

BMDS 3.0 Analysis Report

Marx et al. 2018

For

Liver weight – female – 90-day oral study in rats

18.07.2022 14:23:48

Analysis Info

Analysis Name: Marx et al. 2018 – female

Analysis Description: C:\bmds3201\BMDS3201

Model Type: Continuous

Selected Models:

- Frequentist Log-Logistic (restricted)

Option Sets:

- Option Set #1
 - BMR Type: Std. Dev.
 - BMRF: 1
 - Confidence Level: 0.95
 - Distribution: Normal
 - Variance: Constant
 - Polynomial Restriction: Use dataset adverse direction

Data

| Marx et al. - Liver weight - female | | | |
|---|--------|------|-----------|
| Source: Marx et al. 2018, Table 12, page 21 | | | |
| CBD Dose | N | Mean | Std. Dev. |
| mg/kg bw/day | female | g | g |
| 0 | 10 | 6.42 | 0.4 |
| 25 | 10 | 6.7 | 0.56 |
| 90 | 10 | 7.4 | 0.6 |
| 180 | 10 | 9.21 | 0.54 |

* Note: Dose levels adjusted from hemp extract to CBD assuming 26% of hemp extract are phytocannabinoids, from which 96% are CBD.

Adverse Direction: Automatic

Frequentist Polynomial Restricted Option Set #1

| User Input | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|--|--|-------|--|--------------|-------------------------------------|------------|-----------------------|---------------------|--|---|---------------|--|----------|-----------|------|---|------------------|---|------------------|------|-------------------|--------|--|------------|--|--------------------|--------------|----------------------|---|-------------------------|---|-------------------|-----------|
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| Info | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Model | frequentist Polynomial degree 3 v1.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dataset Name | Marx et al. - Liver weight - female | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| User notes | [Add user notes here] | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose-Response Model | $M[\text{dose}] = g + b_1 * \text{dose} + b_2 * \text{dose}^2 + \dots$ | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Model Options | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| BMR Type | Std. Dev. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| BMRF | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tail Probability | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Confidence Level | 0.95 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Distribution Type | Normal | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Dependent Variable | mg/kg bw/day | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Independent Variable | g | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total # of Observations | 4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adverse Direction | Automatic | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

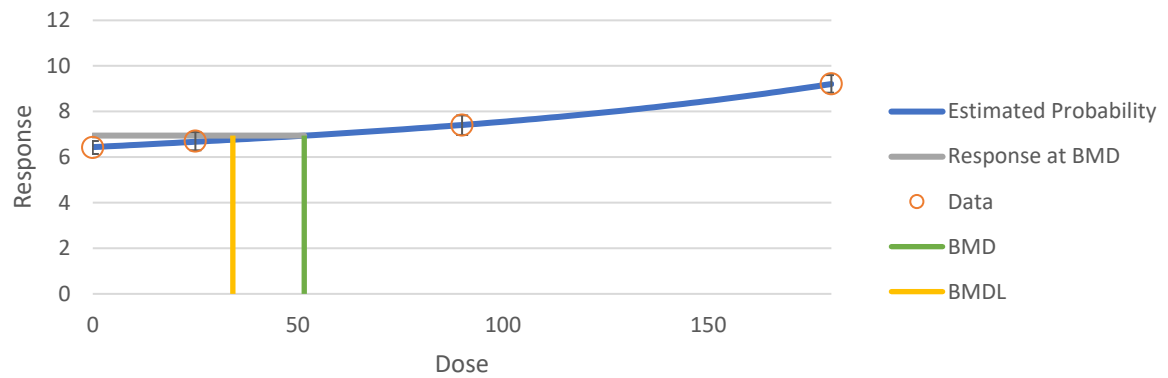
| Model Results | | | | | | | | | | | | | | | |
|---|-------------|------------------|--|-----------------|-------------|----------|-------------|------|-------------|-------|-------------|----------------|-------------|--------|---------|
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| Benchmark Dose | | | | | | | | | | | | | | | |
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| Model Parameters | | | | | | | | | | | | | | | |
| # of Parameters | 5 | | | | | | | | | | | | | | |
| Variable | Estimate | | | | | | | | | | | | | | |
| g | 6.438430792 | | | | | | | | | | | | | | |
| beta1 | 0.00926048 | | | | | | | | | | | | | | |
| beta2 | Bounded | | | | | | | | | | | | | | |
| beta3 | Bounded | | | | | | | | | | | | | | |

