Fusion QbD® – DOE Experimental Design

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Regulatory Guidances – DOE is a Central Element

ICH Q8(R2) Guidance for Industry, Pharmaceutical Development, August, 2009

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".

Check out the recent article titled "A Design for Life Sciences" using the link below.
(The Column, Volume 15, Issue 6, pg 2–7).

http://www.chromatographyonline.com/design-life-sciences

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Regulatory Guidances – DOE is a Central Element

Proposed New USP General Chapter: The Analytical Procedure Lifecycle ⟨1220⟩

Design of experiments (DOE)

is a **fundamental methodology** for the QRM process. It is a systematic method to determine the relationships between variables affecting a process, and it is used to find cause-and-effect relationships.

…

DOE also utilizes statistical data treatment, which allows clear determinations regarding the significance of a variable and/or its interactions towards the output.

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Fusion QbD – DOE Study Parameter Flexibility

Supports All These Separation Modes

Reversed Phase

Normal Phase

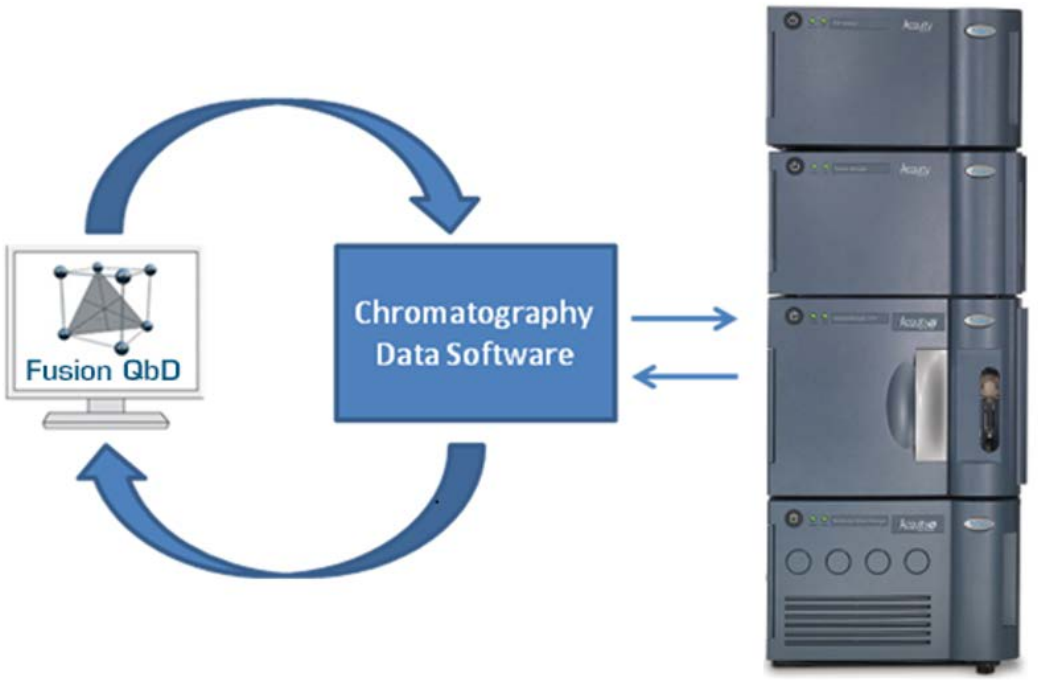
Chiral

HILIC

Ion Exchange

Size Exclusion

SFC



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Fusion QbD – DOE Study Parameter Flexibility

QbD – requires ability to study **any combination** of LC parameters which can **interactively effect** your performance requirements:

