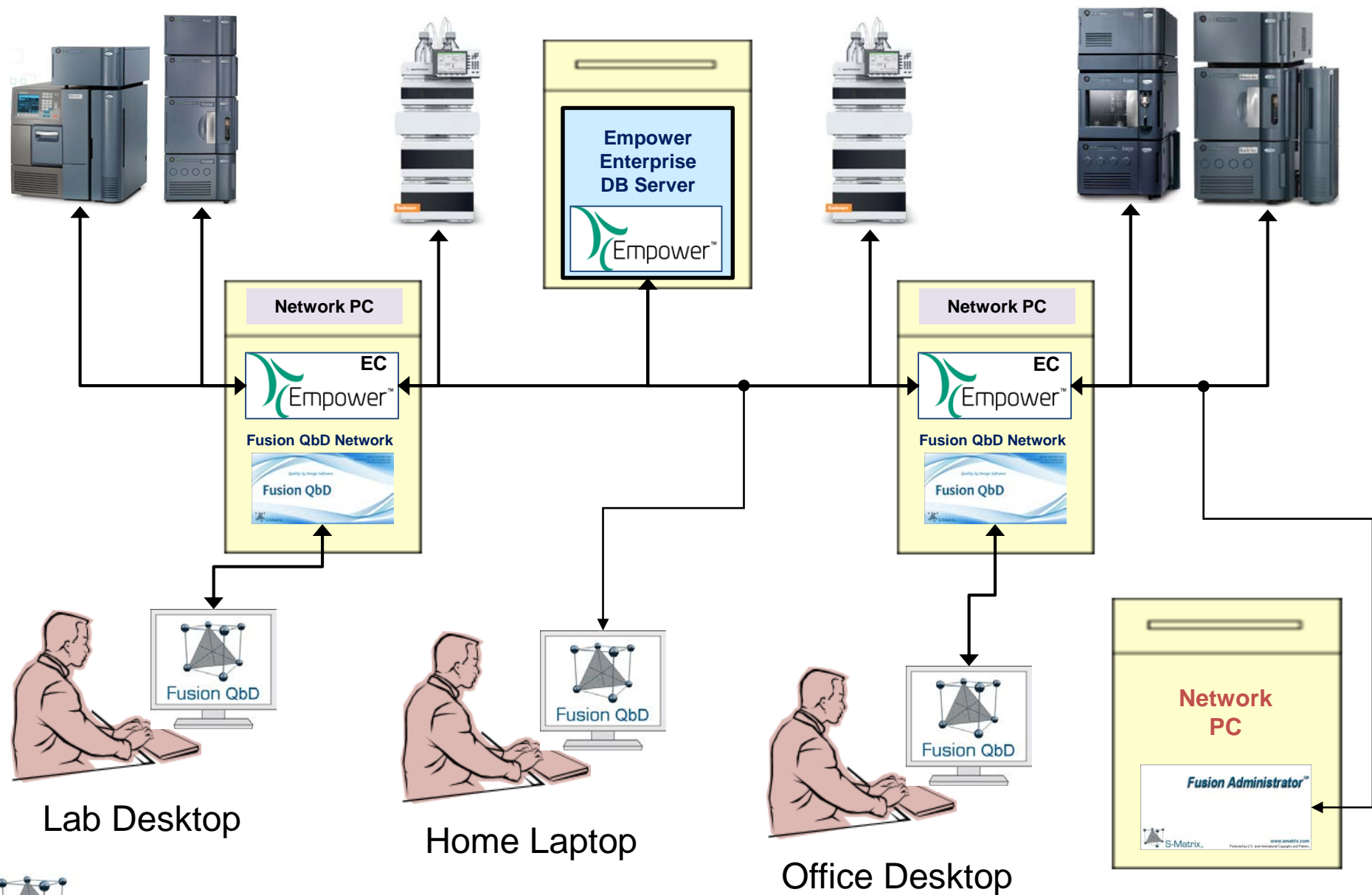


Fully Qualifiable for GxP*



- * - Fusion QbD is operating in the GxP environments of international pharmaceutical companies worldwide.

Fusion QbD – Supports all Install Environments



Supports All These Separation Modes

Reversed Phase

Normal Phase

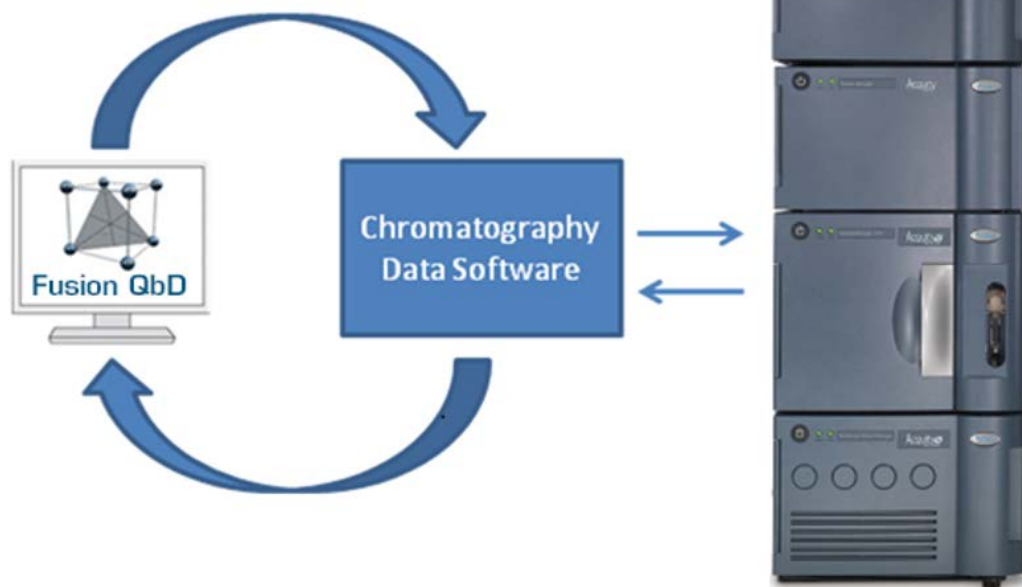
Chiral

HILIC

Ion Exchange

Size Exclusion

SFC



Enables you to study any combination of LC parameters which can interactively effect method performance!

- Isocratic Methods
- Gradient Methods
- Any pump program steps – e.g.
 - Equilibration Time & %
 - Isocratic Hold Time & %
 - Gradient Time & Slope
 - Final Hold Time & %
 - Re-equilibration Time & %
- Strong Solvent Type
- Mobile Phase Solvent Blend
- Column Temperature
- pH
- Column Type
- Flow Rate
- Injection Volume
- Ionic Strength

Initial Chemistry Screening – Built In pH Automation

Buffer Selector... pH Online Blending Mode: One Acid Base Pair pKa of Primary Compound

pH Buffer Settings: No. of Levels: 5

Buffer	Buffer Name	pH Level	Acid %	Base %
Acid	Formic Acid (20 mM)	2.75	100.0	0.0
Base	Ammonium Formate (20 mM)	3.16	80.0	20.0
		3.70	50.0	50.0
		4.34	20.0	80.0
		5.42	5.0	95.0
		6.24	0.0	100.0

Buffer Selector

Select Buffer System: pH 2.75 - 6.24 [Formate System (20 mM)]

Buffer Solutions:

- Formic Acid (20 mM)
- Ammonium Formate (20 mM)

Included	pH	Formic Acid (%)	Ammonium Formate (%)
<input checked="" type="checkbox"/>	2.75	100.00	0.00
<input checked="" type="checkbox"/>	2.78	95.00	5.00
<input checked="" type="checkbox"/>	2.89	90.00	10.00
<input checked="" type="checkbox"/>	3.16	80.00	20.00
<input checked="" type="checkbox"/>	3.38	70.00	30.00
<input checked="" type="checkbox"/>	3.54	60.00	40.00
<input checked="" type="checkbox"/>	3.70	50.00	50.00
<input checked="" type="checkbox"/>	3.88	40.00	60.00
<input checked="" type="checkbox"/>	4.06	30.00	70.00
<input checked="" type="checkbox"/>	4.34	20.00	80.00
<input checked="" type="checkbox"/>	4.91	10.00	90.00
<input checked="" type="checkbox"/>	5.42	5.00	95.00
<input checked="" type="checkbox"/>	6.24	0.00	100.00

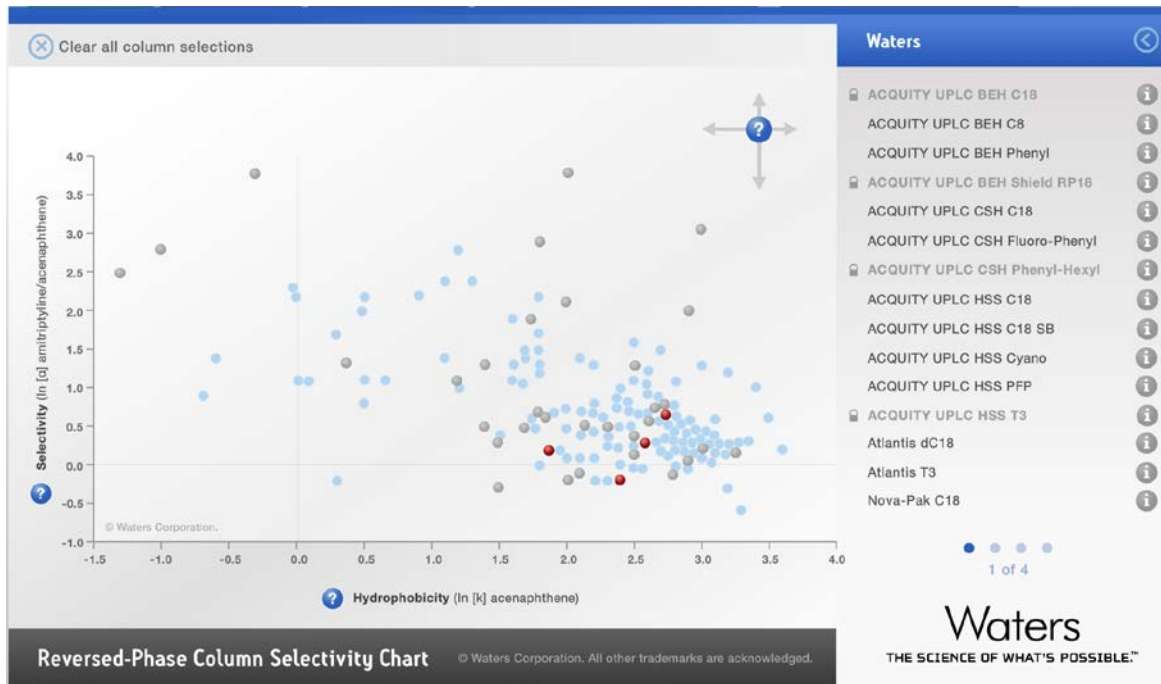
OK Cancel

Built in Buffer System
Titration Curves

Extremely Precise!



