BMDExpress2 Workflow

Inputs, Outputs and Best Model Selection

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BMDExpress2 Workflow

- Inputs
  - Hill
  - Power
  - Poly
  - Exponential
- Outputs
  - Hill
  - Power
  - Poly
  - Exponential
- Best Model Selection
  - Select best poly model
  - Select best non-poly
  - Deal with Hill and select best model

BMDExpress2 Workflow – Hill Input

```
Hill
BMDS MODEL RUN
827377983_1553221_at
Hill
0 20 0
250 1.0E-8 1.0E-8 1 1 1 0 0
1 1.349 1 0.95
-9999.0 0.0 -9999.0 -9999.0 -9999.0 -9999.0
0
-9999.0 0.0 -9999.0 -9999.0 -9999.0 -9999.0
DOSE RESPONSE
0.0 6.96377
0.0 7.05445
0.0 6.97254
0.0 7.09836
1.0E-6 7.17683
1.0E-6 7.12809
1.0E-6 7.17259
1.0E-6 7.04538
1.0E-4 7.09178
1.0E-4 7.12637
1.0E-4 6.82033
1.0E-4 7.30107
0.001 6.92979
0.001 7.15551
0.001 7.04346
0.001 7.2716
1.0 7.00026
1.0 6.75487
1.0 6.62335
1.0 6.77612
```

individual animal data	# observations	adverse direction
0	*20	0

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	v	n	k
-9999.0	*0.0	-9999.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	v	n	k
-9999.0	*0.0	-9999.0	-9999.0	-9999.0	-9999.0

** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Power Input

```
Power
BMDS MODEL RUN
539667114_1553221_at_power.(d)
539667114_1553221_at_power.out
0 20 0
250 1.0E-8 1.0E-8 1 1 1 0 0
1 1.349 1 0.95
-9999.0 0.0 -9999.0 -9999.0 -9999.0
0
-9999.0 0.0 -9999.0 -9999.0 -9999.0
DOSE RESPONSE
0.0 6.96377
0.0 7.05445
0.0 6.97254
0.0 7.09836
1.0E-6 7.17683
1.0E-6 7.12809
1.0E-6 7.17259
1.0E-6 7.04538
1.0E-4 7.09178
1.0E-4 7.12637
1.0E-4 6.82033
1.0E-4 7.30107
0.001 6.92979
0.001 7.15551
0.001 7.04346
0.001 7.2716
1.0 7.00026
1.0 6.75487
1.0 6.62335
1.0 6.77612
```

individual animal data	# observations	adverse direction
0	*20	0

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	**1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	v	k
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	v	k
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Linear Input

```
Polynomial
BMDS MODEL RUN
1046541146_1369698_at_poly1.(d)
1046541146_1369698_at_poly1.out
1
0 20 0
250 1.0E-8 1.0E-8 1 0 1 0 0
1 1.349 1 0.95
-9999.0 0.0  -9999 -9999
0
-9999.0 -9999.0  -9999 -9999
DOSE RESPONSE
0.0 6.36402
0.0 6.92206
0.0 6.61179
0.0 6.92453
0.0 6.65686
62.25284 7.21893
62.25284 7.62579
62.25284 7.74661
124.50568 7.15564
124.50568 7.3435
124.50568 8.19571
248.643 8.69687
248.643 8.18887
248.643 9.26876
497.286 8.75149
497.286 9.40085
497.286 9.32163
994.572 9.30575
994.572 9.48015
994.572 9.88832
```

Degree of polynomial
1

individual animal data	# observations	adverse direction
0	*20	0

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	0	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	beta0	beta1
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	beta0	beta1
-9999.0	-9999.0	-9999.0	-9999.0	-9999.0

** user supplied

* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Poly 2 Input

```
Polynomial
BMDS MODEL RUN
1369455_at_poly2.(d)
1369455_at_poly2.out
2
0 20 -1
250 1.0E-8 1.0E-8 1 0 1 0 0
1 1.349 1 0.95
-9999.0 0.0  -9999 -9999 -9999
0
-9999.0 -9999.0  -9999 -9999 -9999
DOSE RESPONSE
0.0 8.92202
0.0 9.45966
0.0 9.09868
0.0 8.08736
0.0 8.99072
62.25284 8.27227
62.25284 8.69945
62.25284 7.82115
124.50568 8.39911
124.50568 8.82903
124.50568 8.20693
248.643 6.90384
248.643 8.38869
248.643 7.79296
497.286 6.89847
497.286 7.50204
497.286 6.73566
994.572 6.0226
994.572 6.8384
994.572 6.84474
```

Degree of polynomial
2

individual animal data	# observations	adverse direction
0	*20	***1 AND -1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	0	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	beta0	beta1
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	beta0	beta1
-9999.0	-9999.0	-9999	-9999	-9999

