

1,3,5-トリス (2,3-エポキシプロピル) ヘキサヒドロ-1,3,5-トリアジン-  
2,4,6-トリオンの p53 KO マウスを用いた強制経口投与による  
中期発がん性試験報告書

試験番号 : 0923, 0924

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TABLE A 1

SURVIVAL ANIMAL NUMBERS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 0-0   | 1-1            | 1-2            | 1-3            | 1-4            | 1-5            | 1-6            | 1-7            | 2-1            | 2-2            | 2-3            | 2-4            | 2-5            | 2-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 2-7   | 3-1            | 3-2            | 3-3            | 3-4            | 3-5            | 3-6            | 3-7            | 4-1            | 4-2            | 4-3            | 4-4            | 4-5            | 4-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 4-7   | 5-1            | 5-2            | 5-3            | 5-4            | 5-5            | 5-6            | 5-7            | 6-1            | 6-2            | 6-3            | 6-4            | 6-5            | 6-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 6-7   | 7-1            | 7-2            | 7-3            | 7-4            | 7-5            | 7-6            | 7-7            | 8-1            | 8-2            | 8-3            | 8-4            | 8-5            | 8-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 8-7   | 9-1            | 9-2            | 9-3            | 9-4            | 9-5            | 9-6            | 9-7            | 10-1           | 10-2           | 10-3           | 10-4           | 10-5           | 10-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 10-7  | 11-1           | 11-2           | 11-3           | 11-4           | 11-5           | 11-6           | 11-7           | 12-1           | 12-2           | 12-3           | 12-4           | 12-5           | 12-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 23/25<br>92.0   | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 21/25<br>84.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 12-7  | 13-1           | 13-2           | 13-3           | 13-4           | 13-5           | 13-6           | 13-7           | 14-1           | 14-2           | 14-3           | 14-4           | 14-5           | 14-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 17/25<br>68.0   | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 14-7  | 15-1           | 15-2           | 15-3           | 15-4           | 15-5           | 15-6           | 15-7           | 16-1           | 16-2           | 16-3           | 16-4           | 16-5           | 16-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 17/25<br>68.0   | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  | 17/25<br>68.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 16-7  | 17-1           | 17-2           | 17-3           | 17-4           | 17-5           | 17-6           | 17-7           | 18-1           | 18-2           | 18-3           | 18-4           | 18-5           | 18-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 17/25<br>68.0   | 17/25<br>68.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 18-7  | 19-1           | 19-2           | 19-3           | 19-4           | 19-5           | 19-6           | 19-7           | 20-1           | 20-2           | 20-3           | 20-4           | 20-5           | 20-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 30 mg/kg        | 25                  | 16/25<br>64.0   | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 16/25<br>64.0  | 15/25<br>60.0  | 15/25<br>60.0  | 15/25<br>60.0  | 15/25<br>60.0  | 15/25<br>60.0  | 15/25<br>60.0  | 15/25<br>60.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 20-7  | 21-1           | 21-2           | 21-3           | 21-4           | 21-5           | 21-6           | 21-7           | 22-1           | 22-2           | 22-3           | 22-4           | 22-5           | 22-6           |                |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 30 mg/kg        | 25                  | 15/25<br>60.0   | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 14/25<br>56.0  | 13/25<br>52.0  | 13/25<br>52.0  | 13/25<br>52.0  | 11/25<br>44.0  | 11/25<br>44.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 22-7  | 23-1           | 23-2           | 23-3           | 23-4           | 23-5           | 23-6           | 23-7           | 24-1           | 24-2           | 24-3           | 24-4           | 24-5           | 24-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 22/25<br>88.0  | 21/25<br>84.0  |
| 30 mg/kg        | 25                  | 11/25<br>44.0   | 11/25<br>44.0  | 10/25<br>40.0  | 10/25<br>40.0  | 10/25<br>40.0  | 10/25<br>40.0  | 10/25<br>40.0  | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 24-7  | 25-1           | 25-2           | 25-3           | 25-4           | 25-5           | 25-6           | 25-7           | 26-1           | 26-2           | 26-3           | 26-4           | 26-5           | 26-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 21/25<br>84.0   | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 19/25<br>76.0  | 19/25<br>76.0  | 19/25<br>76.0  | 19/25<br>76.0  | 18/25<br>72.0  |
| 30 mg/kg        | 25                  | 9/25<br>36.0  | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 9/25<br>36.0   | 8/25<br>32.0   | 8/25<br>32.0   | 8/25<br>32.0   | 8/25<br>32.0   |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days) |                |
|-----------------|---------------------|-----------------------|----------------|
|                 |                     | 26-7                  | 27-1           |
| Vehicle Control | 25                  | 24/25<br>96.0         | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 25/25<br>100.0        | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 18/25<br>72.0         | 18/25<br>72.0  |
| 30 mg/kg        | 25                  | 8/25<br>32.0          | 7/25<br>28.0   |