Initial Chemistry Screening – Built In Column Switching Automation



Fusion QbD Automation
Supports Column
Compartments with
Multi-position Valves!



Column Settings

	Name	Valve Position	Condition Column Time	pH Upper Bound
1	BEH C18	Position 1 ▼	2.0	14.00
2	BEH Shield RP18	Position 2 ▼	2.0	14.00
3	HSS T3	Position 3 ▼	2.0	14.00
4	CSH Phenyl Hexyl	Position 4 ▼	2.0	14.00

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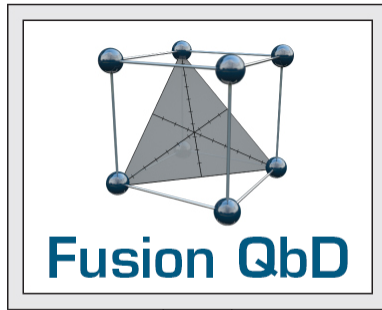
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FDA Statement –

As long as the **data integrity** associated with the method development work matches what would be done in a formal Validation Robustness effort, then the results are acceptable.

**USP Workshop – Enhanced Approaches for Analytical Procedure Lifecycle:
An Alternative to Traditional Validation**

(Sept. 24-25, 2018)



Fusion QbD

Generates QbD-aligned
DOE Experiment

Automatically Builds
Sequence and All
Instrument Methods

Chromatography Data Software (CDS)

Text Mix pH in S-Matrix - MD DemoLC Tutorial - Sample Workup as System/Administrator - Sample Set Method Editor

File Edit View Help

Apply Table Preferences Sample Set Method

Vial	Inj Vol (uL)	# of Injs	Label	SampleName	Level	Function	Method Set / Report Method	Label Reference	Processing	Run Time (Minutes)	Data Start (Minutes)	Next Inj. Delay (Minutes)	Column Position	Auto Additions	SampleWeight	Dilution
1						Condition Column				6.70	0.00	0.00	No Change			
2						Condition Column	Text Mix pH 001_017			0.10	0.00	0.00	No Change			
3						Equilibrate	Text Mix pH 001_017			3.00	0.00	7.95	No Change			
4	1	2.0	1	Unk-000-000	Blank - 1	Inject Samples	Text Mix pH 001_017		Normal	10.50	0.00	1.50			1.00000	1.00000
5						Condition Column	Text Mix pH 001_001			0.10	0.00	0.00	No Change			
6						Equilibrate	Text Mix pH 001_001			3.00	0.00	0.00	No Change			
7	2	2.0	1	Unk-001-001	1.a.1.a	Inject Samples	Text Mix pH 001_001		Normal	10.50	0.00	1.50			1.00000	1.00000
8						Condition Column	Text Mix pH 001_002			0.10	0.00	0.00	No Change			
9						Equilibrate	Text Mix pH 001_002			3.00	0.00	0.00	No Change			
10	2	2.0	1	Unk-001-002	2.a.1.a	Inject Samples	Text Mix pH 001_002		Normal	10.50	0.00	1.50			1.00000	1.00000
11						Condition Column				6.70	0.00	0.00	No Change			
12						Condition Column	Text Mix pH 001_003			0.10	0.00	0.00	No Change			
13						Equilibrate	Text Mix pH 001_003			3.00	0.00	0.00	No Change			
14	2	2.0	1	Unk-001-003	3.a.1.a	Inject Samples	Text Mix pH 001_003		Normal	10.50	0.00	1.50			1.00000	1.00000
15						Condition Column				6.70	0.00	0.00	No Change			
16						Condition Column	Text Mix pH 001_004			0.10	0.00	0.00	No Change			
17						Equilibrate	Text Mix pH 001_004			3.00	0.00	0.00	No Change			
18	2	2.0	1	Unk-001-004	4.a.1.a	Inject Samples	Text Mix pH 001_004		Normal	10.50	0.00	1.50			1.00000	1.00000
19						Condition Column	Text Mix pH 001_005			0.10	0.00	0.00	No Change			
20						Equilibrate	Text Mix pH 001_005			3.00	0.00	0.00	No Change			
21	2	2.0	1	Unk-001-005	5.a.1.a	Inject Samples	Text Mix pH 001_005		Normal	10.50	0.00	1.50			1.00000	1.00000
22						Condition Column				6.70	0.00	0.00	No Change			
23						Condition Column	Text Mix pH 001_006			0.10	0.00	0.00	No Change			
24						Equilibrate	Text Mix pH 001_006			3.00	0.00	0.00	No Change			

**Eliminate Transcription Errors.
Maintain Data in Audited Environment.**

Fusion QbD Automation Supports Full Data Integrity

Full integration of **all e-record** and **all e-signature** features and functions required to support full 21 CFR 11 compliance.

Secure **Workflow** and **Project Management** systems.

Full audit trail, including **bi-directional auditing** of all data exchanges with the CDS.

Fusion QbD Automation – Maintains Data Integrity

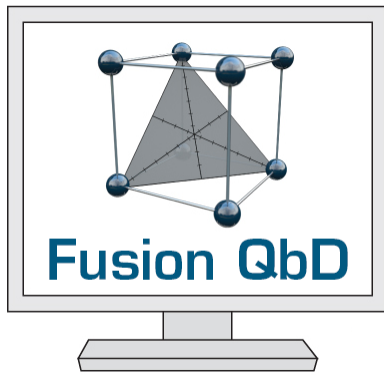
The screenshot displays the S-Matrix software interface. The main window shows a table of methods with columns for Method Name, Method Type, and a date. A 'Method Properties' dialog box is open, showing details for the 'AAA_Demo' method. The dialog includes a 'Method Information' section with fields for Name, Type, and Last Modified By, along with 'Lock' and 'Clear' buttons. Below this is a 'Method History' table with columns for Method Name, Method Type, and a description. The history table shows one entry for 'AAA_Demo' created by Fusion QbD. At the bottom of the dialog are 'OK', 'Cancel', and 'Help' buttons. The main window's table has a 'Filter By' dropdown set to 'Default' and a 'Methods' tab selected. The status bar at the bottom indicates '166 total'.

Method Name	Method Type	
1 AAA_Demo	Sample Set	7/17/201
2 AAA_Demo 001_001	Method Set	7/17/201
3 AAA_Demo 001_001	Instrument	7/17/201
4 AAA_Demo 001_002	Method Set	7/17/201
5 AAA_Demo 001_002	Instrument	7/17/201
6 AAA_Demo 001_003	Method Set	7/17/201
7 AAA_Demo 001_003	Instrument	7/17/201
8 AAA_Demo 001_004	Method Set	7/17/201
9 AAA_Demo 001_004	Instrument	7/17/2018 8:28:16 AM PDT
10 AAA_Demo 001_005	Method Set	7/17/2018 8:28:20 AM PDT
11 AAA_Demo 001_005	Instrument	7/17/2018 8:28:19 AM PDT

Method Name	Method Type	
1 AAA_Demo	Sample Set	Created by Fusion QbD: C:\Program Files

Audited Data Exchange – Assures Data Integrity

Fusion QbD Automation – Maintains Data Integrity

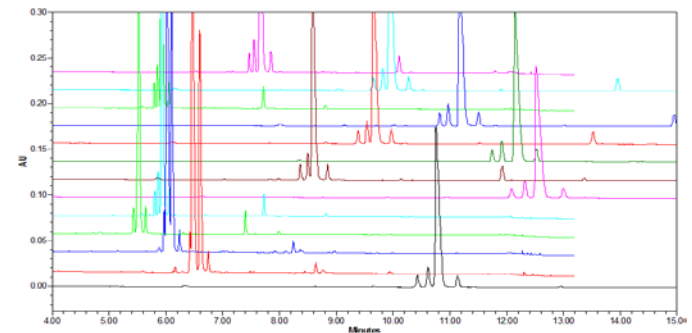


Automatically Retrieves
All Chromatogram
Results Data

Automated analysis,
graphing, and reporting.
Report formats:
RTF, DOC, HTML, PDF,
XLSX, XML

Chromatography Data Software (CDS)