*** Model is run twice.
** user supplied.
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Poly 3 Input

```
Polynomial
BMDS MODEL RUN
1367973_at_poly3.(d)
1367973_at_poly3.out
3
0 20 -1
250 1.0E-8 1.0E-8 1 0 1 0 0
1 1.349 1 0.95
-9999.0 0.0  -9999 -9999 -9999 -9999
0
-9999.0 -9999.0  -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 5.13006
0.0 5.28306
0.0 4.68202
0.0 4.43633
0.0 5.0756
62.25284 5.12553
62.25284 4.69764
62.25284 4.84382
124.50568 5.22581
124.50568 5.16417
124.50568 4.59141
248.643 5.47681
248.643 5.1392
248.643 4.7894
497.286 5.8716
497.286 8.38535
497.286 9.12474
994.572 5.64268
994.572 6.73895
994.572 5.24267
```

Degree of polynomial
3

individual animal data	# observations	adverse direction
0	*20	***1 AND -1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	0	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	beta0	beta1
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	beta0	beta1
-9999.0	-9999.0	-9999	-9999	-9999

*** Model is run twice.
** user supplied.
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Poly 4 Input

```
Polynomial
BMDS MODEL RUN
184556520_1367973_at_poly4.(d)
184556520_1367973_at_poly4.out
4
0 20 1
250 1.0E-8 1.0E-8 1 0 1 0 0
1 1.349 1 0.95
-9999.0 0.0  -9999 -9999 -9999 -9999 -9999
0
-9999.0 -9999.0  -9999 -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 5.13006
0.0 5.28306
0.0 4.68202
0.0 4.43633
0.0 5.0756
62.25284 5.12553
62.25284 4.69764
62.25284 4.84382
124.50568 5.22581
124.50568 5.16417
124.50568 4.59141
248.643 5.47681
248.643 5.1392
248.643 4.7894
497.286 5.8716
497.286 8.38535
497.286 9.12474
994.572 5.64268
994.572 6.73895
994.572 5.24267
```

Degree of polynomial
4

individual animal data	# observations	adverse direction
0	*20	***1 AND -1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	restrict n> 1	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	0	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	Intercept	beta0	beta1
-9999.0	*0.0	-9999.0	-9999.0	-9999.0

Initialize Parameters
0

Alpha	Rho	Intercept	beta0	beta1
-9999.0	-9999.0	-9999	-9999	-9999

*** Model is run twice.
** user supplied.
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Exponential Model 2 Input

```
Exponential
BMDS MODEL RUN
975549689_1369698_at
Exponential
0 20 0 1000 11 0 1
250 1.0E-8 1.0E-8 1 1 0 0
1 1.349 1 0.95
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 6.36402
0.0 6.92206
0.0 6.61179
0.0 6.92453
0.0 6.65686
62.25284 7.21893
62.25284 7.62579
62.25284 7.74661
124.50568 7.15564
124.50568 7.3435
124.50568 8.19571
248.643 8.69687
248.643 8.18887
248.643 9.26876
497.286 8.75149
497.286 9.40085
497.286 9.32163
994.572 9.30575
994.572 9.48015
994.572 9.88832
```

Per exponential model

individual animal data	# observations	adverse direction	Run Models	Span	Distribution Curve	MLE Solution
0	*20	0	***1000	11	0	1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

Initialize Parameters
0

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

*** select which exponential model to run
** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Exponential Model 3 Input

```
Exponential
BMDS MODEL RUN
382189664_1371076_at
Exponential
0 20 0 0100 22 0 1
250 1.0E-8 1.0E-8 1 1 0 0
1 1.349 1 0.95
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 12.176
0.0 11.4719
0.0 10.5891
0.0 11.9201
0.0 12.4076
62.25284 12.4037
62.25284 12.8316
62.25284 12.9837
124.50568 13.2358
124.50568 12.7977
124.50568 13.1576
248.643 13.3875
248.643 13.7481
248.643 14.0329
497.286 13.7985
497.286 14.119
497.286 13.9534
994.572 14.1499
994.572 14.3232
994.572 14.4362
```

Per exponential model

individual animal data	# observations	adverse direction	Run Models	Span	Distribution Curve	MLE Solution
0	*20	0	***0100	22	0	1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

Initialize Parameters
0

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

*** select which exponential model to run
** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Exponential Model 4 Input

```
Exponential
BMDS MODEL RUN
1063430922_1368905_at
Exponential
0 20 0 0010 33 0 1
250 1.0E-8 1.0E-8 1 1 0 0
1 1.349 1 0.95
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 8.98136
0.0 8.8966
0.0 8.76269
0.0 8.93936
0.0 9.03612
62.25284 9.31748
62.25284 9.9288
62.25284 9.85866
124.50568 9.75641
124.50568 9.75798
124.50568 9.89225
248.643 10.5597
248.643 10.5111
248.643 10.513
497.286 10.9022
497.286 11.1703
497.286 10.9194
994.572 12.3686
994.572 11.2348
994.572 11.9283
```