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

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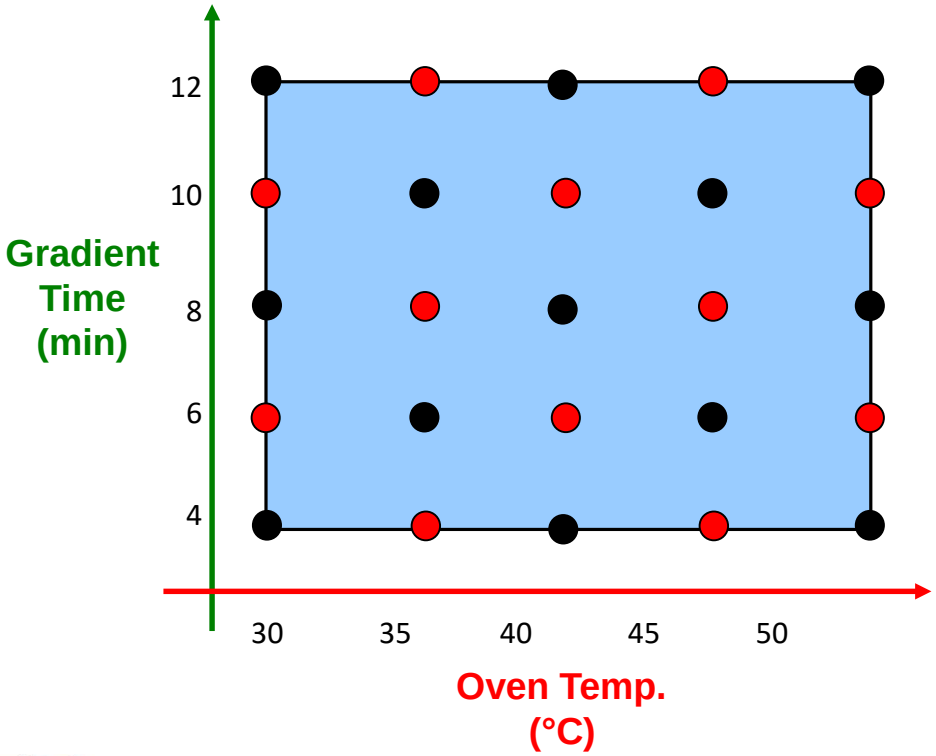
DOE = Statistical Sampling (Efficient Multifactor Studies)

Consider two variables – five study levels each:

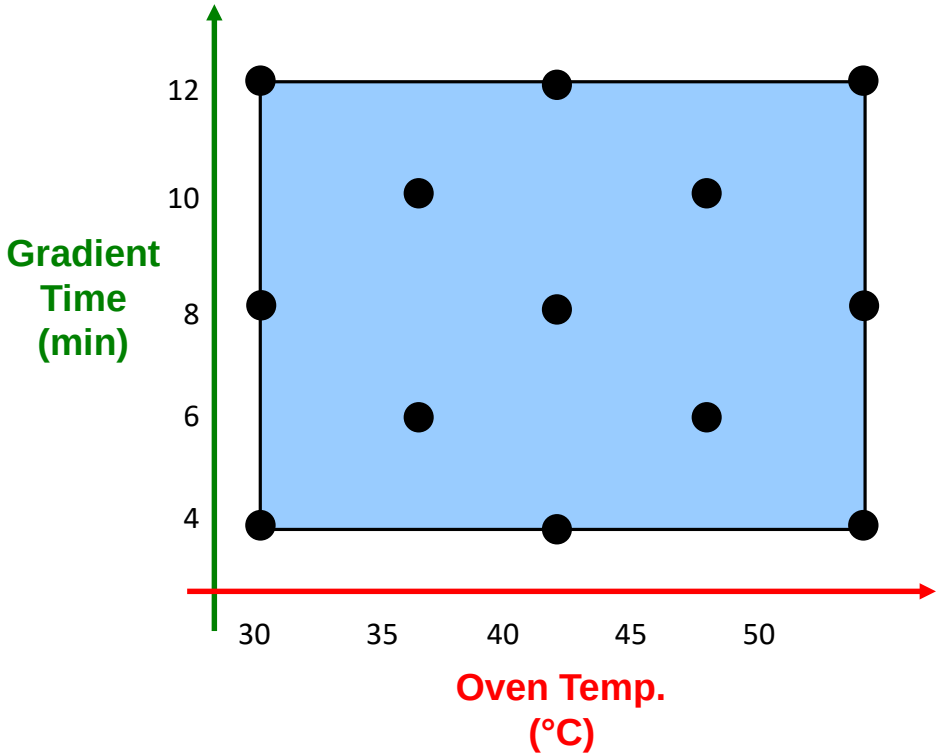
Brute Force Approach = All Possible Combinations