Run	File No.	# of PIP	Label	Sample Name	Level	Function	Method Set / Report Method	Label Reference	Processing	Run Time (minutes)	QMS Start (minutes)	Method ID (minutes)	Column Position	Auto Addition	Sample/Injct	Column
11						Condition Column	Test file pH 01_017			8.70	0.00	0.00	No Change			
21						Condition Column	Test file pH 01_017			0.10	0.00	0.00	No Change			
31						Equilibrate	Test file pH 01_017			3.00	0.00	0.00	No Change			
41	1	2.0	1	UPL-001-001	Blank-1	Inject Samples	Test file pH 01_017		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
51						Condition Column	Test file pH 01_021			0.10	0.00	0.00	No Change			
61						Equilibrate	Test file pH 01_021			3.00	0.00	0.00	No Change			
71	2	2.0	1	UPL-001-001	1.a.1.a	Inject Samples	Test file pH 01_021		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
81						Condition Column	Test file pH 01_022			0.10	0.00	0.00	No Change			
91						Equilibrate	Test file pH 01_022			3.00	0.00	0.00	No Change			
101	2	2.0	1	UPL-001-002	2.a.1.a	Inject Samples	Test file pH 01_022		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
111						Condition Column	Test file pH 01_023			8.70	0.00	0.00	No Change			
121						Condition Column	Test file pH 01_023			0.10	0.00	0.00	No Change			
131						Equilibrate	Test file pH 01_023			3.00	0.00	0.00	No Change			
141	2	2.0	1	UPL-001-001	2.a.1.a	Inject Samples	Test file pH 01_023		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
151						Condition Column	Test file pH 01_024			8.70	0.00	0.00	No Change			
161						Condition Column	Test file pH 01_024			0.10	0.00	0.00	No Change			
171						Equilibrate	Test file pH 01_024			3.00	0.00	0.00	No Change			
181	2	2.0	1	UPL-001-004	4.a.1.a	Inject Samples	Test file pH 01_024		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
191						Condition Column	Test file pH 01_025			0.10	0.00	0.00	No Change			
201						Equilibrate	Test file pH 01_025			3.00	0.00	0.00	No Change			
211	2	2.0	1	UPL-001-005	5.a.1.a	Inject Samples	Test file pH 01_025		Normal	10.50	0.00	1.50	No Change		1.00000	1.00000
221						Condition Column	Test file pH 01_026			8.70	0.00	0.00	No Change			
231						Condition Column	Test file pH 01_026			0.10	0.00	0.00	No Change			
241						Equilibrate	Test file pH 01_026			3.00	0.00	0.00	No Change			



**Eliminate Transcription Errors.
Maintain Data in Audited Environment.**

Fusion QbD Automation – Maintains Data Integrity

The screenshot displays the S-Matrix software interface. The top menu bar includes File, Edit, Activity, Tools, Window, and Help. The left sidebar contains a navigation tree with categories like Design of Experiments, Data Entry / Analysis, Best Answer Searches, Visualization Graphics, and Reporting Toolkit. The main window shows an Audit Log report for Administrator, dated 14 NOV 2019 10:21:21 PST [UTC-08:00]. The report includes an 'Import Response Settings' table and a 'Response Data' table.

Name: Administrator
Company: S-Matrix Corporation
Project: Project 1
Date: 17 NOV 2019 14:04:21 PST [UTC-08:00]

Audit Log
14 NOV 2019 10:21:21 PST [UTC-08:00] - Administrator

Event Type: Import Responses

Import Response Settings

Setting	Value
Target CDS	EMPOWER
Empower Version	Empower 3 Software Build 3471 SPs Installed: Feature Release 4 DB ID: 2660033392
Empower Database	(local)
Empower User	system
Project Name	RD1 - Screen - 9_9_0
Result Set(ID)	FMD_RD1_Screen (1485)
Processed Channel	PDA Ch1 225nm@4.8nm, Time offset by 0.020 mins.
Activate PeakTracker	Unchecked
Auto-imported Response(s)	Height, RetentionTime, WidthAt150Pct, USPTailing, WidthAtTangentUSPResolution, Area
Trend Response(s)	USPResolution
Import Chromatogram Trace Data	Checked
Import Prediction Chromatogram Data	Checked
Total Import Time	00:00:18
Locale	English (United States)

Response Data

Run No.	Result ID	No. of Peaks	No. of Peaks >= 1.50 - USPResolution	No. of Peaks >= 2.00 - USPResolution	No. of Peaks <= 1.50 - USPTailing
1	1748	8	2	2	0
2	1750	6	3	3	0
3	1826	8	5	5	3
4	1824	8	4	4	2
5	1756	7	2	2	0

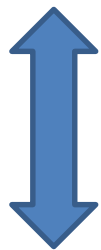
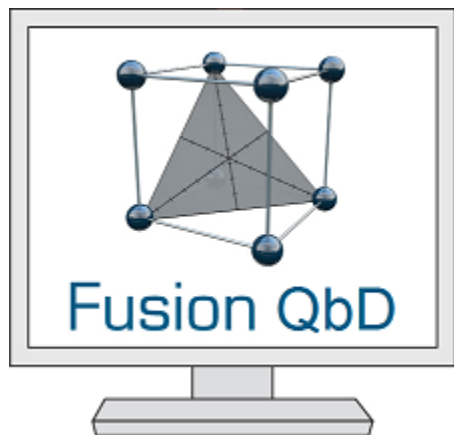
1 of 6

Audited Data Exchange – Assures Data Integrity

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Fusion QbD – PeakTracker™



**Acquity H-Class
With PDA**



**Acquity QDa
Mass Detector**



**6 Column
Capacity**



Fusion QbD – Auto-imports UV and MS Spectra Data for Tracking

Select a Project and Result Set

Select Project

Find Filter Reset

- Projects
 - Customers
 - Distributors
 - S-Matrix
 - ADL
 - FIT
 - FMD Tutorial - 9_9_0
 - RD1 - Screen - 9_9_0
 - RD2 - 9_9_0 - Named Peaks
 - RD2 - Optimization - 9_9_0
 - FMV - A_L_R
 - Internal Development
 - RD1 - Demo Screening Expt
 - RD2 - Demo Optimization Expt
 - Test

Select Result Set(s)

Result Set Name	ID	Date	Sample Set
RD2 Optimization	9001	6/4/2019 8:48:34 AM EDT	RD2 Optimization

Fetch Selected Result Sets

Select Processed Channel:
PDA Ch1 225nm@4.8nm, Time offset by 0.020 mins.

Result(s) for Import

Sample	ID	Date	Type	Channel ID	Result
1	9155	6/4/2019 8:50:34 AM	LC	6737	9001
10	9048	6/4/2019 8:48:51 AM	LC	6812	9001
11	9191	6/4/2019 8:57:34 AM	LC	6820	9001
12	9058	6/4/2019 8:48:54 AM	LC	6828	9001
13	9063	6/4/2019 8:48:56 AM	LC	6836	9001
14	9201	6/4/2019 8:58:48 AM	LC	6844	9001
15	9073	6/4/2019 8:48:59 AM	LC	6852	9001
16	9078	6/4/2019 8:49:00 AM	LC	6860	9001

PeakTracker Data Import

Select Raw PDA Channel: Select Raw MS Channel: MS Time Offset (min):

Spectra Extraction Points: Leading (%) Trailing (%) Threshold Setting: MS Intensity

Select Processed MS Channel: Track Non-absorbing Peaks

User Types (logged in as 'Owner')

Ready

Next >> Cancel ?

Fusion QbD – Auto-imports UV and MS Spectra Data for Tracking

Select a Project and Result Set

Select Project

Select Result Set(s)

Result Set Name	ID	Date	Sample Set
RD2 Optimization	1114	2/19/2019 7:23:52 PM EST	RD2 Optimization

Select Processed Channel:
PDA Ch1 225nm@4.8nm, Time offset by 0.020 mins.

Result(s) for Import

Sample	ID	Date	Type	Channel ID	Result
1	1449	2/19/2019 7:56:43 PM	LC	1112	1114
10	1405	2/19/2019 7:43:08 PM	LC	1196	1114
11	1407	2/19/2019 7:44:13 PM	LC	1205	1114
12	1409	2/19/2019 7:44:53 PM	LC	1214	1114
	1411	2/19/2019 7:45:20 PM	LC	1223	1114
	1413	2/19/2019 7:45:47 PM	LC	1232	1114
	1415	2/19/2019 7:46:04 PM	LC	1241	1114
	1252	2/19/2019 7:24:36 PM	LC	1250	1114

Used for samples with peaks which Do Not Ionize

Activate Peak Tracker

Select Raw PDA Channel: PDA Spectrum

Select Raw MS Channel: QDa Positive Scan

MS Time Offset (min): 0.02

Spectra Extraction Points: Leading (%) 30.00, Trailing (%) 30.00

Threshold Setting: MS Intensity 50000

Select Processed MS Channel: QDa Positive Scan MS TIC, Smoothed by 59 Point Savitzky-Golay Filter, [QDa Positive Scan (100.00-12

Track Non-absorbing Peaks

Used for samples with peaks which Do Not Absorb

Ready

Next >> Cancel ?

Fusion QbD – Auto-imports all Results for Modeling, & Simulation

Select Responses

PDA Spectrum PDA 225.0 nm (PDA Spectrum (190-400)nm), Time offset by 0.020 mins.

Trend Responses

Add Delete Undo Changes Restore Defaults

		Operator	Value	Response
1	<input checked="" type="checkbox"/>	No. of Peaks		
2	<input checked="" type="checkbox"/>	No. of Peaks >=	1.50 USPResolution	
3	<input checked="" type="checkbox"/>	No. of Peaks >=	2.00 USPResolution	
4	<input checked="" type="checkbox"/>	No. of Peaks <=	1.20 USPTailing	
5	<input checked="" type="checkbox"/>	Max Peak	1 USPResolution	

Select All Select None I = Incomplete D = Duplicate

Named Compounds in CDS

Auto-imported Responses...