Per exponential model

individual animal data	# observations	adverse direction	Run Models	Span	Distribution Curve	MLE Solution
0	*20	0	***0010	33	0	1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

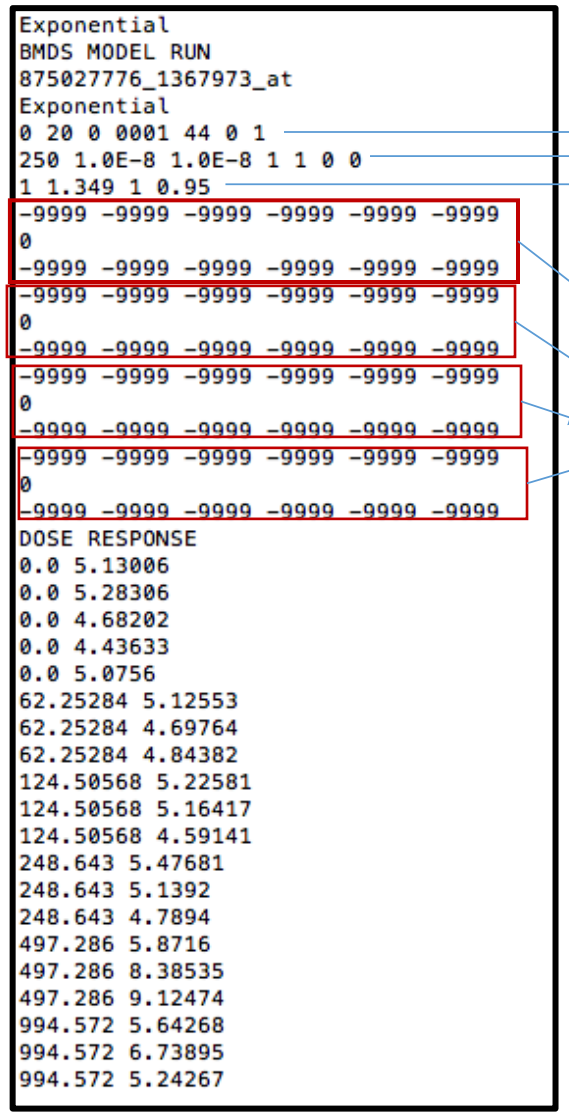
Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

Initialize Parameters
0

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

*** select which exponential model to run
** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Exponential Model 5 Input



```
Exponential
BMDS MODEL RUN
875027776_1367973_at
Exponential
0 20 0 0001 44 0 1
250 1.0E-8 1.0E-8 1 1 0 0
1 1.349 1 0.95
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
-9999 -9999 -9999 -9999 -9999 -9999
0
-9999 -9999 -9999 -9999 -9999 -9999
DOSE RESPONSE
0.0 5.13006
0.0 5.28306
0.0 4.68202
0.0 4.43633
0.0 5.0756
62.25284 5.12553
62.25284 4.69764
62.25284 4.84382
124.50568 5.22581
124.50568 5.16417
124.50568 4.59141
248.643 5.47681
248.643 5.1392
248.643 4.7894
497.286 5.8716
497.286 8.38535
497.286 9.12474
994.572 5.64268
994.572 6.73895
994.572 5.24267
```

Per exponential model

individual animal data	# observations	adverse direction	Run Models	Span	Distribution Curve	MLE Solution
0	*20	0	***0001	44	0	1

Maximum iterations	rel function convergence	parameter convergence	BMDL curve calculation	BMD calculation	append or overwrite output file	smooth option
**250	1.0E-8	1.0E-8	1	1	0	0

BMR Type	BMR Level	Constant Variance	Confidence Level
1	**1.349	**1	**0.95

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

Initialize Parameters
0

Alpha	Rho	a	b	c	d
-9999	-9999	-9999	-9999	-9999	-9999

*** select which exponential model to run
** user supplied
* BMDExpress2 calculated based on user input

BMDExpress2 Workflow – Hill Output

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.0648651	0.0205122	0.024662	0.105068
intercept	6.55888	0.0636716	6.43408	6.68367
v	-1.77745	135.706	-267.757	264.202
n	3.06055	515.18	-1006.67	1012.8
k	0.739444	49.3537	-95.9921	97.471

Intercept	V	n	k
6.55888	-1.77745	3.06055	0.739444

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	17.856850	6	-23.713700
A2	19.237895	10	-18.475789
A3	17.856850	6	-23.713700
fitted	17.354452	5	-24.708904
R	1.273745	2	1.452511

AIC	Log (likelihood)
-24.708904	17.354452

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Adverse direction
-1 (if v < 0)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	35.9283	8	<.0001
Test 2	2.76209	4	0.5984
Test 3	2.76209	4	0.5984
Test 4	1.0048	1	0.3162

