JMP Tools for Pharmaceutical Companies: Stability Analysis and Assessing Consistency in Manufacturing

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JMP Tools for Pharmaceutical Companies: Stability Analysis and Assessing Consistency in Manufacturing

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JMP has multiple tools for to help Pharmaceutical companies achieve their goals. I will discuss two common challenges in the Pharmaceutical industry and show how to use JMP for analysis and decision making for two of these: Stability Analysis and Consistency in Manufacturing. For Stability Analysis, JMP has built in statistical tests for determining batch pooling using the ICH Guidelines. When data in non-linear, there are options for transforming data that allow for standard analysis. JMP also has a non-linear platform for fitting complex non-linear models and equivalence testing. JMP tools for monitoring and assessing consistency in a manufacturing process allow tracking and trending of operations and products. Interactive tools such as Control Chart Builder and Distributions facilitate deep understanding of single processes or products, including metrics to understand if specification limits are being met. Process Screening and Process Capability scale up to investigating multiple product or processes simultaneously. There are additional tools in JMP for identifying root causes when problems arise, as well as innovative tools for identifying drift in processes.

Pharmaceutical Industry Needs Specialized Tools for Data Driven Decisions

- Stability Analysis
  - Drug Degradation and Expiration

- Consistency in Manufacturing
  - Tracking and Trending of Manufacturing Operations and Products

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Stability Analysis: Drug Degradation and Expiration

- Statistical tests for determining batch pooling
- ICH Guidelines
- Non-linear Data: data transformation for standard analysis

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Stability Analysis: Drug Degradation and Expiration

- Statistical tests for determining batch pooling
- ICH Guidelines

Stability – Characterization of how important properties of a pharmaceutical or biologic products change over time, such as:

- Decreases in potency, purity, etc.
- Increases in impurities, moisture, etc.

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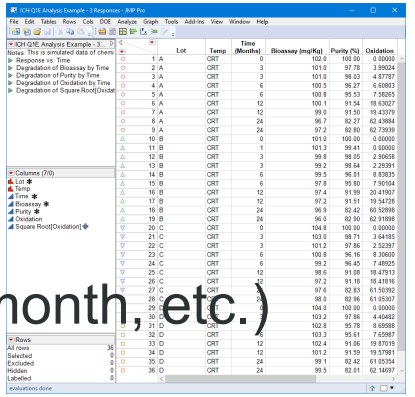
JMP Stability Demo



Key Data Columns:

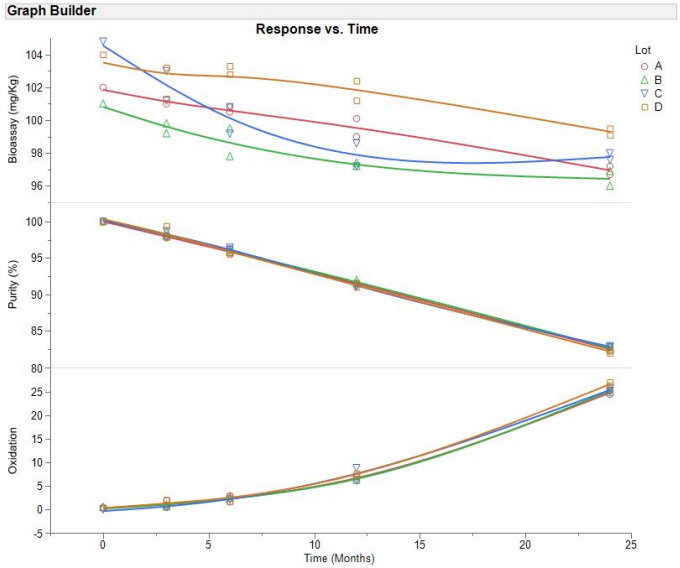
- **Time:** Number of months (0- Before storage, 1 = one month, etc.)
- **Batch:** Manufacturing lot or batch (A, B, C, etc.)