Available Included

Auto-imported Responses

Auto-imported Responses

Response
BasePeak
AssignedMass
AssignedMassValue
RetentionTime
MigrationTime
PctAmount
PctArea
Height
Amount
Area
EndPV
EndTime
EPPlateCount
USPSignalToNoise
EPSignalToNoise
JPSignalToNoise
SignalToNoise
KPrime
...

Close

<< Back Next >> Cancel ?

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 - b. Composite Chromatogram Modeling & Visualization

PeakTracker – Displays UV & MS Chromatograms / Auto-builds GTM

The screenshot displays the PeakTracker software interface. On the left is a 'Run No.' list with '15' selected. The main area shows two chromatograms: a UV Chromatogram (top) and a Total Ion Chromatogram (TIC) (middle). Both show peaks at retention times 262.2, 193.1, 336.8, 274.2, 288.2, 304.1, and 360.2. Below the chromatograms is a 'Peak Table' and a 'Global Tracking Method' table.

UV Chromatogram
 D: 1241: Channel: PDA Ch1 225nm@4.8nm: Channel Type: 2D
 Fusion QbD Plot

Total Ion Chromatogram (TIC)
 Channel Type: 2D

Peak Table - PDA Ch1 225nm@4.8nm - Run No. 15

	Name	RT (min)	Base Peak (m/z)	AMV (m/z)	Area (uV*sec)	Height (uV)
1		1.037	262.2	262.2	973,202	523,791
2		3.061	193.1	193.1	110,123	37,394
3		4.656	336.8	336.8	296,881	160,622
4		4.926	274.2	274.2	397,548	230,388
5		5.122	288.2	288.2	1,247,109	670,465

Global Tracking Method
 Mass | UV | Options
 Display Intensity Columns

Component Name	Expected Mass 1	Expected Mass 2	Expected Mass 3	Expected Mass 4	Expected Mass 5
1	262.2	263.2	284.2	279.1	264.2
2	193.1	215.1	132.1	407.3	194.1
			673.4	278.9	160.2
			329.9	126.0	279.1
			310.1	279.2	126.1
			333.1	126.1	279.0

Global Tracking Method (GTM)
PeakTracker automatically builds a customizable **GTM** by scanning all UV and TIC chromatograms to identify all integrated peaks.

PeakTracker can automatically address these complex separation and tracking challenges:

- Auto-deconvolution of partially and completely co-eluted peaks,
- Two or more peaks with identical mass data.
- Non-ionizing and non-absorbing compounds.

Peak Tracking Fingerprint Data

PeakTracker – Displays Tracking Results and Peak Spectra Data

PeakTracker

Run No. 15: Result ID: 1415; Channel ID: 1241; Channel: PDA.Ch1 225nm@4.8nm; Channel Type: 2D

Run No. 15: Result ID: 1509; Channel ID: 1245; Channel: MS_T.C; Channel Type: 2D

Extracted Spectra: Row 6 (API)

Detected Mass (Da)	Leading (Intensity)	Apex (Intensity)	Trailing (Intensity)
1 288	0	8,044.328	2,607.084
2 289	0	1,295.965	461.805
3 310	0	341.743	110.963
4 279	109.578	153.287	103.860
5 126	138.762	141.044	192.051
6 290	0	76.088	0
7 326	0	74.274	0
8 311	0	72.460	0
9 144	148.356	0	0

Mass and UV Spectral Analysis Window in Fusion QbD

Peak Table - PDA.Ch1 225nm@4.8nm - Run No. 15

Name	RT (min)	Base Peak (m/z)	AMV (m/z)	Area (uV*sec)	Height (uV)
1 B	1.037	262.2	262.2	973.202	523.791
2 G					
3 H*					
4 F					
5 A					
6 API					
7 D-Deg					
8 E					
9 D					

Show Spectra for Peak...

Clear Component Assignment

Assign Missing Component-MS...

Assign Missing Component-UV...

Insert Co-eluted Component(s)-MS...

Insert Co-eluted Component(s)-UV...

Add Peak to Global Tracking Method

Remove Peak

Copy

Global Tracking Method

Mass | UV | Options

Component Name	Expected Mass 1	Expected Intensity 1	Expected Mass 2	Expected Intensity 2	Expected Mass 3
1 B	262.2	6,850.432	263.2	1,137,543	264.2
2 G	193.1	1,667.393	215.1	876,505	237.1
3 F	336.8	1,502.819	672.4	690,817	673.4
4 A	274.1	3,460.414	275.2	460,235	276.3
5 API	288.1	8,044.328	289.1	1,295,965	290.1
6 D-Deg	332.1	1,393.173	344.9	310,529	345.9
7 E	304.1	9,383.768	305.1	1,577.671	306.1

Commands: Create Tracking Method... Track Peaks... Update Responses Close

Flexible Tracking Editor

PeakTracker – Instant Preview of Tracking Results

Run No.

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30

Run No.: 15; Result ID: 9073; Channel ID: 6852; Channel: PDA Ch1 225nm@4.8nm; Channel Type: 2D Fusion QbD Plot

Run No.: 15; Result ID: 9262; Channel ID: 9075; Channel: MS_TIC; Channel Type: 2D

	Run No.	No. of Peaks	B RetentionTime	G RetentionTime	H* RetentionTime	F RetentionTime	A RetentionTime	API RetentionTime	D-Deg RetentionTime	E RetentionTime	D RetentionTime
1	1	8	0.913	1.949	3.561	4.688	5.008	5.261	5.820	5.998	7.908
2	2	8	0.872	1.893	3.349	3.929	4.226	4.369	4.621	4.756	5.760
3	3	8	1.375	3.058	4.914	5.755	6.259	6.496	6.947	7.208	9.122
4	4	8	1.361	3.044	4.571	4.865	5.297	5.432	5.626	5.808	6.776
5	5	8	1.357	3.030	4.559	4.856	5.287	5.423	5.616	5.798	6.783
6	6	8	0.848	1.863	3.297	3.868	4.162	4.307	4.562	4.695	5.715
7	7	8	1.338	2.984	4.843	5.717	6.223	6.470	6.943	7.202	9.136
8	8	8	1.307	3.661	4.489	5.118	5.481	5.673	5.867	6.199	7.691
9	9	8	1.906	4.846	5.053	5.235	5.654	5.786	5.745	6.101	7.119
10	10	7	1.205	3.633	3.904	4.316	4.583	4.721	4.721	5.045	6.085

Select Mode Data Review Peak Tracking

Commands

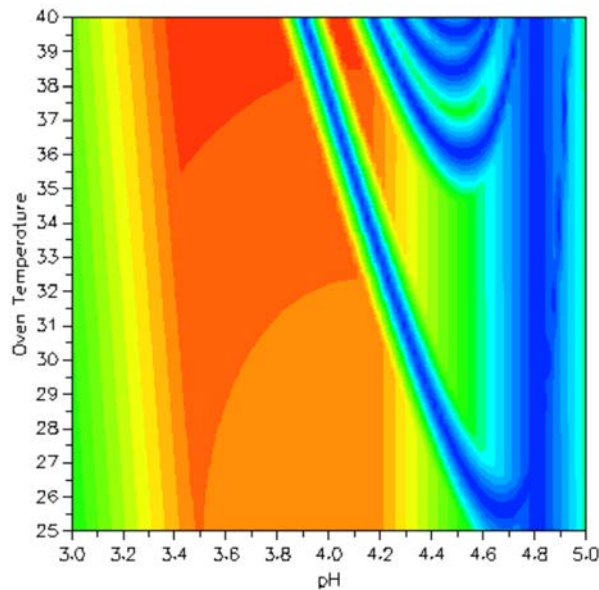
Easy edit mode.

- Blue Background for data auto-updated by **PeakTracker**.
- Yellow Background for missing data which can be edited by user.

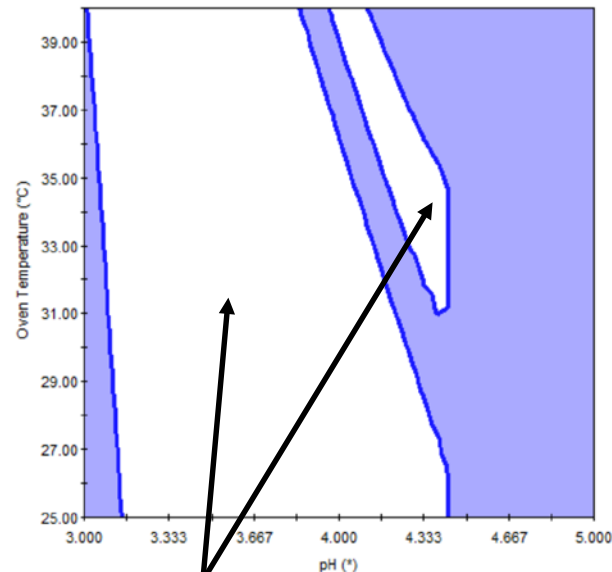
Fusion QbD – *Rs-Map Response*

Fusion QbD now uses its hyper-accurate modeling technologies to predict USP or EP Resolutions for all peaks for any method conditions using standard Resolution equations. Graphical and numerical displays update in real time as you change method conditions.