Fit P-Value
0.3162

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1.349

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

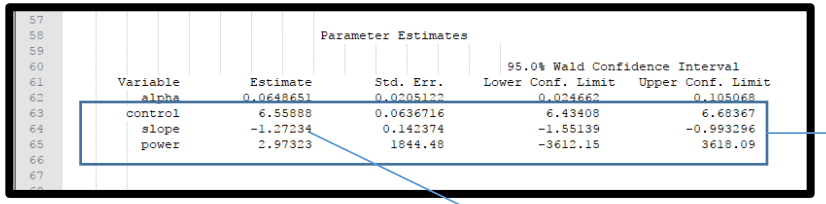
BMD = 0.463624

BMDL = 0.00117758

BMDU = 0.949156

BMD	BMDL	BMDU
0.463624	0.00117758	0.949156

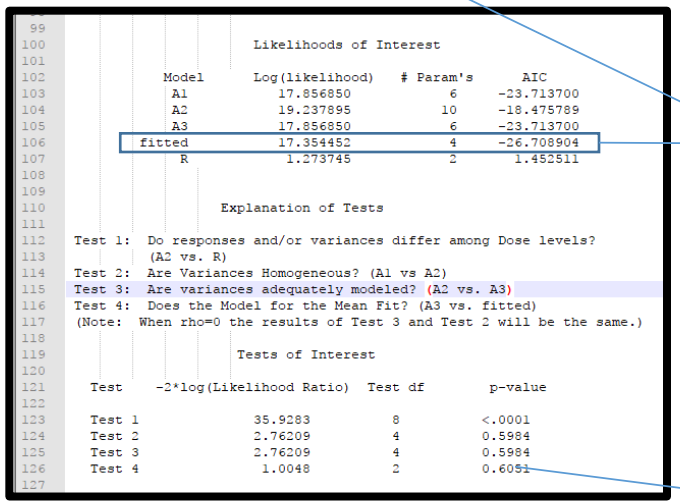
BMDExpress2 Workflow – Power Output



Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.0648651	0.0205122	0.024662	0.105068
control	6.55888	0.0636716	6.43408	6.68367
slope	-1.27234	0.142374	-1.55139	-0.993296
power	2.97323	1844.48	-3612.15	3618.09

control	Slope	Power
6.55888	-1.27234	2.97323



Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	17.856850	6	-23.713700
A2	19.237895	10	-18.475789
A3	17.856850	6	-23.713700
fitted	17.354452	4	-26.708904
R	1.273745	2	1.452511

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

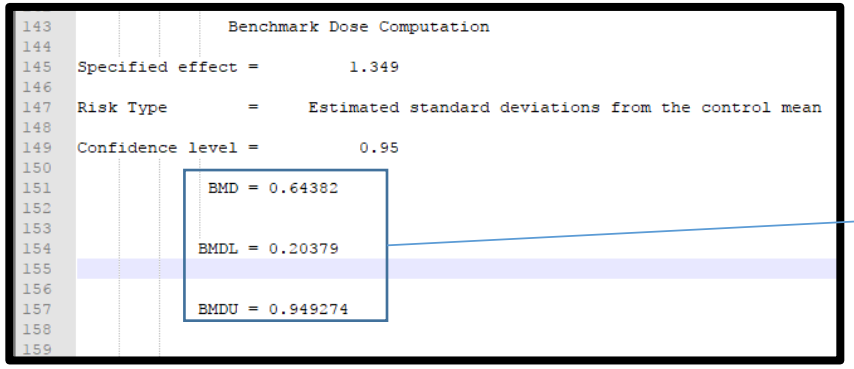
Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	35.9283	8	<.0001
Test 2	2.76209	4	0.5984
Test 3	2.76209	4	0.5984
Test 4	1.0048	2	0.6051

AIC	Log (likelihood)
-26.708904	17.354452

Adverse direction
-1 (if slope < 0)

Fit P-Value
0.6051



Benchmark Dose Computation

Specified effect = 1.349

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 0.64382

BMDL = 0.20379

BMDU = 0.949274

BMD	BMDL	BMDU
0.64382	0.20379	0.949274

BMDExpress2 Workflow – Linear Output

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.342072	0.108173	0.130058	0.554087
beta_0	7.24842	0.172144	6.91102	7.58582
beta_1	0.00278456	0.000387207	0.00202565	0.00354348

Beta_0	Beta_1	
7.24842	0.00278456	

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	13.010761	7	-12.021522
A2	15.035038	12	-6.070077
A3	13.010761	7	-12.021522
fitted	0.727337	3	4.545327
R	-12.042515	2	28.085029

