Sneak Peek

CMC Statistics

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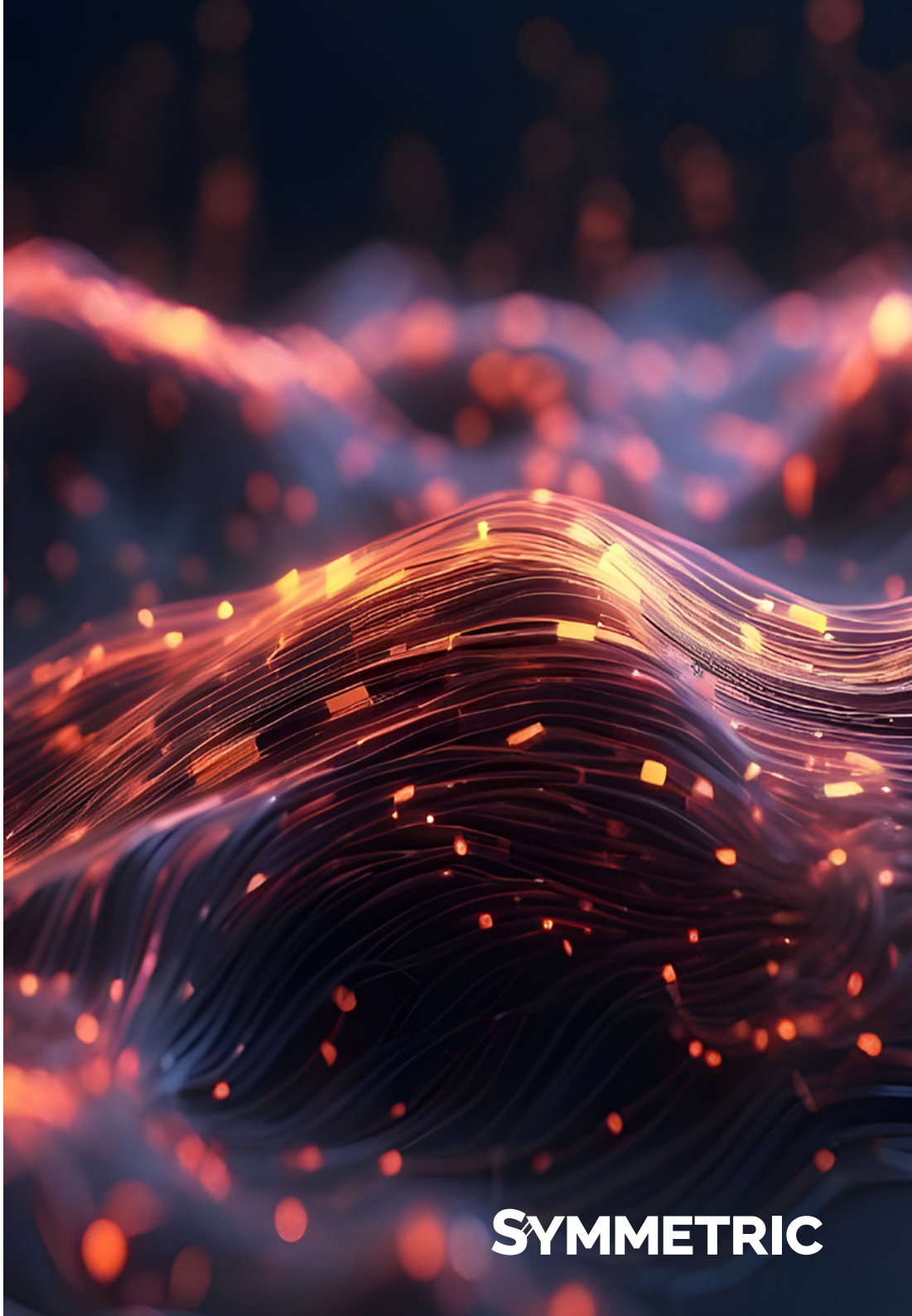
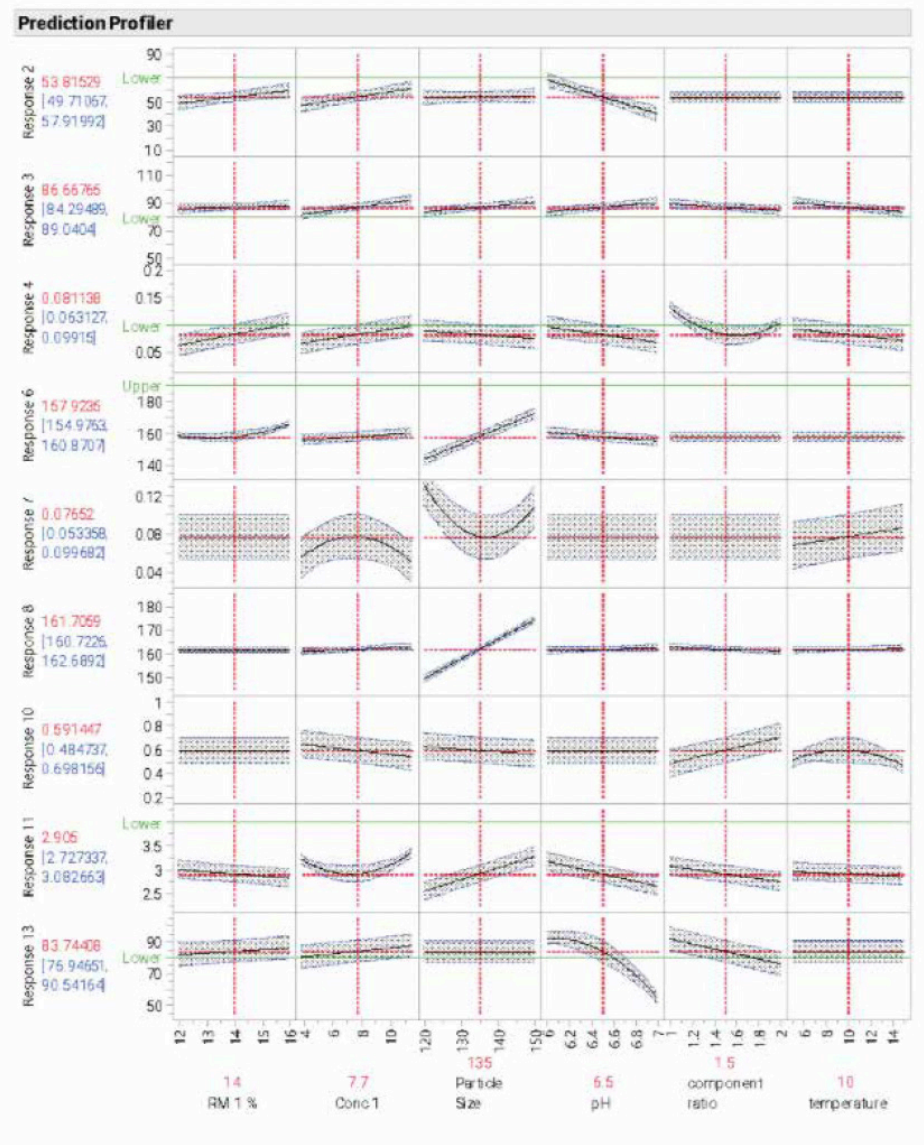
Principal