25 Methods



Design of Experiments = Statistical Sampling

13 Methods



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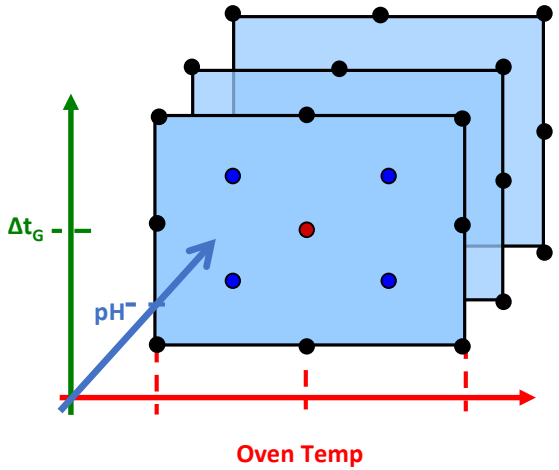
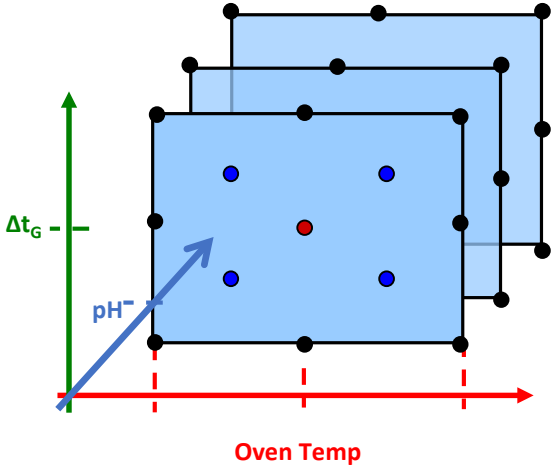
DOE – Adding a 3rd and 4th Factor to the Study

3rd Variable – pH

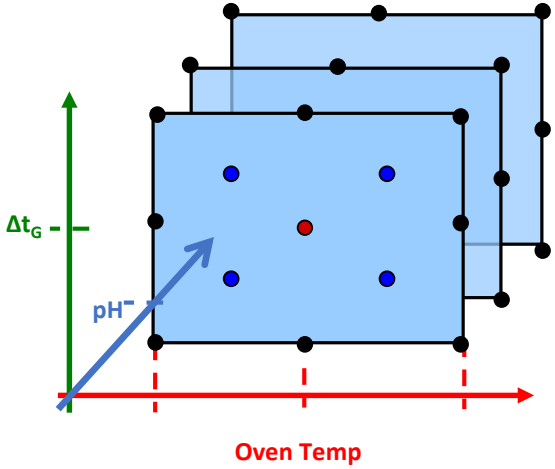


Studies can become very complex – difficult to carry out

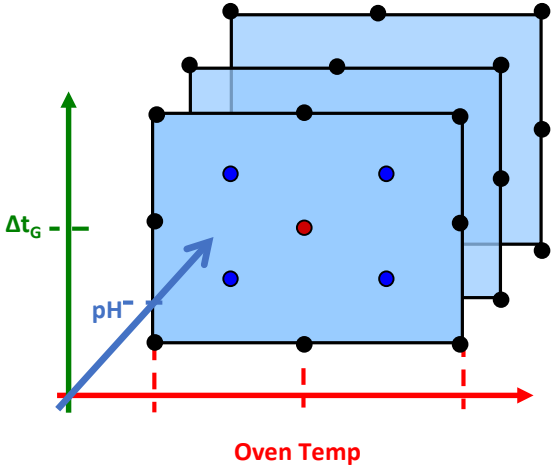
4th Variable – Column Type



C18



Phenyl



C8

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Fusion QbD – Experiment Automation to the Rescue!

Built-in **Design Wizard** which **Automatically Selects the most efficient DOE design** for your stage of work (e.g. chemistry screening or method optimization) and the LC parameters you selected for study.

- **Automatically organizes the design for efficient execution.**
- **Automatically builds the instrument methods and sequence** – automated error-free execution.

	Run No.	Gradient Time	pH	Column Type
1	Condition Column - 1	2	2.73	BEH C18
2	Condition Column - 2	2	2.73	BEH Shield RP18
3	Condition Column - 3	2	2.73	HSS T3
4	Condition Column - 4	2	2.73	CSH Phenyl Hexyl
5	1	25	2.73	BEH C18
6	2	10	2.73	BEH C18
7	3	25	2.73	BEH Shield RP18
8	4	10	2.73	BEH Shield RP18
9	5	25	2.73	HSS T3
10	6	10	2.73	HSS T3
11	7	17.5	2.73	CSH Phenyl Hexyl
12	8	17.5	2.73	CSH Phenyl Hexyl
13	Condition Column - 5	2	3.2	BEH C18
14	Condition Column - 6	2	3.2	BEH Shield RP18
15	Condition Column - 7	2	3.2	HSS T3
16	Condition Column - 8	2	3.2	CSH Phenyl Hexyl
17	9	21.3	3.2	BEH C18
18	10	13.8	3.2	HSS T3
19	11	17.5	3.2	BEH Shield RP18
20	12	17.5	3.2	CSH Phenyl Hexyl
21	Condition Column - 9	2	3.69	BEH C18
22	Condition Column - 10	2	3.69	BEH Shield RP18
23	Condition Column - 11	2	3.69	HSS T3
24	Condition Column - 12	2	3.69	CSH Phenyl Hexyl
25	13	17.5	3.69	BEH C18
26	14	17.5	3.69	BEH Shield RP18
27	15	17.5	3.69	HSS T3
28	16	17.5	3.69	CSH Phenyl Hexyl
29	17	25	3.69	CSH Phenyl Hexyl
30	18	10	3.69	CSH Phenyl Hexyl
31	19	17.5	3.69	BEH C18
32	20	17.5	3.69	BEH Shield RP18