AIC	Log (likelihood)
4.545327	0.727337

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Adverse direction
1 (if beta_1 >0) (beta_1 is used for all degrees of polynomial)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	54.1551	10	<.0001
Test 2	4.04855	5	0.5424
Test 3	4.04855	5	0.5424
Test 4	24.5668	4	<.0001

Fit P-Value
<.0001

Benchmark Dose Computation

Specified effect = 1.349
Risk Type = Estimated standard deviations from the control mean
Confidence level = 0.95

BMD = 283.344
BMDL = 209.504
BMDU = 429.163

BMD	BMDL	BMDU
283.344	209.504	429.163

BMDExpress2 Workflow – Poly 2 Output

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.208956	0.0660776	0.079446	0.338465
beta_0	12.0154	0.164256	11.6935	12.3373
beta_1	0.00705918	0.00112587	0.00485251	0.00926585
beta_2	-4.8569e-06	1.10941e-06	-7.03131e-06	-2.6825e-06

Beta_0	Beta_1	Beta_2
12.0154	0.00705918	-4.8569E-06

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	10.199374	7	-6.398748
A2	17.911202	12	-11.822404
A3	10.199374	7	-6.398748
fitted	5.656331	4	-3.312662
R	-10.185971	2	24.371942

AIC	Log (likelihood)
-3.312662	5.656331

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Adverse direction
1 (if beta_1 > 0) (beta_1 is used for all degrees of polynomial)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	56.1943	10	<.0001
Test 2	15.4237	5	0.008698
Test 3	15.4237	5	0.008698
Test 4	9.08609	3	0.02817

Fit P-Value
0.02817

Benchmark Dose Computation

Specified effect = 1.349
Risk Type = Estimated standard deviations from the control mean
Confidence level = 0.95
BMD = 93.35
BMDL = 66.7565
BMDU = 151.278

BMD	BMDL	BMDU
93.35	66.7565	151.278

BMDExpress2 Workflow – Poly 3 Output

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.141058	0.0446066	0.0536311	0.228486
beta_0	11.7785	0.155067	11.4745	12.0824
beta_1	0.0137887	0.00235794	0.00916722	0.0184102
beta_2	-2.67325e-05	7.10916e-06	-4.06662e-05	-1.27988e-05
beta_3	1.55071e-08	4.99791e-09	5.71136e-09	2.53028e-08

Beta_0	Beta_1	Beta_2	Beta_3
11.7785	0.0137887	-2.67325E-05	1.55071E-08

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	10.199374	7	-6.398748
A2	17.911202	12	-11.822404
A3	10.199374	7	-6.398748
fitted	9.585815	5	-9.171630
R	-10.185971	2	24.371942

AIC	Log (likelihood)
-9.171630	9.585815

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	56.1943	10	<.0001
Test 2	15.4237	5	0.008698
Test 3	15.4237	5	0.008698
Test 4	1.22712	2	0.5414

Adverse direction
1(if beta_1 > 0) (beta_1 is used for all degrees of polynomial)