ONLINE
TRAINING



Using Doe to Determine Design Space

- Simultaneously evaluate multiple responses at various factor levels
- Easily see which factors have largest influence on each response
- Easily see magnitude of noise



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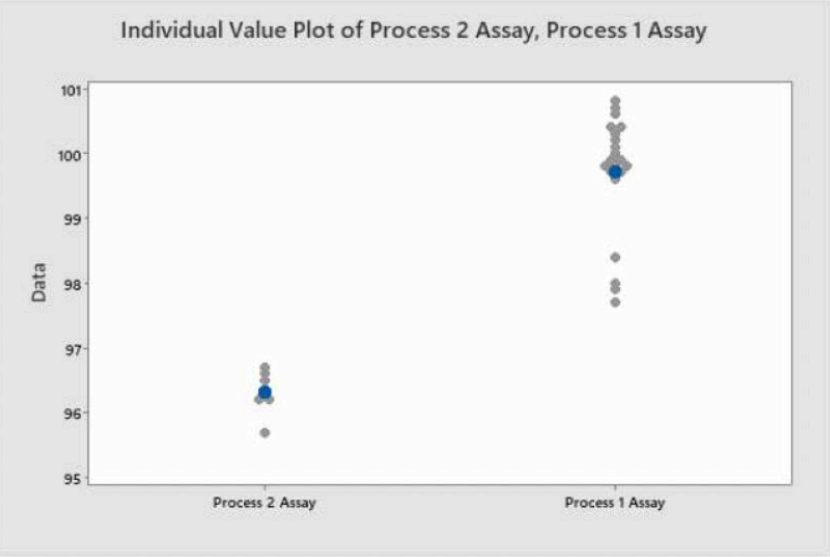
Establish Process Compatibilty Using Equivalence Margins



