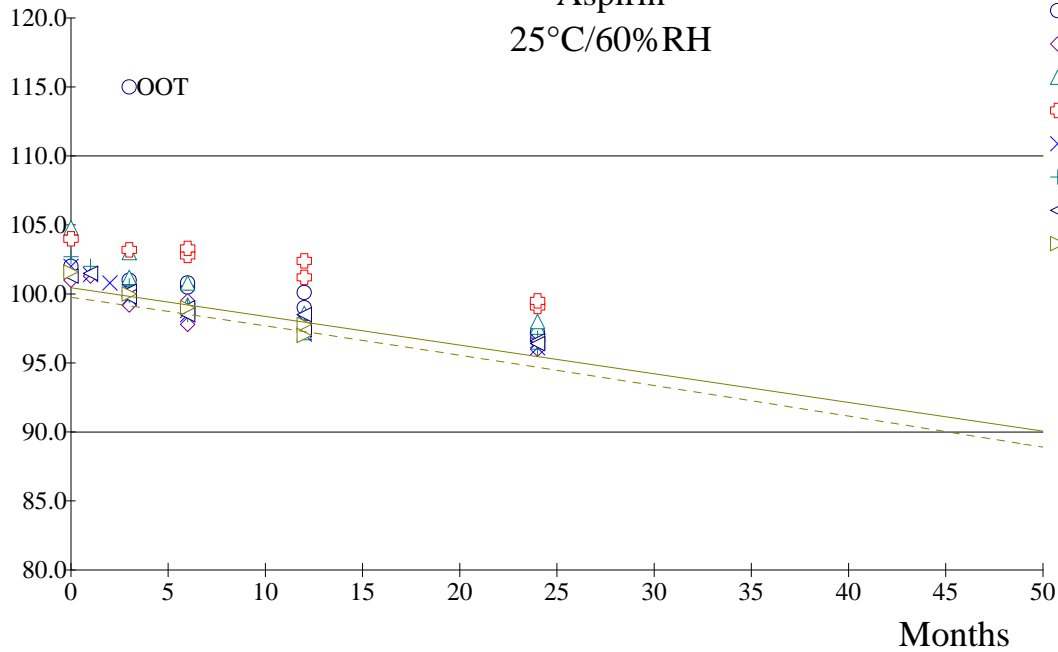


Shelf Life Projection

Kurital Tablets
Aspirin
25°C/60%RH

mg/tablet

Study



Model 2: Common Slope but Different Intercepts (95.0% CI)

Test Category: HPLC High Spec: 110.0 Low Spec: 90.0

Original FDA Data Set with an OOT Result added...

File: C:\Program Files (x86)\SLIM\Demo\Standard Conditions.SST User: Craig Hamilton

SLIMStat Regression Analysis and Pooling of Data.

Original Raw Data (Time in units of Months):

Study	Time (Months)	Results (mg/tablet)
Study 1 _11	0.0	102.00
	3.0	101.00
	3.0	115*
	6.0	100.50
	6.0	100.80
	12.0	100.10
	12.0	99.00
	24.0	96.70
	24.0	97.20
Study 2 _12	0.0	101.00
	1.0	101.30
	3.0	99.80
	3.0	99.20
	6.0	99.50
	6.0	97.80
	12.0	97.40
	12.0	97.20
	24.0	96.90
Study 3 _13	0.0	104.80
	3.0	103.00
	3.0	101.20
	6.0	100.80
	6.0	99.20
	12.0	98.60
	12.0	97.20
	24.0	97.60
	24.0	98.00
Study 4 _14	0.0	104.00
	3.0	103.20
	6.0	102.80
	6.0	103.30
	12.0	102.40
	12.0	101.20
	24.0	99.10
	24.0	99.50
	24.0	99.50
Study 5 _161	0.0	102.00
	1.0	101.40
	2.0	100.80
	3.0	100.20
	3.0	99.70
	6.0	98.80
	6.0	98.50
	12.0	98.00
	12.0	97.10
Study 6 _162	0.0	102.70
	1.0	102.00
	3.0	100.60
	3.0	99.90
	6.0	99.20
	6.0	98.50
	12.0	98.10
	12.0	97.60
	24.0	96.80
Study 7 _163	0.0	101.30
	1.0	101.50
	3.0	100.20
	3.0	99.80
	6.0	99.00
	6.0	98.50
	12.0	98.50
	12.0	97.40
	24.0	96.00

Time : 24.0 24.0
Results: 96.60 96.40

Study 8 _164
Time : 0.0 3.0 6.0 12.0 12.0
Results: 101.60 100.00 99.00 97.80 97.00

Original Raw Data Treatment:

- a. Less than (<) results are ignored.
- b. Greater than (>) results are ignored.
- c. A result marked with a question (?) is "Selected for Testing" and is ignored.
- d. Results marked by an asterisk (*) are "Out of Trend (OOT)" and are ignored.
- e. Results marked by a pound (#) are "Forcibly Excluded (EXC)" and are ignored.