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Number of survival/ Number of effective animals  
Survival rate(%)

TABLE A 2

SURVIVAL ANIMAL NUMBERS : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 0-0   | 1-1            | 1-2            | 1-3            | 1-4            | 1-5            | 1-6            | 1-7            | 2-1            | 2-2            | 2-3            | 2-4            | 2-5            | 2-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 2-7   | 3-1            | 3-2            | 3-3            | 3-4            | 3-5            | 3-6            | 3-7            | 4-1            | 4-2            | 4-3            | 4-4            | 4-5            | 4-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0924

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days) |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|-----------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 4-7                   | 5-1            | 5-2            | 5-3            | 5-4            | 5-5            | 5-6            | 5-7            | 6-1            | 6-2            | 6-3            | 6-4            | 6-5            | 6-6            |
| Vehicle Control | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |

Number of survival/ Number of effective animals  
Survival rate(%)

STUDY NO. : 0924

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days) |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|-----------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 6-7                   | 7-1            | 7-2            | 7-3            | 7-4            | 7-5            | 7-6            | 7-7            | 8-1            | 8-2            | 8-3            | 8-4            | 8-5            | 8-6            |
| Vehicle Control | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0        | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |

Number of survival/ Number of effective animals  
Survival rate(%)

STUDY NO. : 0924

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 8-7   | 9-1            | 9-2            | 9-3            | 9-4            | 9-5            | 9-6            | 9-7            | 10-1           | 10-2           | 10-3           | 10-4           | 10-5           | 10-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 23/25<br>92.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

(HAN360)

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STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 10-7  | 11-1           | 11-2           | 11-3           | 11-4           | 11-5           | 11-6           | 11-7           | 12-1           | 12-2           | 12-3           | 12-4           | 12-5           | 12-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 23/25<br>92.0   | 23/25<br>92.0  | 23/25<br>92.0  | 23/25<br>92.0  | 22/25<br>88.0  | 22/25<br>88.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 21/25<br>84.0  | 20/25<br>80.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 12-7  | 13-1           | 13-2           | 13-3           | 13-4           | 13-5           | 13-6           | 13-7           | 14-1           | 14-2           | 14-3           | 14-4           | 14-5           | 14-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| 30 mg/kg        | 25                  | 20/25<br>80.0   | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 20/25<br>80.0  | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 14-7  | 15-1           | 15-2           | 15-3           | 15-4           | 15-5          | 15-6          | 15-7          | 16-1          | 16-2          | 16-3          | 16-4          | 16-5          | 16-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 30 mg/kg        | 25                  | 18/25<br>72.0   | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0  | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 18/25<br>72.0 | 17/25<br>68.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |               |               |               |               |               |               |               |               |               |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |               |               |               |               |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 16-7  | 17-1          | 17-2          | 17-3          | 17-4          | 17-5          | 17-6          | 17-7          | 18-1          | 18-2          | 18-3          | 18-4          | 18-5          | 18-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 30 mg/kg        | 25                  | 17/25<br>68.0   | 17/25<br>68.0 | 17/25<br>68.0 | 17/25<br>68.0 | 17/25<br>68.0 | 17/25<br>68.0 | 16/25<br>64.0 | 16/25<br>64.0 | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |               |               |               |               |               |               |               |               |               |               |               |               |               |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |               |               |               |               |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 18-7  | 19-1          | 19-2          | 19-3          | 19-4          | 19-5          | 19-6          | 19-7          | 20-1          | 20-2          | 20-3          | 20-4          | 20-5          | 20-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 23/25<br>92.0 | 23/25<br>92.0 | 23/25<br>92.0 | 23/25<br>92.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 |
| 30 mg/kg        | 25                  | 15/25<br>60.0   | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 | 15/25<br>60.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 | 14/25<br>56.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |               |               |               |               |               |               |               |               |               |               |               |               |               |