T-test

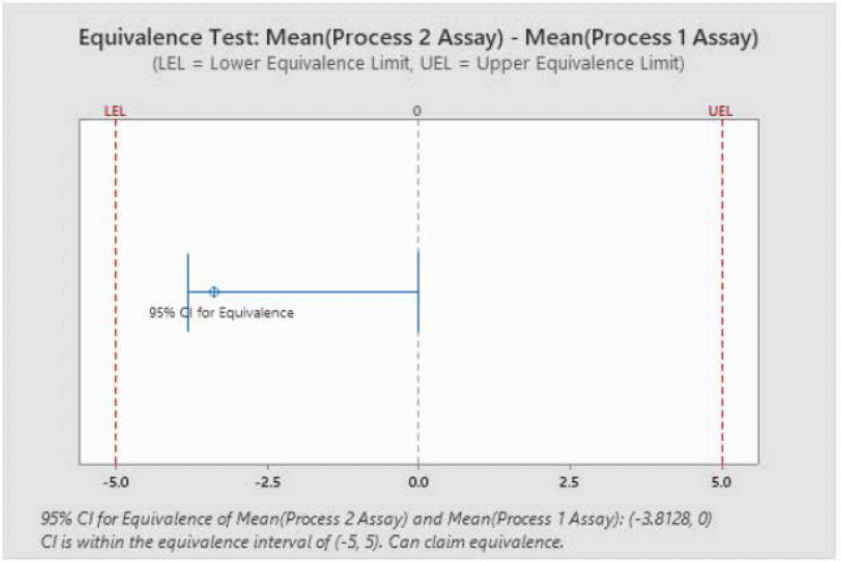
Estimation for Difference

Difference	95% CI for Difference
-3.383	(-3.902, -2.864)

Test

Null hypothesis	$H_0: \mu_1 - \mu_2 = 0$
Alternative hypothesis	$H_1: \mu_1 - \mu_2 \neq 0$

T-Value	DF	P-Value
-13.56	21	0.000



95% CI for Equivalence of Mean(Process 2 Assay) and Mean(Process 1 Assay): (-3.8128, 0)
CI is within the equivalence interval of (-5, 5). Can claim equivalence.

Equivalence Margin -5, +5

Difference: Mean(Process 2 Assay) - Mean(Process 1 Assay)

Difference	SE	95% CI for Equivalence	Equivalence Interval
-3.3833	0.24956	(-3.81275, 0)	(-5, 5)

CI is within the equivalence interval. Can claim equivalence.

Test

Null hypothesis:	Difference ≤ -5 or Difference ≥ 5
Alternative hypothesis:	-5 < Difference < 5
α level:	0.05

Null Hypothesis	DF	T-Value	P-Value
Difference ≤ -5	21	6.4782	0.000
Difference ≥ 5	21	-33.593	0.000

The greater of the two P-Values is 0.000. Can claim equivalence.

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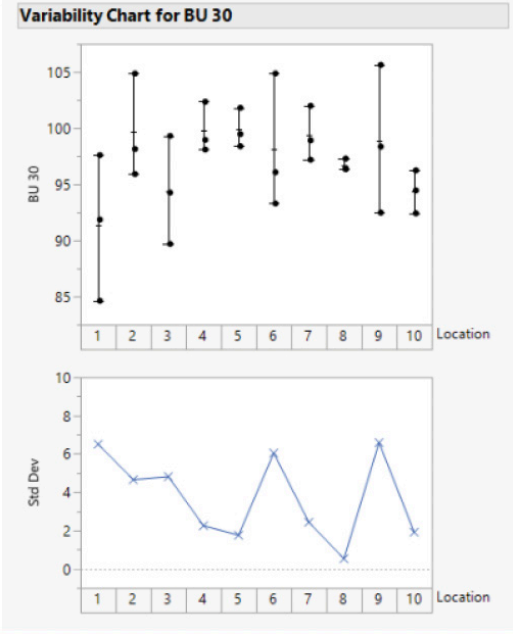
Asses Influence of Variability Sources Measurement or Process?