Step 1. Fit each individual regression equation and compute the residual sum of squares.

1 Study: _11
OOT[3.0,115.00][Mult.=3,SD= 0.385432721]Expected= 101.265753425±1.156298162(100.109455262 to 102.422051587) mg/tablet
Linear Least Squares: $Y = -0.20359x + 101.87652$ (n = 8)
Residual Sum of Squares (i = 1) = 0.89135
 R^2 (Coefficient of Determination) = 0.96394
Standard Deviation of Residuals = 0.38543 mg/tablet
Standard Error of Slope = 0.01608
P Value of Slope = 0.00001. Slope significant (user selected P = 0.25).

2 Study: _12
Linear Least Squares: $Y = -0.18013x + 100.24914$ (n = 10)
Residual Sum of Squares (i = 2) = 6.54335
 R^2 (Coefficient of Determination) = 0.77705
Standard Deviation of Residuals = 0.90439 mg/tablet
Standard Error of Slope = 0.03411
P Value of Slope = 0.00075. Slope significant (user selected P = 0.25).

3 Study: _13
Linear Least Squares: $Y = -0.23397x + 102.38413$ (n = 9)
Residual Sum of Squares (i = 3) = 19.81530
 R^2 (Coefficient of Determination) = 0.63509
Standard Deviation of Residuals = 1.68249 mg/tablet
Standard Error of Slope = 0.06703
P Value of Slope = 0.01012. Slope significant (user selected P = 0.25).

4 Study: _14
Linear Least Squares: $Y = -0.19615x + 104.07065$ (n = 8)
Residual Sum of Squares (i = 4) = 1.08023
 R^2 (Coefficient of Determination) = 0.95344
Standard Deviation of Residuals = 0.42431 mg/tablet
Standard Error of Slope = 0.01770
P Value of Slope = 0.00003. Slope significant (user selected P = 0.25).

5 Study: _161
Linear Least Squares: $Y = -0.20861x + 100.78187$ (n = 11)
Residual Sum of Squares (i = 5) = 6.41360
 R^2 (Coefficient of Determination) = 0.83553
Standard Deviation of Residuals = 0.84417 mg/tablet
Standard Error of Slope = 0.03085
P Value of Slope = 0.00008. Slope significant (user selected P = 0.25).

6 Study: _162
Linear Least Squares: $Y = -0.22256x + 101.16533$ (n = 10)
Residual Sum of Squares (i = 6) = 7.94614
 R^2 (Coefficient of Determination) = 0.81419
Standard Deviation of Residuals = 0.99663 mg/tablet
Standard Error of Slope = 0.03759
P Value of Slope = 0.00035. Slope significant (user selected P = 0.25).

7 Study: _163
Linear Least Squares: $Y = -0.18839x + 100.63436$ (n = 10)
Residual Sum of Squares (i = 7) = 4.18927
 R^2 (Coefficient of Determination) = 0.85622
Standard Deviation of Residuals = 0.72364 mg/tablet
Standard Error of Slope = 0.02729
P Value of Slope = 0.00012. Slope significant (user selected P = 0.25).

8 Study: _164
Linear Least Squares: $Y = -0.33021x + 101.25938$ (n = 5)
Residual Sum of Squares (i = 8) = 0.60687
 R^2 (Coefficient of Determination) = 0.95391
Standard Deviation of Residuals = 0.44977 mg/tablet
Standard Error of Slope = 0.04190
P Value of Slope = 0.00426. Slope significant (user selected P = 0.25).

Model using Different Slopes and Different Intercepts
Total residual Sum of Squares for this model = 47.48613

Step 2. Fit each individual regression equation with different intercepts and a common slope.