| Goodness of Fit | | | | | | | | |
|-----------------|------|------------------|---------------|---------------|--------------|-----------|-------------|-----------------|
| Dose | Size | Estimated Median | Calc'd Median | Observed Mean | Estimated SD | Calc'd SD | Observed SD | Scaled Residual |
| 0 | 10 | 6.438430792 | 6.42 | 6.42 | 0.50312864 | 0.4 | 0.4 | -0.115841709 |
| 25 | 10 | 6.672899785 | 6.7 | 6.7 | 0.50312864 | 0.56 | 0.56 | 0.170330999 |
| 90 | 10 | 7.409835735 | 7.4 | 7.4 | 0.50312864 | 0.6 | 0.6 | -0.061819829 |
| 180 | 10 | 9.209011272 | 9.21 | 9.21 | 0.50312864 | 0.54 | 0.54 | 0.006214381 |

| Likelihoods of Interest | | | |
|-------------------------|-----------------|-----------------|------------|
| Model | Log Likelihood* | # of Parameters | AIC |
| A1 | -29.28365975 | 5 | 68.5673195 |
| A2 | -28.41912111 | 8 | 72.8382422 |
| A3 | -29.28365975 | 5 | 68.5673195 |
| fitted | -29.30680603 | 3 | 64.6136121 |
| R | -63.96325219 | 2 | 131.926504 |

| Tests of Interest | | | |
|-------------------|--------------------------|---------|------------|
| Test | -2*Log(Likelihood Ratio) | Test df | p-value |
| 1 | 71.08826215 | 6 | <0.0001 |
| 2 | 1.729077269 | 3 | 0.63048872 |
| 3 | 1.729077269 | 3 | 0.63048872 |
| 4 | 0.046292569 | 2 | 0.97711954 |

Frequentist Polynomial Degree 3 Model with BMR of 1 Std.
Dev. for the BMD and 0.95 Lower Confidence Limit for the
BMDL



Frequentist Polynomial Restricted Option Set #1

| User Input | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|--|--|-------|---|--------------|-------------------------------------|------------|-----------------------|---------------------|--|---|---------------|--|----------|-----------|------|---|------------------|---|------------------|------|-------------------|--------|--|------------|--|--------------------|--------------|----------------------|---|-------------------------|---|-------------------|-----------|
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| Info | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Dataset Name | Marx et al. - Liver weight - female | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Model Options | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| BMR Type | Std. Dev. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| BMRF | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tail Probability | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Confidence Level | 0.95 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Distribution Type | Normal | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Model Data | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dependent Variable | mg/kg bw/day | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Independent Variable | g | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total # of Observations | 4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adverse Direction | Automatic | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