Contour Graph

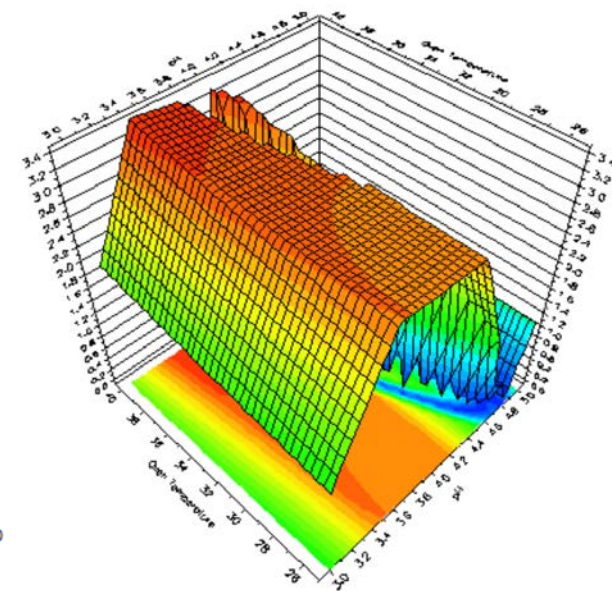


Overlay Graph

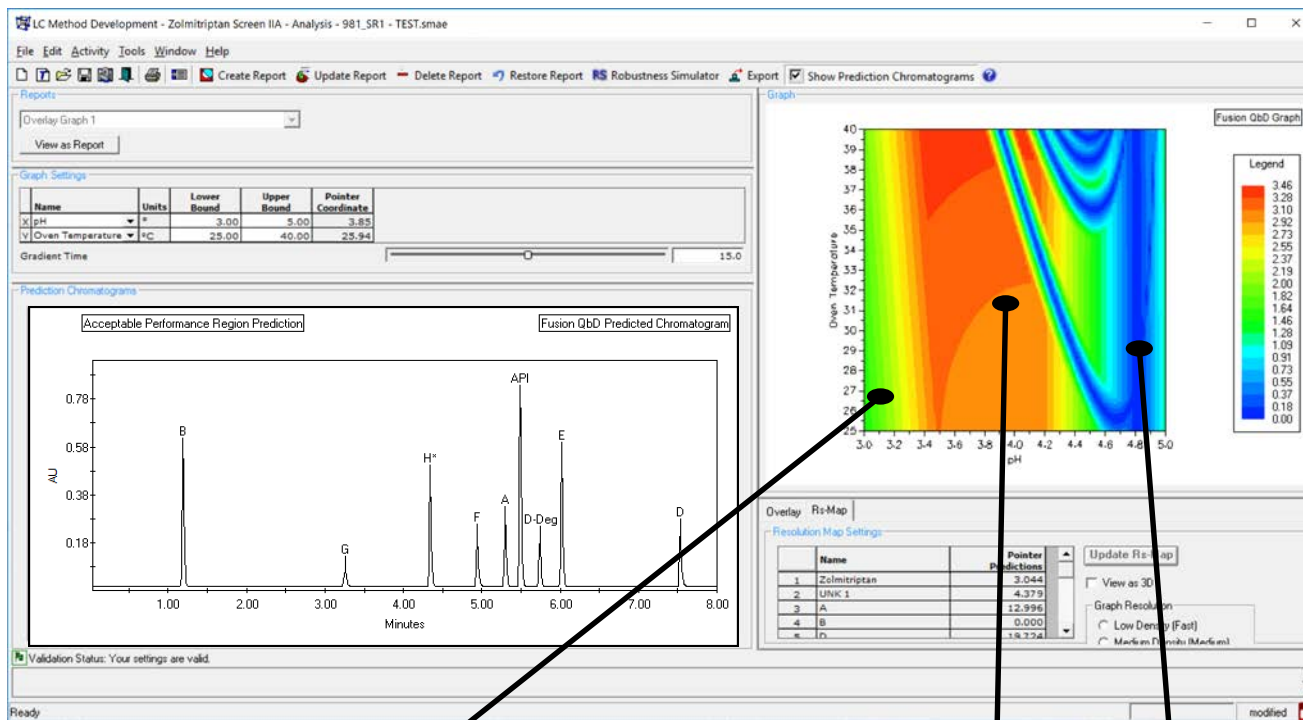


$R_s \geq 2.00$

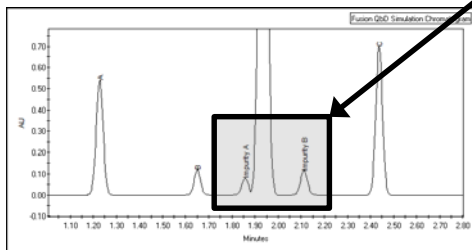
Response Surface Graph



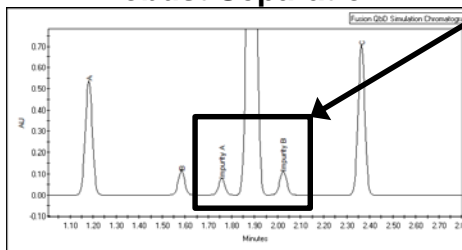
Rs-Map Response



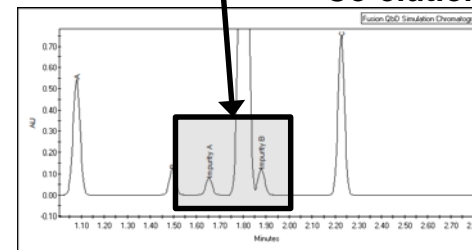
Co-elution



Robust Separation



Co-elution



Robust Method Optimization – Robustness Modeling Throughout MODR

The screenshot displays the Robustness Simulator interface. The main window is titled "Robustness Simulator" and contains a "Response Settings" section with a table of response parameters. A dialog box titled "Robustness Simulator - Select Rs Responses for Individual Compounds" is open, showing a list of responses with checkboxes. A blue arrow points from the "Add Individual Rs Responses..." button in the main window to the dialog box.

Robustness Simulator - Response Settings

Enabled	Response	Robustness Index	Specification Limit Delta (\pm)	LSL	USL	Target	Additional Error	Additional Error Amount ($\pm 1\sigma$ Value)
<input checked="" type="checkbox"/>	B - RetentionTime	Cpk		0.900			<input type="checkbox"/>	
<input checked="" type="checkbox"/>	A - Rs-Map USP Resolution	Cpk			1.500		<input type="checkbox"/>	
<input checked="" type="checkbox"/>	API - Rs-Map USP Resolution	Cpk			1.500		<input type="checkbox"/>	
<input checked="" type="checkbox"/>	D-Deg - Rs-Map USP Resolution	Cpk			1.500		<input type="checkbox"/>	
<input checked="" type="checkbox"/>	E - Rs-Map USP Resolution	Cpk			1.500		<input type="checkbox"/>	

Robustness Simulator - Select Rs Responses for Individual Compounds

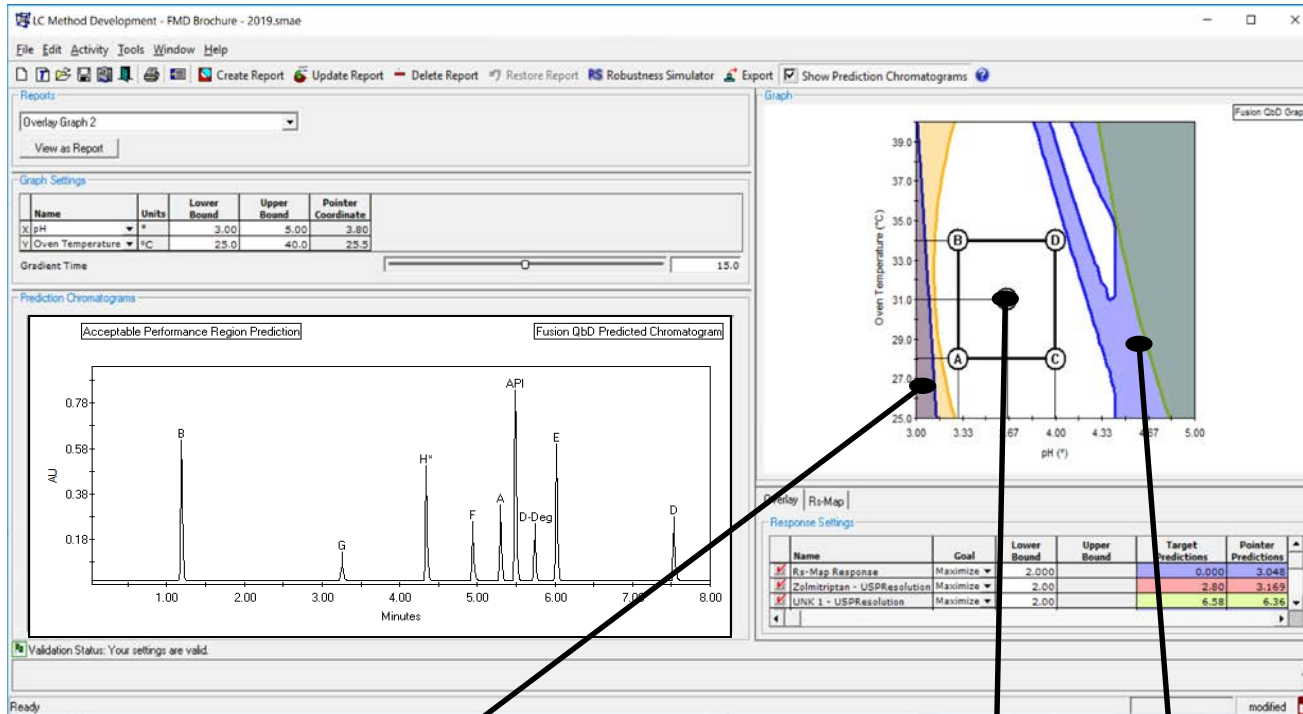
Include	Response
<input type="checkbox"/>	G - Rs-Map USP Resolution
<input type="checkbox"/>	H* - Rs-Map USP Resolution
<input type="checkbox"/>	F - Rs-Map USP Resolution
<input checked="" type="checkbox"/>	A - Rs-Map USP Resolution
<input checked="" type="checkbox"/>	API - Rs-Map USP Resolution
<input checked="" type="checkbox"/>	D-Deg - Rs-Map USP Resolution
<input checked="" type="checkbox"/>	E - Rs-Map USP Resolution
<input type="checkbox"/>	D - Rs-Map USP Resolution

The "Add Individual Rs Responses..." button in the main window is highlighted with a red box. The "E - Rs-Map USP Resolution" row in the dialog box is highlighted with a blue box. The "0.900" value in the LSL column of the main window table is also highlighted with a red box.