- **Bioassay:** How active is my product relative to standard preparation expectations. (Lower Specification Limit of 95)
- **Purity:** What proportion of the active product is comprised of drug (Lower Specification Limit of 90)
- **Oxidation:** Level of oxidation Impurity (Upper Specification Limit of 20)

JMP Stability Demo

Data Visualization in Graph Builder

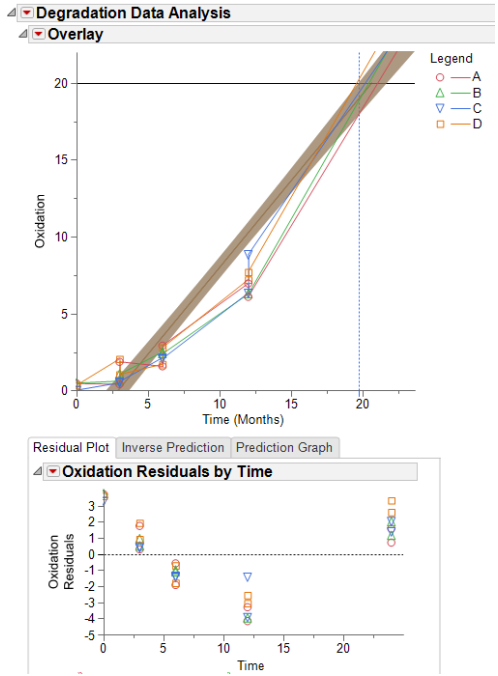
- Visual assessment of the different batches and measurements over time for overview and to look for any potential issues with further analysis
- Fit a smooth line to check for possible curvature in the responses: Oxidation might cause problems with the analysis



JMP Stability Demo

Degradation/Stability Analysis Platform

- Regression of product property over time for each batch
- Residual Plot for each response to look for a pattern indicating non-linear

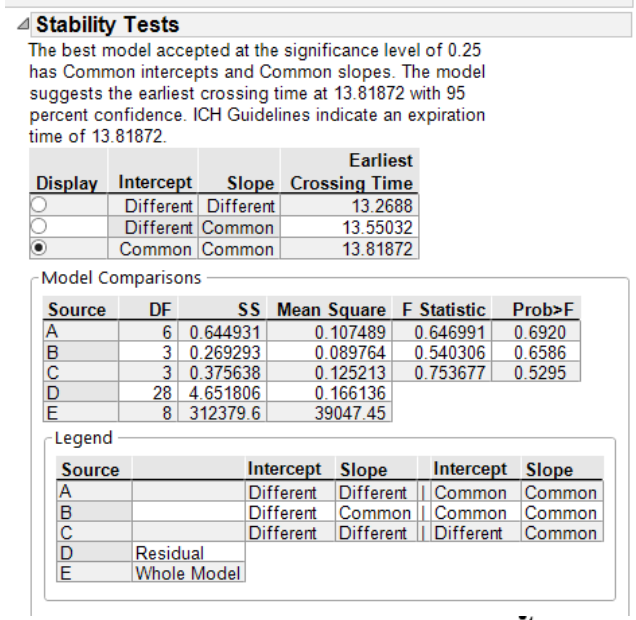


- Need to transform Oxidation. Simplest is to use a square root transformation
- Right-click on Oxidation column allows selection of a New Formula
- Choosing Transform>Square Root creates a new column with the square root of Oxidation column

JMP Stability Demo

Degradation/Stability Analysis Platform

- **Regression Results:**
- Looking for Batch and Batch * Time effects above .25 guidance
- Do not need to run each model separately (same slope/different slope and same intercept/different intercept tests run automatically)
- Find earliest crossing time that matches upper or lower specification limit at edge of 95% confidence limit, expiration time is 13.8 months



Stability Tests

The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time at 13.81872 with 95 percent confidence. ICH Guidelines indicate an expiration time of 13.81872.

Display	Intercept	Slope	Earliest Crossing Time
○	Different	Different	13.2688
○	Different	Common	13.55032
◉	Common	Common	13.81872

Model Comparisons

Source	DF	SS	Mean Square	F Statistic	Prob>F
A	6	0.644931	0.107489	0.646991	0.6920
B	3	0.269293	0.089764	0.540306	0.6586
C	3	0.375638	0.125213	0.753677	0.5295
D	28	4.651806	0.166136		
E	8	312379.6	39047.45		

Legend

Source		Intercept	Slope	Intercept	Slope
A		Different	Different	Common	Common
B		Different	Common	Common	Common
C		Different	Different	Different	Common
D	Residual				
E	Whole Model				

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Conclusions:

Stability Analysis: Drug Degradation and Expiration

- Analysis quickly assessed batch stability and establish pooled degradation linear fits
- Oxidation needed a simple transformation before we could establish the proper stability degradation line
- Expiration time was 13.8 months for Purity levels according to ICH Q1E guidelines

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  - Tracking and Trending of Manufacturing Operations and Products

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Consistency in Manufacturing:

Tracking and Trending of Manufacturing Operations and Products

- Process Monitoring - Process Control
- Process/Product Consistency - capability and specification limits
- identifying drift in processes