Auto-built for walk-away execution in the CDS.

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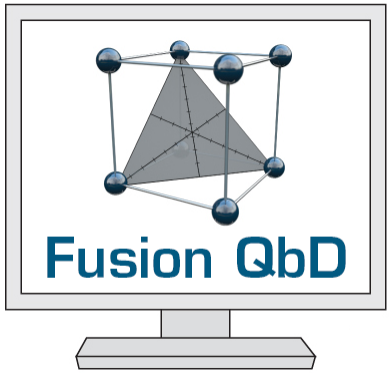
Fusion QbD – Automated DOE Experiment Workflow



Generates QbD-aligned DOE Experiment

Automatically Builds Sequence and All Instrument Methods

Chromatography Data Software (CDS)

Text Mix pH in S-Matrix - MD Demo\LC 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.

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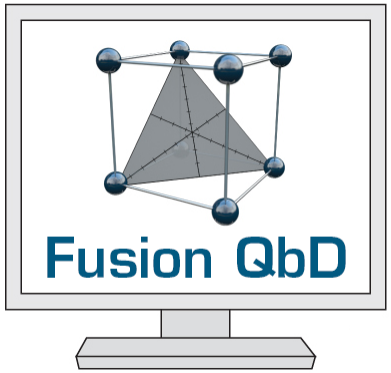
Fusion QbD – Automated DOE Experiment Workflow

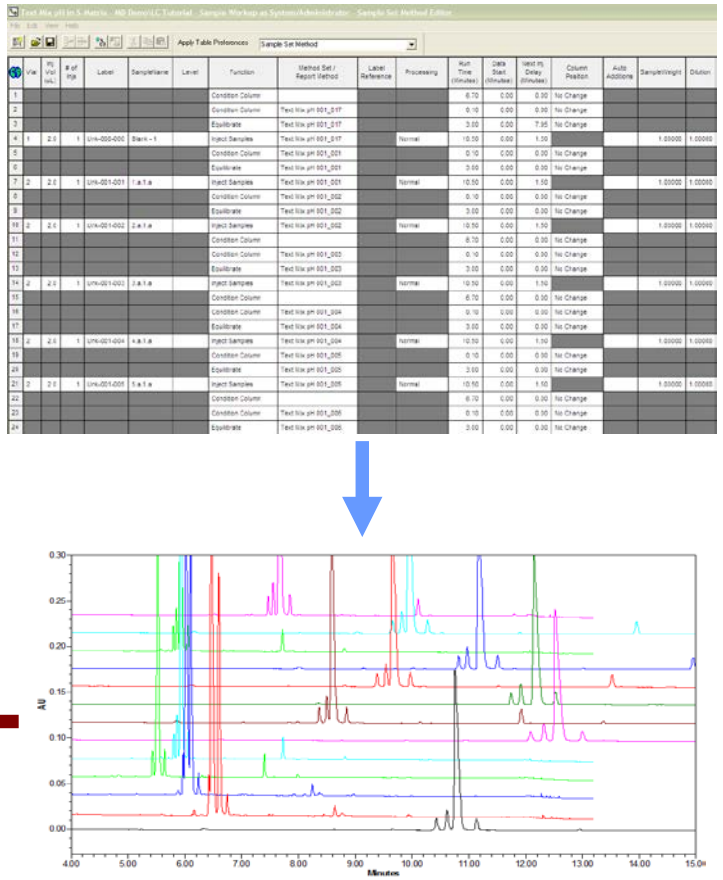


Automatically Retrieves
All Chromatogram
Results Data

Automated analysis, graphing, and reporting.

Report formats:
RTF, DOC, HTML, PDF, XLSX, XML

Chromatography Data Software (CDS)



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