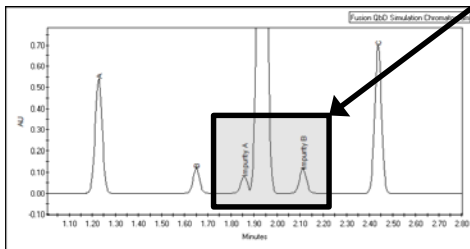
Robustness is calculated for each key performance metric.

Robust Method Optimization – Robustness Modeled Throughout MODR

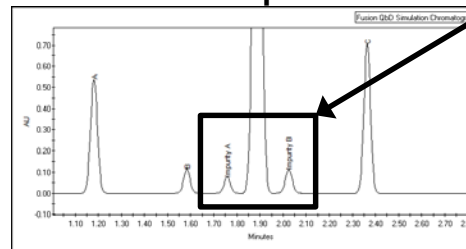
- Mean Performance and Robustness Throughout MODR.
- Include Performance Requirements for Critical Peaks and Peak Pairs.



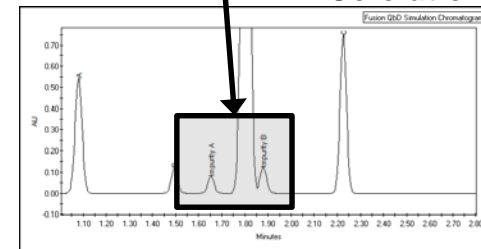
Co-elution



Robust Separation



Co-elution



Presentation Outline

1. Introduction to the Fusion QbD[®] Software Platform
 - a. QbD Method Development Experiment Automation
 - b. Cross-platform Data Integrity
1. **PeakTracker** – UV & MS Spectra Based Peak Tracking
 - a. Data Integration for Automated Modeling
 - b. Tracking Automation
2. Forced Degradation Study Automation
 - a. Peak Tracking in Forced Degradation Studies
 - b. Composite Chromatogram Modeling & Visualization

Fusion QbD – *Forced Degradation Studies*

Fusion QbD enables users to set up an experiment execution protocol in which each experiment run will be repeated according to user-specified Replication Strategy which can be any combination of Sample Preparation and/or Injection replicates – with the replicates taken from the same vial or assigned different vials.

Experiment Setup | **Replication Settings**

Replication Strategy

- Forced Degradation Study
- No. of preparation replicates per sample: 3
- No. of injections per preparation replicate: 1
- Obtain all injection repeats from the same vial

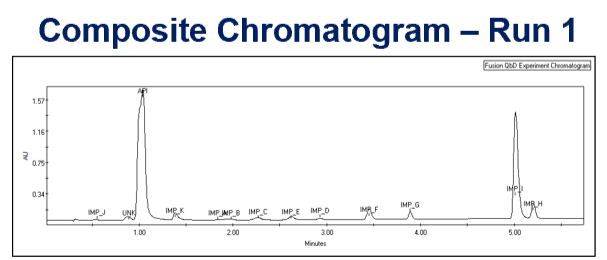
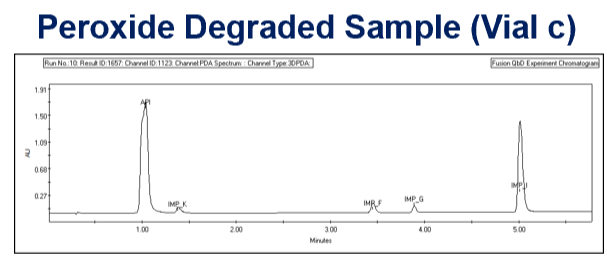
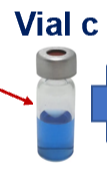
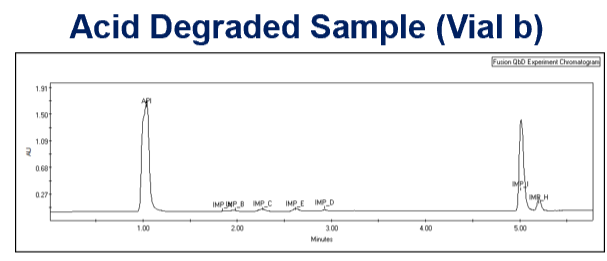
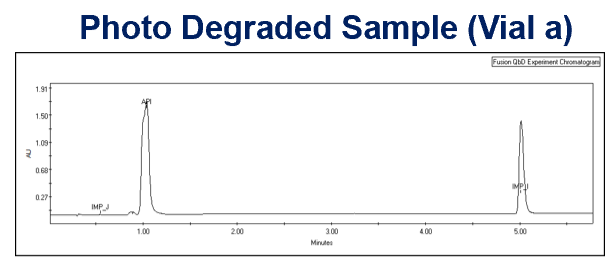
S-Matrix has now created a new **“Forced Degradation Study”** mode to support experiments in which the different Sample Preparation replicates represent different degradation paths such as photo degradation, acid degradation, and peroxide degradation. This activates an entirely new technology which aggregates peak data from the replicates for each run into a “Composite Chromatogram” data set for the run to be used in robust method optimization and prediction chromatogram visualization.

Fusion QbD – Forced Degradation Study (FDS) Automation

Forced Degradation Studies – Full Automation Support

Experiment Design Matrix

Run No.	Pump Flow Rate (mL/min)	Gradient Time (min)	Oven Temperature (°C)	pH
Condition Column - 1	0.400	2.0	35.0	3.20
1.a	0.300	5.0	35.0	3.20
1.b	0.300	5.0	35.0	3.20
1.c	0.300	5.0	35.0	3.20
2.a	0.500	5.0	35.0	3.20
2.b	0.500	5.0	35.0	3.20
2.c	0.500	5.0	35.0	3.20
3.a	0.300	15.0	35.0	3.20
3.b	0.300	15.0	35.0	3.20
3.c	0.300	15.0 <td 35.0	3.20	



Full Automation Support

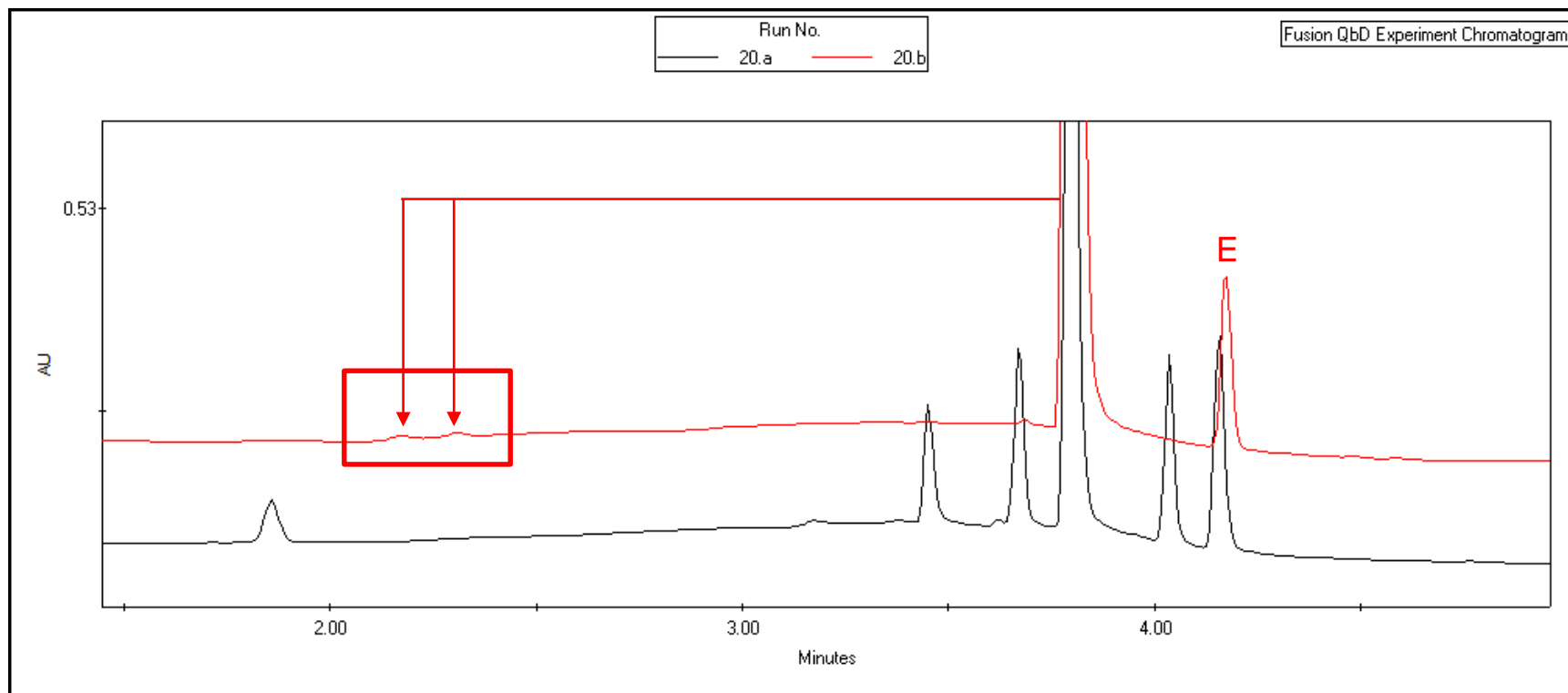
- ✓ Each experiment run is replicated for each degradation path sample.
- ✓ Each peak is tracked in each degradation path sample chromatogram.
- ✓ All peaks from all degradation path sample chromatograms are aggregated into one chromatogram for the run.