Fit P-Value
0.5414

Benchmark Dose Computation

Specified effect = 1.349

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

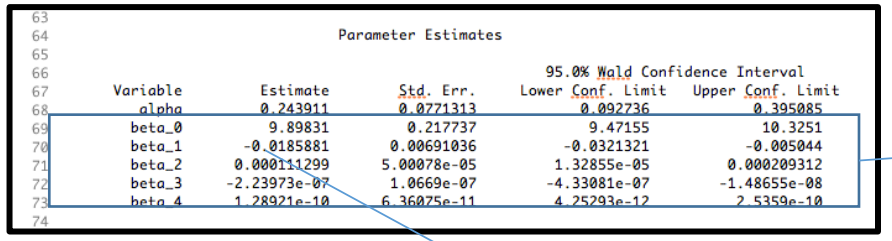
BMD = 39.7345

BMDL = 28.0789

BMDU = 65.8564

BMD	BMDL	BMDU
39.7345	28.0789	65.8564

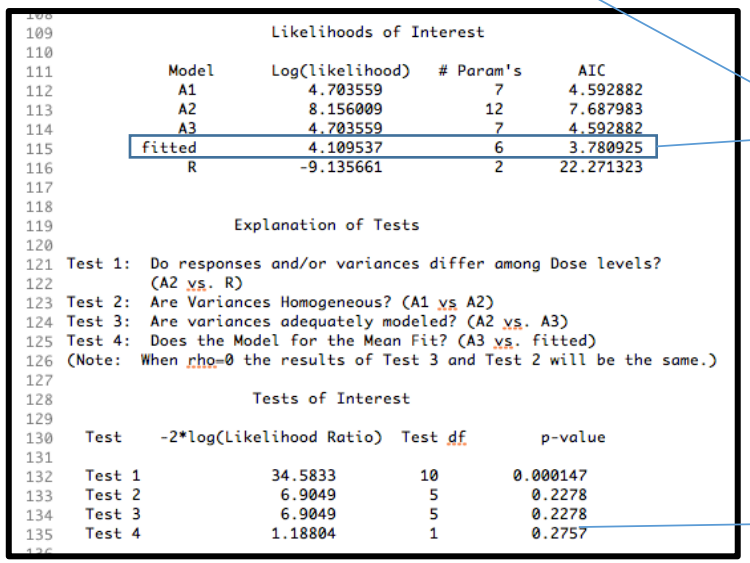
BMDExpress2 Workflow – Poly 4 Output



Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.243911	0.0771313	0.092736	0.395085
beta_0	9.89831	0.217737	9.47155	10.3251
beta_1	-0.0185881	0.00691036	-0.0321321	-0.005044
beta_2	0.000111299	5.00078e-05	1.32855e-05	0.000209312
beta_3	-2.23973e-07	1.0669e-07	-4.33081e-07	-1.48655e-08
beta_4	1.28921e-10	6.36075e-11	4.25293e-12	2.5359e-10

Beta_0	Beta_1	Beta_2	Beta_3	Beta_4
9.89831	-0.0185881	0.000111299	-2.23973E-07	1.28921E-10



Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	4.703559	7	4.592882
A2	8.156009	12	7.687983
A3	4.703559	7	4.592882
fitted	4.109537	6	3.780925
R	-9.135661	2	22.271323

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

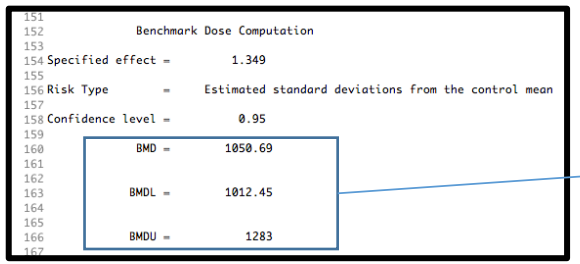
Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	34.5833	10	0.000147
Test 2	6.9049	5	0.2278
Test 3	6.9049	5	0.2278
Test 4	1.18804	1	0.2757

AIC	Log (likelihood)
3.780925	4.109537

Adverse direction
-1 (if beta_1 < 0) (beta_1 is used for all degrees of polynomial)

Fit P-Value
0.2757



Benchmark Dose Computation

Specified effect = 1.349
Risk Type = Estimated standard deviations from the control mean
Confidence level = 0.95
BMD = 1050.69
BMDL = 1012.45
BMDU = 1283

BMD	BMDL	BMDU
1050.69	1012.45	1283

BMDExpress2 Workflow – Exponential Model 2 Output

Parameter Estimates

Variable	Model 2	Std. Err.
lnalpha	0.116966	0.355466
a	5.1112	0.296453
b	0.000261759	0.000110746

a	b	c	d
5.1112	0.000261759		

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-0.9400467	7	15.88009
A2	8.940436	12	6.119129
A3	-0.9400467	7	15.88009
R	-13.44641	2	30.89283
2	-11.16966	3	28.33932

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

AIC	Log (likelihood)
-11.16966	28.33932

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	44.77	10	< 0.0001
Test 2	19.76	5	0.001386
Test 3	19.76	5	0.001386
Test 4	20.46	4	0.0004052

Adverse direction
1 (use trend test)

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.111	1.06	-0.4003
62.25	5.195	1.06	-0.5002
124.5	5.281	1.06	-0.4684
248.6	5.455	1.06	-0.5224
497.3	5.822	1.06	3.222
994.6	6.631	1.06	-1.236

Fit P-Value
0.0004052

Benchmark Dose Computations:

Specified Effect = 1.349000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 942.56

BMDL = 576.845

BMDU = 3727.1

BMD	BMDL	BMDU
942.56	576.845	3727.1

BMDExpress2 Workflow – Exponential Model 3 Output

Parameter Estimates

Variable	Model 3	Std. Err.
lnalpha	-0.855175	0.134463
a	12.4617	0.186879
b	0.000166351	3.0549e-05
d	1	NA

a	b	c	d
12.4617	0.000166351		1

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	10.19937	7	-6.398748
A2	17.9112	12	-11.8224
A3	10.19937	7	-6.398748
R	-10.18597	2	24.37194
3	-1.448242	3	8.896484

Additive constant for all log-likelihoods = -18.38. This constant added to above values gives the log-likelihood including the term that does not depend on the model parameters.