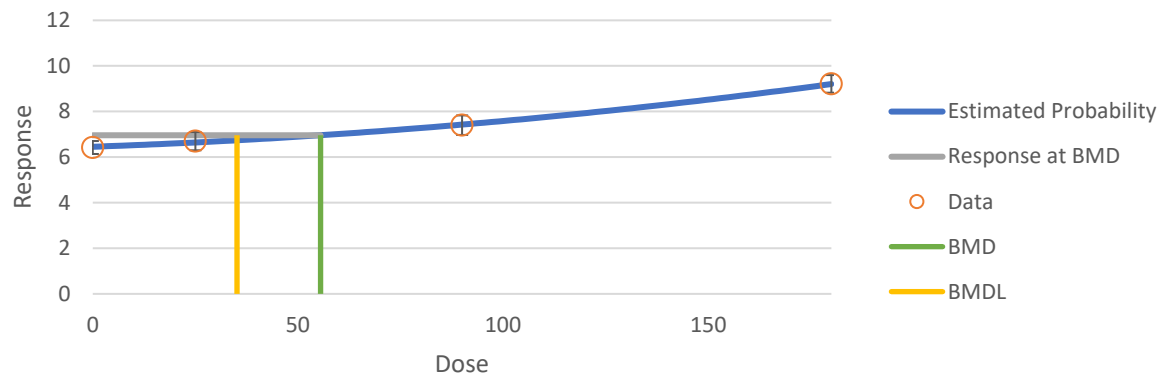
| Model Results | | | | | | | | | | | | | | | |
|---|-------------|------------------|--|-----------------|-------------|----------|-------------|------|-------------|-------|-------------|----------------|-------------|--------|---|
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| # of Parameters | 4 | | | | | | | | | | | | | | |
| Variable | Estimate | | | | | | | | | | | | | | |
| g | 6.454825157 | | | | | | | | | | | | | | |
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| beta2 | 4.97303E-05 | | | | | | | | | | | | | | |

| Goodness of Fit | | | | | | | | |
|-----------------|------|------------------|---------------|---------------|--------------|-----------|-------------|-----------------|
| Dose | Size | Estimated Median | Calc'd Median | Observed Mean | Estimated SD | Calc'd SD | Observed SD | Scaled Residual |
| 0 | 10 | 6.454825157 | 6.42 | 6.42 | 0.50442482 | 0.4 | 0.4 | -0.218321561 |
| 25 | 10 | 6.644003235 | 6.7 | 6.7 | 0.50442482 | 0.56 | 0.56 | 0.351047985 |
| 90 | 10 | 7.426788568 | 7.4 | 7.4 | 0.50442482 | 0.6 | 0.6 | -0.167939572 |
| 180 | 10 | 9.20438304 | 9.21 | 9.21 | 0.50442482 | 0.54 | 0.54 | 0.035213153 |

| Likelihoods of Interest | | | |
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| Model | Log Likelihood* | # of Parameters | AIC |
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| R | -63.96325219 | 2 | 131.926504 |

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| 2 | 1.729077269 | 3 | 0.63048872 |
| 3 | 1.729077269 | 3 | 0.63048872 |
| 4 | 0.200846052 | 1 | 0.6540388 |

Frequentist Polynomial Degree 2 Model with BMR of 1 Std.
Dev. for the BMD and 0.95 Lower Confidence Limit for the
BMDL



Summary of Results

| Option set #1 (Hover for details) | | | | | | | | | | | |
|--|---------------|-------------|-----------|----------|----------|-----------|----------------|-------------|--|----------------------|---------------------------|
| Model | Analysis Type | Restriction | RiskType | BMD | BMDL | BMDU | Test 4 P-Value | AIC | Unnormalized Log Posterior Probability | BMDS Recommendation | BMDS Recommendation Notes |
| Polynomial Degree 3 (CV - normal)* | frequentist | Restricted | Std. Dev. | 51.53386 | 34.11537 | 84.631691 | 0.9771195 | 64.61361206 | - | Viable - Recommended | Lowest AIC |
| Polynomial Degree 2 (CV - normal) | frequentist | Restricted | Std. Dev. | 55.52267 | 35.13466 | 84.530023 | 0.6540388 | 66.76816555 | - | Viable - Alternate | |

*Constant variance case presented (BMDS Test 2 p-value = 0.630488719567165), with the selected model in bold; scaled residuals for selected model for doses 0, 25, 90, 180 were -0.115841708701134, 0.170330999055086, -0.061819828632339, 6.21438086272044E-03 [units], respectively.