Forced Degradation Study (FDS) – 2 New Degradants Discovered

Black Trace – Undegraded Sample (Note – API material contained Related Compound “E”)

Red Trace – Peroxide Degraded API (generated 2 new degradants)

Chromatogram formatting – zoom, stack, offset, and annotate to get best presentation view.



PeakTracker – Instant Preview of Tracking Results

PeakTracker

Run No.: 24.b; Result ID: 2555; Channel ID: 2350; Channel: UV 225nm; Channel Type: 2D

Run No.: 24.b; Result ID: 2557; Channel ID: 2354; Channel: MS TIC; Channel Type: 2D

Tracks peaks in all Deg Path replicates of each experiment run injection.

Run No.	No. of Peaks	B RetentionTime	G RetentionTime	F RetentionTime	H* RetentionTime	A RetentionTime	API RetentionTime	DDeg RetentionTime	E RetentionTime	D RetentionTime	OxDeg_1 RetentionTime	OxDeg_2 RetentionTime
43 22.a	7	2.023	5.168	5.259	5.349	5.614	5.712	5.712	5.957	6.848		
44 22.b	3								6.781		5.748	5.790
45 23.a	7	1.330	3.799	4.079	3.999	2.309	4.404	4.404	4.633	5.541		
46 23.b	3								4.640		3.643	3.650
47 24.a	8	2.046	6.206	7.064	6.691	7.429	7.646	7.712	8.243	10.410		
48 24.b	3								8.234		5.789	5.917
49 25.a	8	1.311	4.441	5.206	4.783	5.469	5.718	5.868	6.434	8.623	4.264	4.334
50 25.b	3								6.419			

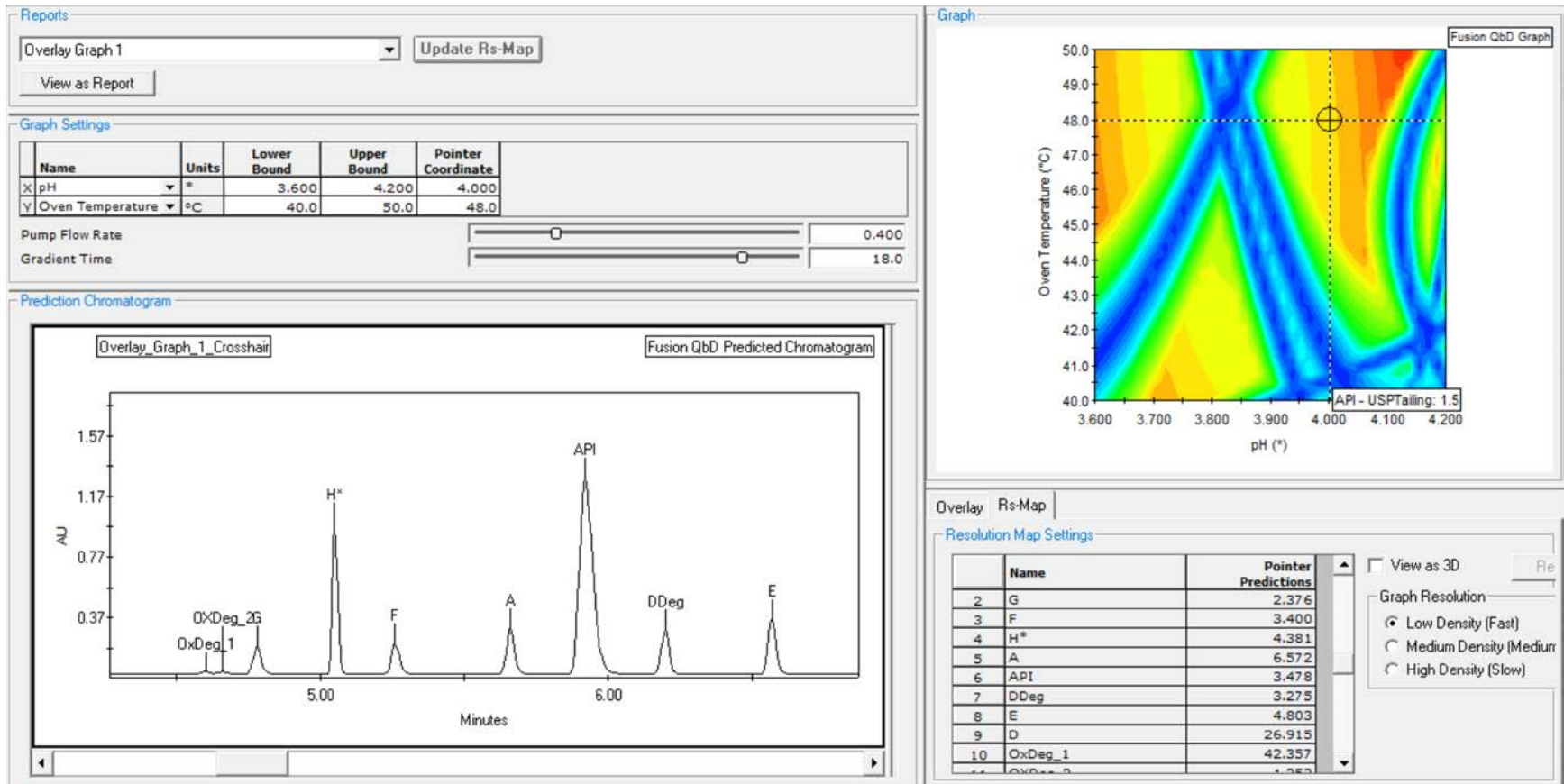
Select Mode: Data Review Peak Tracking

Commands: Create Tracking Method... Track Peaks... Update Data Close ?

Presentation Outline

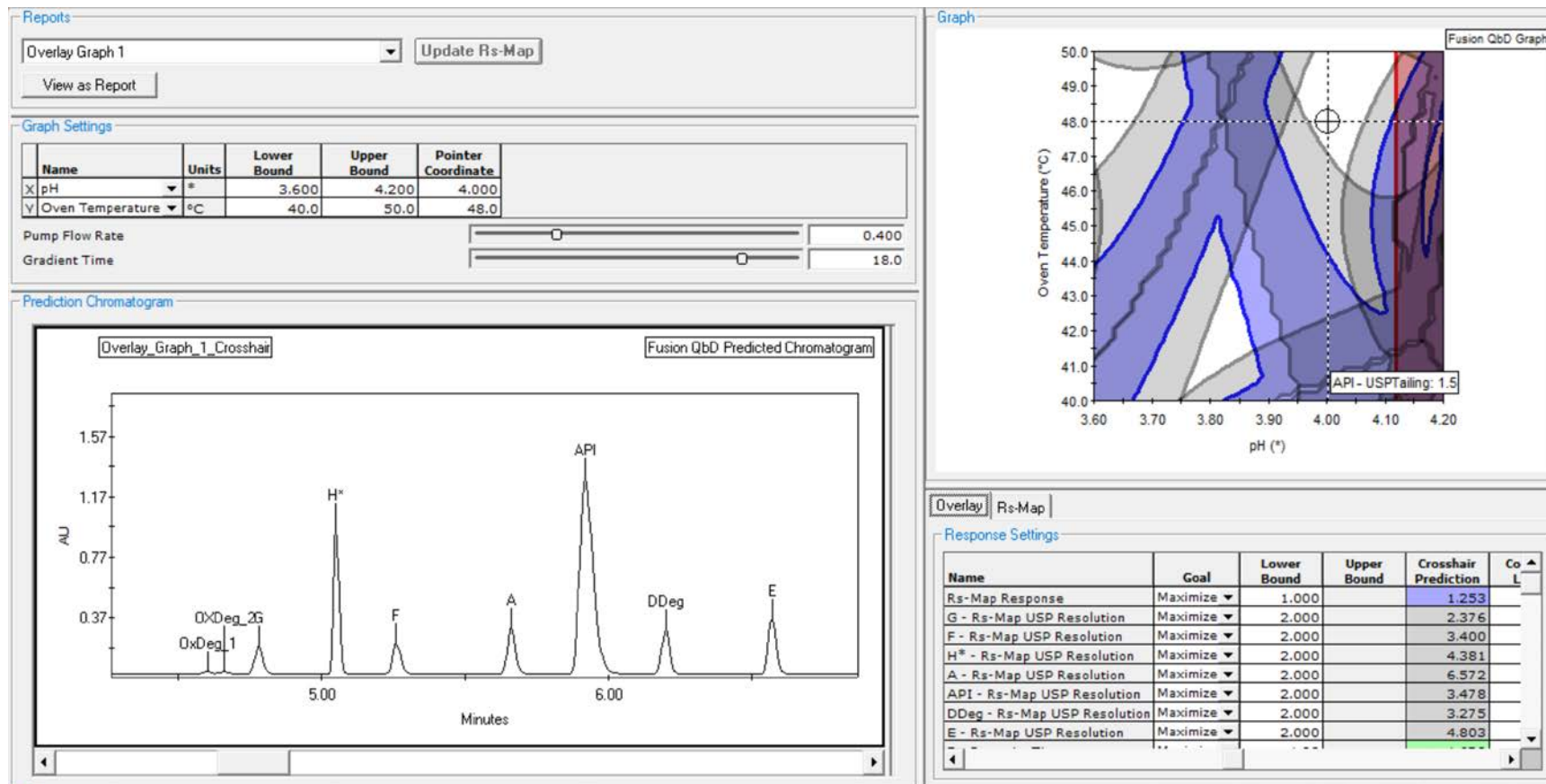
1. Introduction to the Fusion QbD[®] Software Platform
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 - a. Peak Tracking in Forced Degradation Studies
 - b. Composite Chromatogram Modeling & Visualization

Fusion QbD automatically creates a data set of composite chromatograms for peak tracking, modeling, and simulation.