AIC	Log (likelihood)
8.896484	-1.448242

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Adverse direction
1 (use trend test)

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	12.46	0.6521	-2.568
62.25	12.59	0.6521	0.3937
124.5	12.72	0.6521	0.9063
248.6	12.99	0.6521	1.952
497.3	13.54	0.6521	1.117
994.6	14.7	0.6521	-1.064

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	56.19	10	< 0.0001
Test 2	15.42	5	0.008698
Test 3	15.42	5	0.008698
Test 5a	23.3	4	0.0001105

Fit P-Value
0.0001105

Benchmark Dose Computations:

Specified Effect = 1.349000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 410.028

BMDL = 296.801

BMDU = 664.755

BMD	BMDL	BMDU
410.028	296.801	664.755

BMDExpress2 Workflow – Exponential Model 4 Output

Parameter Estimates

Variable	Model 4	Std. Err.
lnalpha	-2.70421	0.021163
a	9.02207	0.104631
b	0.00262571	0.00058857
c	1.32836	0.0283797

a	b	c	d
9.02207	0.00262671	1.32836	

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	20.17103	7	-26.34206
A2	34.02348	12	-44.04696
A3	20.17103	7	-26.34206
R	-10.32324	2	24.64648
4	17.04207	4	-26.08415

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

AIC	Log (likelihood)
-26.08415	17.04207

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	88.69	10	< 0.0001
Test 2	27.7	5	< 0.0001
Test 3	27.7	5	< 0.0001
Test 6a	6.258	3	0.09971

Adverse direction
1 (use trend test)

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	9.022	0.2587	-0.8544
62.25	9.469	0.2587	1.559
124.5	9.848	0.2587	-0.3077
248.6	10.44	0.2587	0.5725
497.3	11.18	0.2587	-1.235
994.6	11.77	0.2587	0.5146

Fit P-Value
0.09971

Benchmark Dose Computations:

Specified Effect = 1.349000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 47.7341

BMDL = 33.6597

BMDU = 75.432

BMD	BMDL	BMDU
47.7341	33.6597	75.432

BMDExpress2 Workflow – Exponential Model 5 Output

Parameter Estimates

Variable	Model 5	Std. Err.
lnalpha	-2.73545	0.0205122
a	6.55888	0.0636716
b	1.6131	33179
c	0.804078	633.024
d	3.19964	9306.47

a	b	c	d
6.55888	1.6131	0.804078	3.19964

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	17.85685	6	-23.7137
A2	19.23789	10	-18.47579
A3	17.85685	6	-23.7137
R	1.273745	2	1.452511
5	17.35445	5	-24.7089

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

AIC	Log (likelihood)
-24.7089	17.35445

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Adverse direction
-1 (use trend test)

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.559	0.2547	-0.8053
1e-006	6.559	0.2547	0.03168
0.0001	6.559	0.2547	0.2616
0.001	6.559	0.2547	0.5119
1	5.287	0.2547	-7.734e-010

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	35.93	8	< 0.0001
Test 2	2.762	4	0.5984
Test 3	2.762	4	0.5984
Test 7a	1.005	1	0.3162

Fit P-Value
0.3162

Benchmark Dose Computations:

Specified Effect = 1.349000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 0.430382