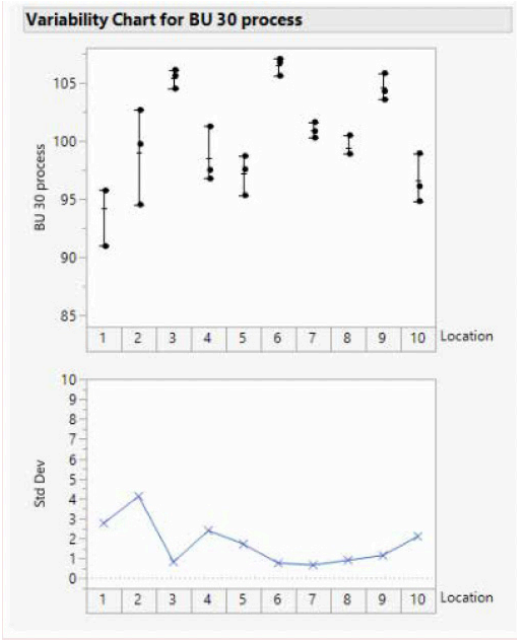
BU 30 Variance Component Analysis

Random Effect	Var Ratio	Var Component	Std Error	95% Lower	95% Upper	Wald p-Value	Pct of Total
Location	0.135812	2.5130555	4.5333343	-6.372116	11.398228	0.5793	11.957
Residual		18.503923	5.8514543	10.830633	38.58691		88.043
Total		21.016979	5.6536973	13.200632	38.617884		100.000



BU 30 Process Variance Component Analysis

Random Effect	Var Ratio	Var Component	Std Error	95% Lower	95% Upper	Wald p-Value	Pct of Total
Location	3.6409493	15.202354	7.8349282	-0.153823	30.558531	0.0523	78.453
Residual		4.1753821	1.3203717	2.4439158	8.7070774		21.547
Total		19.377736	7.8719265	9.9914766	52.478186		100.000



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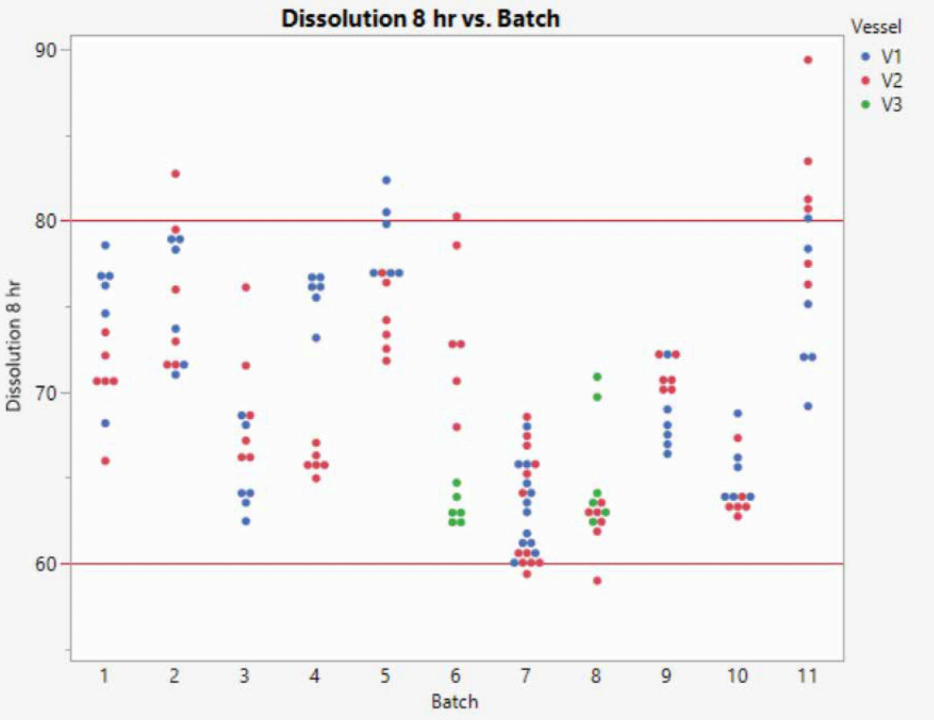
Data Visualization of Oos Dissolution

04



Hypothesis: the dissolution measurement vessel used influences dissolution result

A random pattern among the vessels would negate any influence

In some cases, there is a difference between vessels; however, the relative behavior is not consistent. That is, the same vessel is not always the highest.