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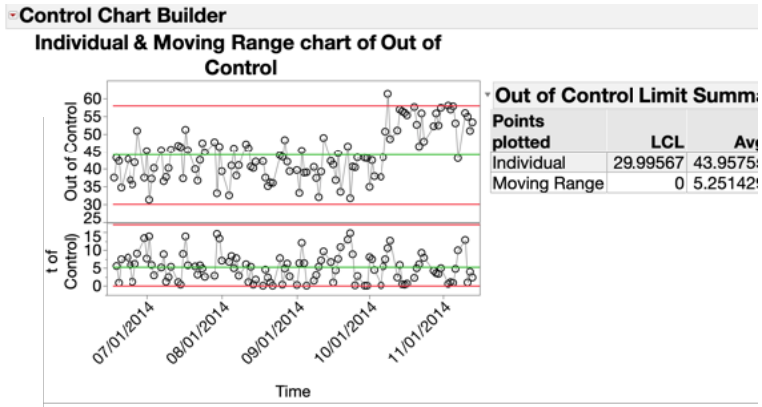
Process Monitoring - Process Control

Three Tools for Control Charts

- Control Chart Builder
  - Great for exploring data
  - Design and replicate a template
  - All control charts in one place
    - Don't have to be a CC expert to get the right chart
- Control Charts
  - Quick selection of control chart type from menu
  - Easy to generate and quickly view many many charts
  - Generate easy to use graph scripts for automation
- Process Screening
  - Summary control chart statistics
  - Great for looking at hundreds of process parameters



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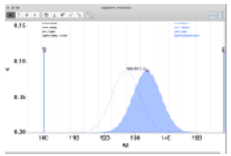
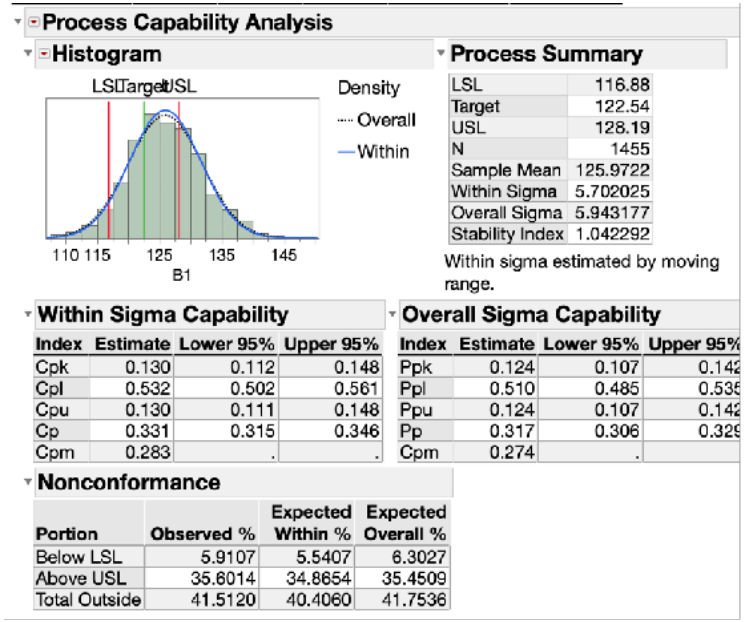
Process/Product Consistency - capability and specification limits

- Distribution
- Control Charts
- Process Screening
- Process Capability





Pharmaceutical Industry Needs Specialized Tools for Data Driven Decisions

Conclusions:

- Consistency in Manufacturing
  - Tracking and Trending of Manufacturing Operations and Products
    - Many ways to understand process control
    - Flexible platforms for setting and understanding specification limits
    - Process Screening characterizes both control and quality in one interactive platform

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Pharmaceutical Industry Needs Specialized Tools for Data Driven Decisions

Conclusion: JMP has many powerful tools for Pharmaceutical Industry!

- Stability Analysis
  - Drug Degradation and Expiration

- Consistency in Manufacturing
  - Tracking and Trending of Manufacturing Operations and Products

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Bonus material

- Bioassay Analysis:
  - Non-linear platform for fitting complex non-linear models and equivalence testing
- Consistency in Manufacturing
  - Identifying root causes of problems

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Sigma is different for Cpk and Ppk

- Cpk
  - Control chart sigma
  - Dispersion based on average moving range
  - Insensitive to distribution of the data (in most cases)
  - Insensitive to shifts in the mean
- Ppk
  - Standard deviation
  - Dispersion based on variance from the mean
  - Sensitive to mean shifts
  - Distribution is important to consider

Here to help

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