BMDL = 0.00164527

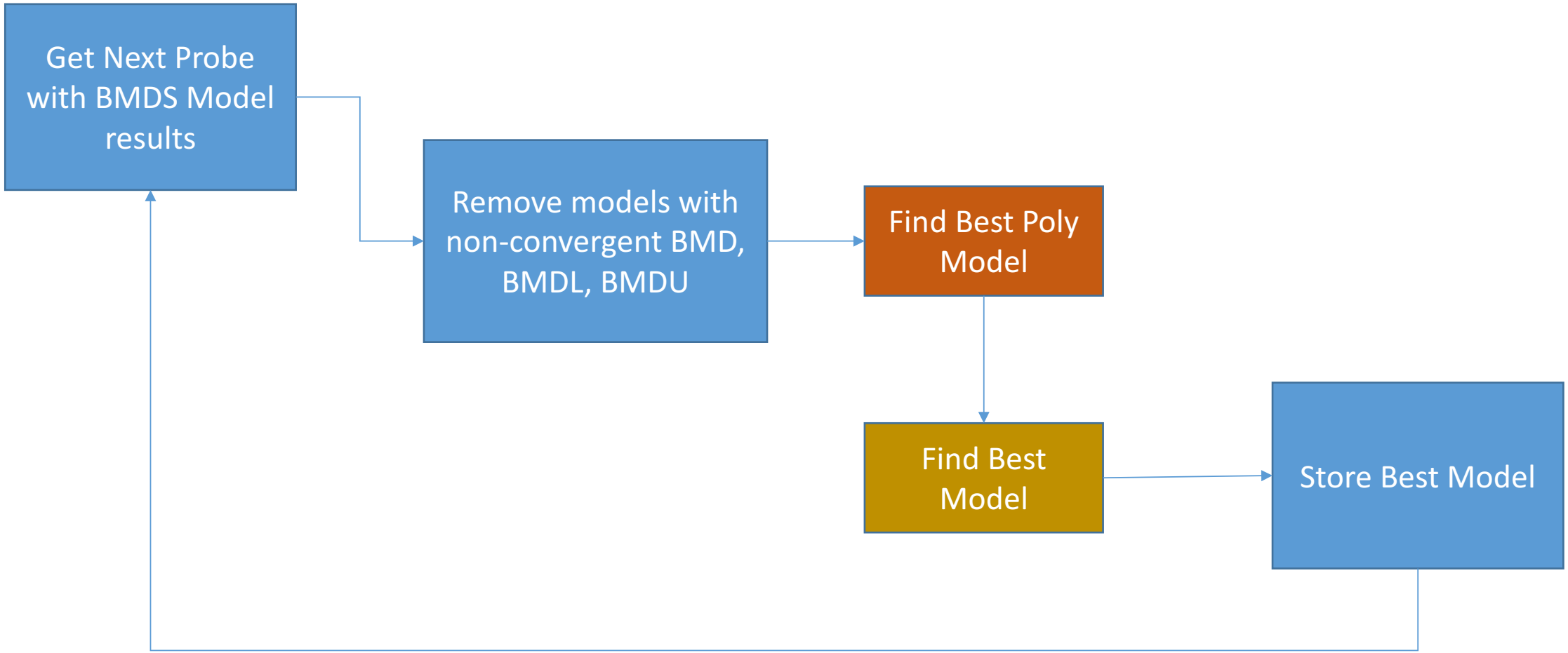
BMDU = 0.946299

BMD	BMDL	BMDU
0.430382	0.00164527	0.946299

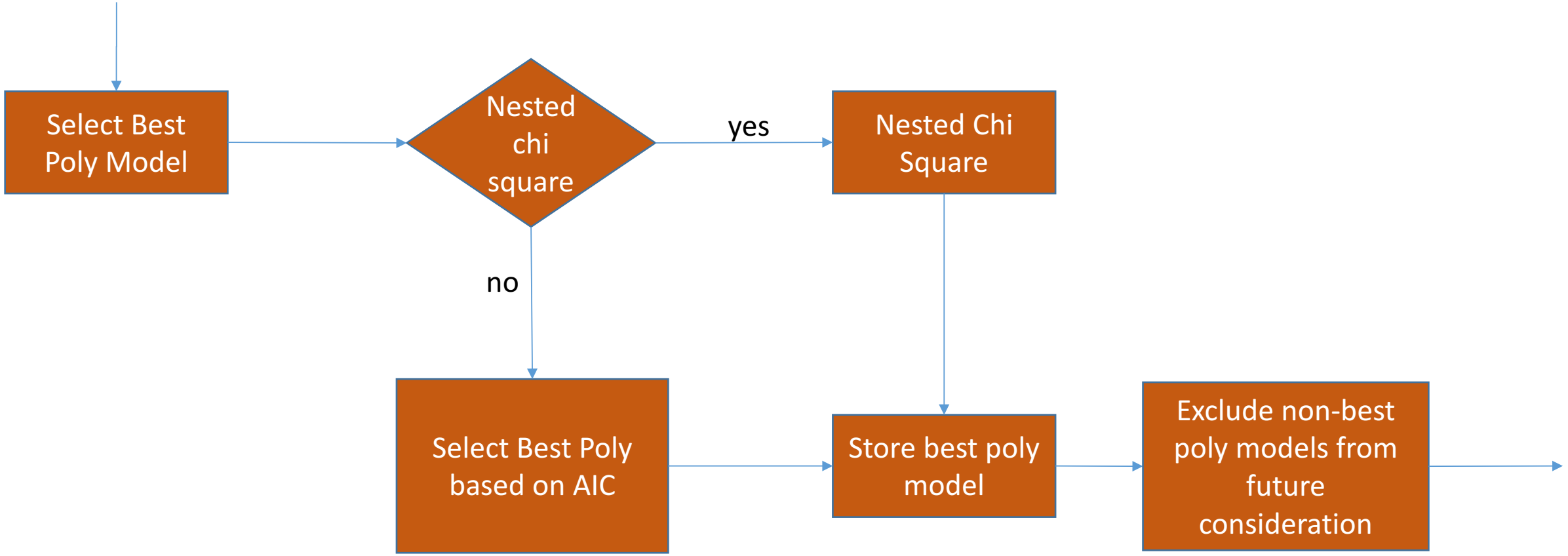
BMDExpress2 Workflow – Best Model Selection

- Best Model Selection
  - Select best poly
    - AIC
    - Nested Chi-squared
  - Select best non-poly
  - Select model from best poly and best non-poly
    - Not Flagged Hill
    - Is Flagged Hill
      - Exclude Flagged Hill from Best
      - Exclude All Hill
      - Modify BMD if Flagged Hill is Best
      - Select next best model with p-value greater than .005

BMDExpress2 Workflow – Select best poly



BMDExpress2 Workflow – Select best poly



BMDExpress2 Workflow – Select best model