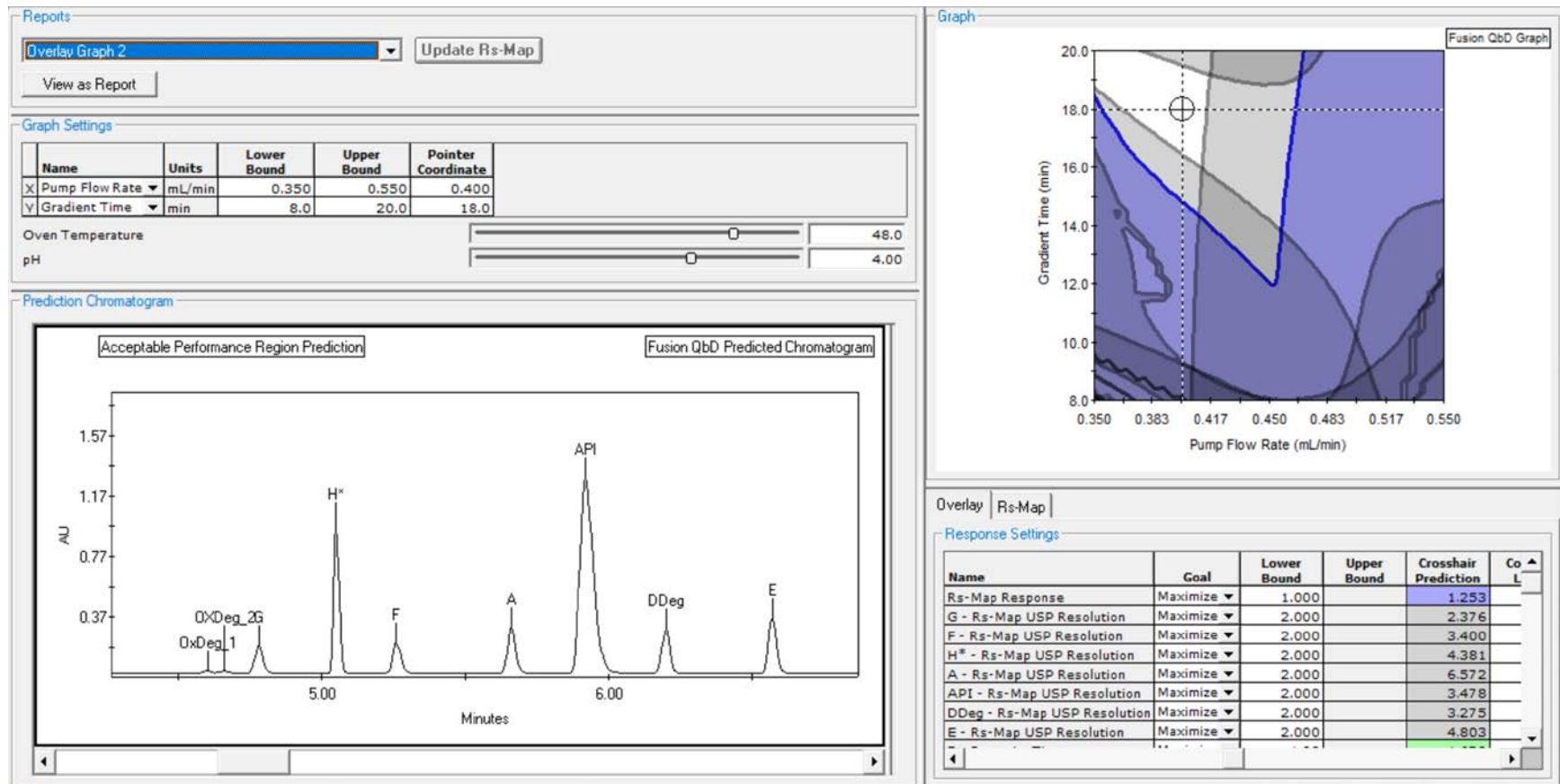
New Degradants Identified – Forced Degradation Study (FDS)

Overlay lets you include mean performance and robustness for any critical performance characteristic across the MODR.



New Degradants Identified – Forced Degradation Study (FDS)

Switch graphed and non-graphed variables – find most robust method overall.



C. Presentations of Design Space

Example 1: Response graphs for dissolution are depicted as a surface plot (Figure 1a) and a contour plot (Figure 1b). Parameters 1 and 2 are factors of a granulation operation that affect the dissolution rate of a tablet (e.g., excipient attribute, water amount, granule size.)

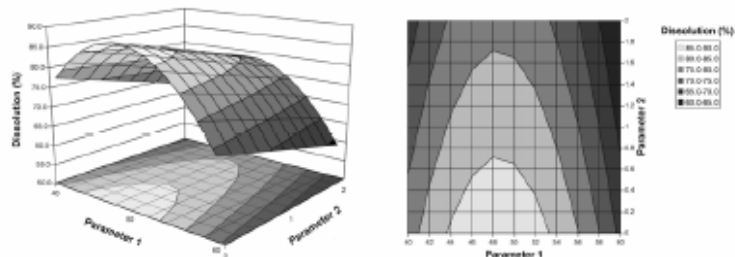


Figure 1a: Response surface plot of dissolution as a function of two parameters of a granulation operation. Dissolution above 80% is desired.

Figure 1b: Contour plot of dissolution from example 1a.

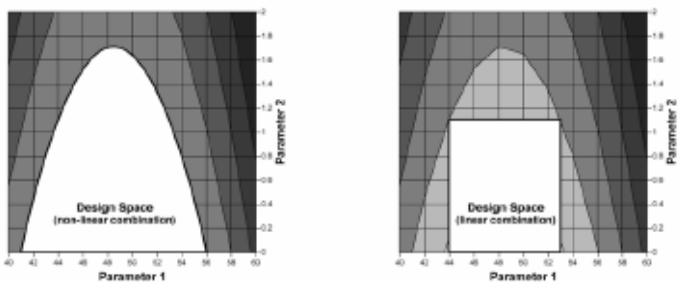


Figure 1c: Design space for granulation parameters, defined by a nonlinear combination of their ranges, that delivers satisfactory dissolution (i.e., >80%).

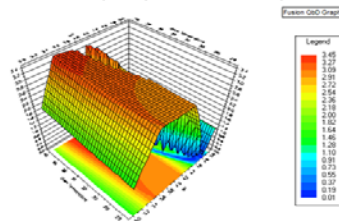
Figure 1d: Design space for granulation parameters, defined by a linear combination of their ranges, that delivers satisfactory dissolution (i.e., >80%).

Name: Administrator
Company: S-Matrix
Project: Project 1
Date: 08 APR 2018 18:38:09 PDT [UTC-07:00]

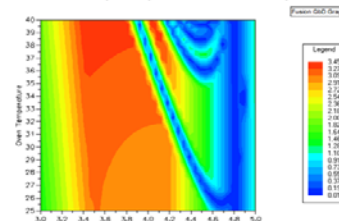


Final Design Space + PARs

Rs-Map Response Surface Graph

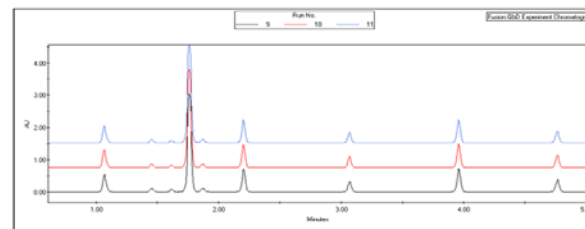
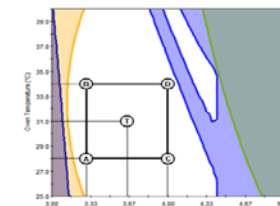


Rs-Map Response Contour Graph



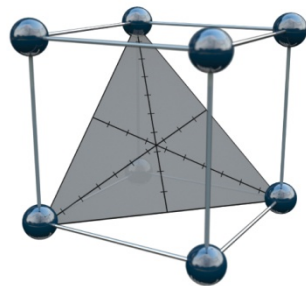
Response	Performance Goal	Color
API – USP Resolution	> 2.00	Red
API – USP Tailing	> 2.00	Blue
Impurity A – USP Resolution	> 2.00	Blue
Impurity B – USP Resolution	> 2.00	Green
API – USP Resolution - Cpk	> 1.33	Orange
Impurity A – USP Resolution - Cpk	> 1.33	Teal
Impurity B – USP Resolution - Cpk	> 1.33	Purple
API – USP Tailing - Cpm	> 1.33	Sky

Multi-Response Overlay with Design Space



END

THANK YOU!



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