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Determing Ppq Intra-Batch Sample Size

$$\bar{X} \pm k\,s$$

From Development Data
Expected Mean = 100.0;
Expected Standard Deviation = 1.0;
ConÞdence = 95%; Coverage = 99%
SpeciÞcation = 90-110

nk		Tolerance Interval Assay
3	12.65	87.4 – 112.6%
4	8.22	91.8 – 108.2% ✓
5	6.60	93.4 – 106.6% ✓

Line of sight to PPQ evidence-based conclusions:

A tolerance interval within specifications provides a ***"high degree of assurance" … "process is capable of consistently producing acceptable quality products"***

Development data → 4-5 intra-batch samples

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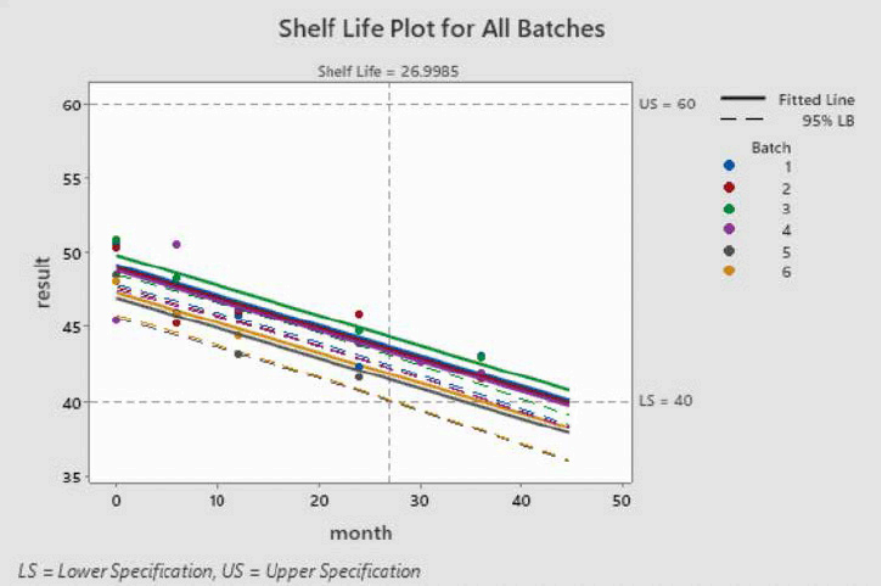
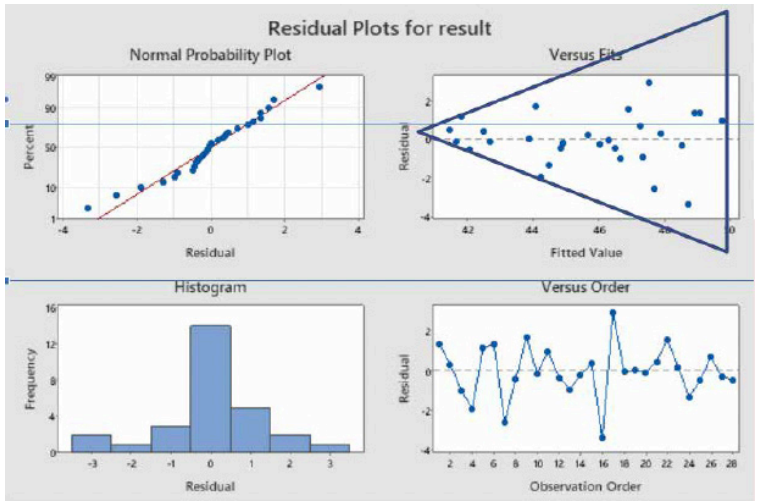
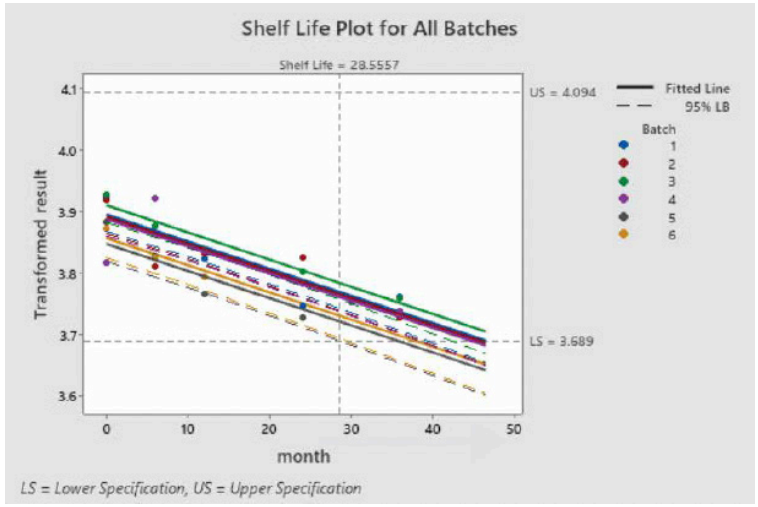
Establishing Shelf Life Using Residuals Plot



Model with same slope, different intercepts



Log transformed results



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Registration

Sneak Peek

CMC Statistics

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