1 Study: _11
Linear Least Squares: $Y = -0.20766x + 101.92085$ (n = 8)

Residual Sum of Squares (i = 1) = 0.90091
 2 Study: _12
 Linear Least Squares: $Y = -0.20766x + 100.49975$ (n = 10)
 Residual Sum of Squares (i = 2) = 7.07644
 3 Study: _13
 Linear Least Squares: $Y = -0.20766x + 102.12109$ (n = 9)
 Residual Sum of Squares (i = 3) = 20.25118
 4 Study: _14
 Linear Least Squares: $Y = -0.20766x + 104.19585$ (n = 8)
 Residual Sum of Squares (i = 4) = 1.15644
 5 Study: _161
 Linear Least Squares: $Y = -0.20766x + 100.77389$ (n = 11)
 Residual Sum of Squares (i = 5) = 6.41427
 6 Study: _162
 Linear Least Squares: $Y = -0.20766x + 101.02975$ (n = 10)
 Residual Sum of Squares (i = 6) = 8.10217
 7 Study: _163
 Linear Least Squares: $Y = -0.20766x + 100.80975$ (n = 10)
 Residual Sum of Squares (i = 7) = 4.45038
 8 Study: _164
 Linear Least Squares: $Y = -0.20766x + 100.45059$ (n = 5)
 Residual Sum of Squares (i = 8) = 2.33683
 Model using Common Slope and Different Intercepts
 Total residual Sum of Squares for this model = 50.68862

Step 3. Fit a single regression line assuming identical degradation curves.
 Linear Least Squares: $Y = -0.19350x + 101.30690$ (n = 71)
 Model using Common Slope and Common Intercept
 Total residual Sum of Squares for this model = 140.77086

Step 4. Partition the total sum of squares (SStot) into sum of squares due to regression (SSreg) and residual sum of squares (SSres).
 Partition: $322.06000(SStot) = 274.57387(SSreg) + 47.48613(SSres)$

STATISTICAL ANALYSIS

Standard Conditions Data Models

- Model 1: Common Slope and Common Intercept
- Model 2: Common Slope but Different Intercepts
- Model 3: Common Intercept but Different Slopes
- Model 4: Different Intercepts and Different Slopes

LOWER ONE-TAILED CONFIDENCE INTERVAL
 PROBABILITY LEVEL = 95.0% (equivalent to two-tail 90.0% probability)

Key to Sources of Variation

Source	Alternative hypothesis	Null hypothesis
A	Separate intercepts, separate slopes	Common intercept, common slope
B	Separate intercepts, common slope	Common intercept, common slope
C	Separate intercepts, separate slopes	Separate intercepts, common slope
D	Residual	
E	Full Model	

TABLE OF STATISTICAL ANALYSIS

Source	SS	DF	MS	F	P
A	93.285	14	6.663	7.7175	0.00000
B	90.082	7	12.869	14.9052	0.00000
C	3.202	7	0.457	0.5299	0.80812
D	47.486	55	0.863		
E	703192.324	16	43949.520		

DECISION RULES

If the p-value of test C < 0.25, then Model 3 or 4 is applicable.
 If the p-value of test C >= 0.25, then test for B.
 If the p-value of test B < 0.25, then Model 2 is applicable.
 If the p-value of test B >= 0.25, then Model 1 is applicable.

Final results based on the decision rules:
 Pooling Allowed (Model 2), Common Slope but Different Intercepts.

1 Study: _11
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 52 Months.
Trend (CI) at 36 Months = 94.4 - 0.8 (\geq 93.7) mg/tablet.

2 Study: _12
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 46 Months.
Trend (CI) at 36 Months = 93.0 - 0.8 (\geq 92.3) mg/tablet.

3 Study: _13
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 53 Months.
Trend (CI) at 36 Months = 94.6 - 0.8 (\geq 93.9) mg/tablet.

4 Study: _14
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 62 Months.
Trend (CI) at 36 Months = 96.7 - 0.8 (\geq 96.0) mg/tablet.

5 Study: _161
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 47 Months.
Trend (CI) at 36 Months = 93.3 - 0.8 (\geq 92.5) mg/tablet.

6 Study: _162
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 48 Months.
Trend (CI) at 36 Months = 93.6 - 0.8 (\geq 92.8) mg/tablet.

7 Study: _163
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 47 Months.
Trend (CI) at 36 Months = 93.3 - 0.8 (\geq 92.6) mg/tablet.

8 Study: _164
One Sided Lower Confidence Interval (95.0% CI).
The expiration date was determined when the low specification was exceeded.
Expiration Date = 45 Months.
Trend (CI) at 36 Months = 93.0 - 0.9 (\geq 92.0) mg/tablet.

Pooled expiration date based on _164

Analysis Complete.

HISTORY INFORMATION

File Version: 5
File Status : ACTIVE
File Name : C:\Program Files (x86)\SLIM\Demo\Standard Conditions.SST
Created : 22 November 2010 at 17:32:34 by Administrator (User ID = 1)
Last Saved : 26 February 2011 at 23:04:41 by Administrator (User ID = 1)