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |               |               |               |               |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 20-7  | 21-1          | 21-2          | 21-3          | 21-4          | 21-5          | 21-6          | 21-7          | 22-1          | 22-2          | 22-3          | 22-4          | 22-5          | 22-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 22/25<br>88.0   | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 | 22/25<br>88.0 |
| 30 mg/kg        | 25                  | 14/25<br>56.0   | 13/25<br>52.0 | 13/25<br>52.0 | 13/25<br>52.0 | 13/25<br>52.0 | 13/25<br>52.0 | 12/25<br>48.0 | 12/25<br>48.0 | 11/25<br>44.0 | 10/25<br>40.0 | 10/25<br>40.0 | 10/25<br>40.0 | 10/25<br>40.0 | 10/25<br>40.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |               |               |               |               |               |               |               |               |               |               |               |               |               |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |               |               |               |               |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 22-7  | 23-1          | 23-2          | 23-3          | 23-4          | 23-5          | 23-6          | 23-7          | 24-1          | 24-2          | 24-3          | 24-4          | 24-5          | 24-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 21/25<br>84.0   | 21/25<br>84.0 | 21/25<br>84.0 | 21/25<br>84.0 | 21/25<br>84.0 | 20/25<br>80.0 | 20/25<br>80.0 | 20/25<br>80.0 | 20/25<br>80.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 |
| 30 mg/kg        | 25                  | 10/25<br>40.0   | 10/25<br>40.0 | 8/25<br>32.0  | 6/25<br>24.0  | 6/25<br>24.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |               |               |               |               |               |               |               |               |               |               |               |               |               |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |               |               |               |               |               |               |               |               |               |               |               |               |               |
|-----------------|---------------------|---|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                 |                     | 24-7  | 25-1          | 25-2          | 25-3          | 25-4          | 25-5          | 25-6          | 25-7          | 26-1          | 26-2          | 26-3          | 26-4          | 26-5          | 26-6          |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0   | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 19/25<br>76.0   | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 | 19/25<br>76.0 |
| 30 mg/kg        | 25                  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  | 5/25<br>20.0  |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |               |               |               |               |               |               |               |               |               |               |               |               |               |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days) |               |
|-----------------|---------------------|-----------------------|---------------|
|                 |                     | 26-7                  | 27-1          |
| Vehicle Control | 25                  | 24/25<br>96.0         | 24/25<br>96.0 |
| 3 mg/kg         | 25                  | 24/25<br>96.0         | 24/25<br>96.0 |
| 10 mg/kg        | 25                  | 18/25<br>72.0         | 18/25<br>72.0 |
| 30 mg/kg        | 25                  | 5/25<br>20.0          | 5/25<br>20.0  |

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Number of survival/ Number of effective animals  
Survival rate(%)

TABLE A 3

CLINICAL OBSERVATION : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 1

| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 1-1<br>1                | 1-1<br>2 | 1-2<br>1 | 1-2<br>2 | 1-3<br>1 | 1-3<br>2 | 1-4<br>1 | 1-4<br>2 | 1-5<br>1 | 1-5<br>2 | 1-6<br>1 | 1-6<br>2 | 1-7<br>1 | 1-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 2

| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 2-1<br>1                | 2-1<br>2 | 2-2<br>1 | 2-2<br>2 | 2-3<br>1 | 2-3<br>2 | 2-4<br>1 | 2-4<br>2 | 2-5<br>1 | 2-5<br>2 | 2-6<br>1 | 2-6<br>2 | 2-7<br>1 | 2-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 3-1<br>1                | 3-1<br>2 | 3-2<br>1 | 3-2<br>2 | 3-3<br>1 | 3-3<br>2 | 3-4<br>1 | 3-4<br>2 | 3-5<br>1 | 3-5<br>2 | 3-6<br>1 | 3-6<br>2 | 3-7<br>1 | 3-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |



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|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 4-1<br>1                | 4-1<br>2 | 4-2<br>1 | 4-2<br>2 | 4-3<br>1 | 4-3<br>2 | 4-4<br>1 | 4-4<br>2 | 4-5<br>1 | 4-5<br>2 | 4-6<br>1 | 4-6<br>2 | 4-7<br>1 | 4-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 5-1<br>1                | 5-1<br>2 | 5-2<br>1 | 5-2<br>2 | 5-3<br>1 | 5-3<br>2 | 5-4<br>1 | 5-4<br>2 | 5-5<br>1 | 5-5<br>2 | 5-6<br>1 | 5-6<br>2 | 5-7<br>1 | 5-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 6-1<br>1                | 6-1<br>2 | 6-2<br>1 | 6-2<br>2 | 6-3<br>1 | 6-3<br>2 | 6-4<br>1 | 6-4<br>2 | 6-5<br>1 | 6-5<br>2 | 6-6<br>1 | 6-6<br>2 | 6-7<br>1 | 6-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 7-1<br>1                | 7-1<br>2 | 7-2<br>1 | 7-2<br>2 | 7-3<br>1 | 7-3<br>2 | 7-4<br>1 | 7-4<br>2 | 7-5<br>1 | 7-5<br>2 | 7-6<br>1 | 7-6<br>2 | 7-7<br>1 | 7-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 8-1<br>1                | 8-1<br>2 | 8-2<br>1 | 8-2<br>2 | 8-3<br>1 | 8-3<br>2 | 8-4<br>1 | 8-4<br>2 | 8-5<br>1 | 8-5<br>2 | 8-6<br>1 | 8-6<br>2 | 8-7<br>1 | 8-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 9-1<br>1                | 9-1<br>2 | 9-2<br>1 | 9-2<br>2 | 9-3<br>1 | 9-3<br>2 | 9-4<br>1 | 9-4<br>2 | 9-5<br>1 | 9-5<br>2 | 9-6<br>1 | 9-6<br>2 | 9-7<br>1 | 9-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 1        | 1        | 1        | 1        | 1        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 0        | 0        | 0        | 0        | 1        | 1        |
| TRAUMA                  | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 0        | 0        | 0        | 0        | 0        | 0        |
| M. FORELIMB             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 1        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |

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|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 10-1<br>1               | 10-1<br>2 | 10-2<br>1 | 10-2<br>2 | 10-3<br>1 | 10-3<br>2 | 10-4<br>1 | 10-4<br>2 | 10-5<br>1 | 10-5<br>2 | 10-6<br>1 | 10-6<br>2 | 10-7<br>1 | 10-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 11-1<br>1               | 11-1<br>2 | 11-2<br>1 | 11-2<br>2 | 11-3<br>1 | 11-3<br>2 | 11-4<br>1 | 11-4<br>2 | 11-5<br>1 | 11-5<br>2 | 11-6<br>1 | 11-6<br>2 | 11-7<br>1 | 11-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 3         | 3         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 1                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |



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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 12-1<br>1               | 12-1<br>2 | 12-2<br>1 | 12-2<br>2 | 12-3<br>1 | 12-3<br>2 | 12-4<br>1 | 12-4<br>2 | 12-5<br>1 | 12-5<br>2 | 12-6<br>1 | 12-6<br>2 | 12-7<br>1 | 12-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 3                       | 4         | 4         | 4         | 4         | 4         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 0         | 0         | 0         | 0         | 2         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 3         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 0         | 0         | 0         | 0         | 3         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 13-1<br>1               | 13-1<br>2 | 13-2<br>1 | 13-2<br>2 | 13-3<br>1 | 13-3<br>2 | 13-4<br>1 | 13-4<br>2 | 13-5<br>1 | 13-5<br>2 | 13-6<br>1 | 13-6<br>2 | 13-7<br>1 | 13-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 14-1<br>1               | 14-1<br>2 | 14-2<br>1 | 14-2<br>2 | 14-3<br>1 | 14-3<br>2 | 14-4<br>1 | 14-4<br>2 | 14-5<br>1 | 14-5<br>2 | 14-6<br>1 | 14-6<br>2 | 14-7<br>1 | 14-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 15-1<br>1               | 15-1<br>2 | 15-2<br>1 | 15-2<br>2 | 15-3<br>1 | 15-3<br>2 | 15-4<br>1 | 15-4<br>2 | 15-5<br>1 | 15-5<br>2 | 15-6<br>1 | 15-6<br>2 | 15-7<br>1 | 15-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 16-1<br>1               | 16-1<br>2 | 16-2<br>1 | 16-2<br>2 | 16-3<br>1 | 16-3<br>2 | 16-4<br>1 | 16-4<br>2 | 16-5<br>1 | 16-5<br>2 | 16-6<br>1 | 16-6<br>2 | 16-7<br>1 | 16-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 17-1<br>1               | 17-1<br>2 | 17-2<br>1 | 17-2<br>2 | 17-3<br>1 | 17-3<br>2 | 17-4<br>1 | 17-4<br>2 | 17-5<br>1 | 17-5<br>2 | 17-6<br>1 | 17-6<br>2 | 17-7<br>1 | 17-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 7                       | 7         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 18-1<br>1               | 18-1<br>2 | 18-2<br>1 | 18-2<br>2 | 18-3<br>1 | 18-3<br>2 | 18-4<br>1 | 18-4<br>2 | 18-5<br>1 | 18-5<br>2 | 18-6<br>1 | 18-6<br>2 | 18-7<br>1 | 18-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 8                       | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 19-1<br>1               | 19-1<br>2 | 19-2<br>1 | 19-2<br>2 | 19-3<br>1 | 19-3<br>2 | 19-4<br>1 | 19-4<br>2 | 19-5<br>1 | 19-5<br>2 | 19-6<br>1 | 19-6<br>2 | 19-7<br>1 | 19-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         |
|                         | 30 mg/kg        | 8                       | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 9         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |



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| Clinical sign           | Group Name      | Administration Week-day |   |      |   |      |   |      |   |      |   |      |   |      |   |
|-------------------------|-----------------|-------------------------|---|------|---|------|---|------|---|------|---|------|---|------|---|
|                         |                 | 20-1                    |   | 20-2 |   | 20-3 |   | 20-4 |   | 20-5 |   | 20-6 |   | 20-7 |   |
|                         |                 | 1                       | 2 | 1    | 2 | 1    | 2 | 1    | 2 | 1    | 2 | 1    | 2 | 1    | 2 |
| DEATH                   | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 1                       | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 1                       | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 |
|                         | 30 mg/kg        | 9                       | 9 | 9    | 9 | 9    | 9 | 9    | 9 | 9    | 9 | 9    | 9 | 9    | 9 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| TRAUMA                  | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| INTERNAL MASS           | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| M. FORELIMB             | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| ANEMIA                  | Vehicle Control | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
| EROSION                 | Vehicle Control | 1                       | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 | 1    | 1 |
|                         | 3 mg/kg         | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 10 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |
|                         | 30 mg/kg        | 0                       | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 | 0    | 0 |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 21-1<br>1               | 21-1<br>2 | 21-2<br>1 | 21-2<br>2 | 21-3<br>1 | 21-3<br>2 | 21-4<br>1 | 21-4<br>2 | 21-5<br>1 | 21-5<br>2 | 21-6<br>1 | 21-6<br>2 | 21-7<br>1 | 21-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 10                      | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 22-1                    |    | 22-2 |    | 22-3 |    | 22-4 |    | 22-5 |    | 22-6 |    | 22-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 10                      | 10 | 11   | 11 | 11   | 11 | 11   | 11 | 13   | 13 | 13   | 13 | 13   | 13 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| TRAUMA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| M. FORELIMB             | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 23-1                    |    | 23-2 |    | 23-3 |    | 23-4 |    | 23-5 |    | 23-6 |    | 23-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 2    | 2  | 2    | 2  | 2    | 2  |
|                         | 30 mg/kg        | 13                      | 13 | 14   | 14 | 14   | 14 | 14   | 14 | 14   | 14 | 14   | 14 | 15   | 15 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| TRAUMA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| M. FORELIMB             | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 24-1                    |    | 24-2 |    | 24-3 |    | 24-4 |    | 24-5 |    | 24-6 |    | 24-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 2                       | 2  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  |
|                         | 30 mg/kg        | 15                      | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| TRAUMA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| M. FORELIMB             | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 25-1                    |    | 25-2 |    | 25-3 |    | 25-4 |    | 25-5 |    | 25-6 |    | 25-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 3                       | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 4  | 4    | 4  |
|                         | 30 mg/kg        | 15                      | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 | 15   | 15 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| TRAUMA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| M. FORELIMB             | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 26-1<br>1               | 26-1<br>2 | 26-2<br>1 | 26-2<br>2 | 26-3<br>1 | 26-3<br>2 | 26-4<br>1 | 26-4<br>2 | 26-5<br>1 | 26-5<br>2 | 26-6<br>1 | 26-6<br>2 | 26-7<br>1 | 26-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 2         | 2         | 2         | 2         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 4                       | 4         | 4         | 5         | 5         | 5         | 5         | 5         | 5         | 5         | 5         | 5         | 5         | 5         |
|                         | 30 mg/kg        | 15                      | 15        | 15        | 15        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |

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| Clinical sign           | Group Name      | Administration Week-day |           |
|-------------------------|-----------------|-------------------------|-----------|
|                         |                 | 27-1<br>1               | 27-1<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 2                       | 2         |
|                         | 30 mg/kg        | 2                       | 2         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 5                       | 5         |
|                         | 30 mg/kg        | 16                      | 16        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| TRAUMA                  | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| EXTERNAL MASS           | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 1                       | 1         |
|                         | 30 mg/kg        | 0                       | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| M. FORELIMB             | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 1                       | 1         |
|                         | 30 mg/kg        | 0                       | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| EROSION                 | Vehicle Control | 1                       | 0         |
|                         | 3 mg/kg         | 1                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 1                       | 1         |



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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 1-1<br>1                | 1-1<br>2 | 1-2<br>1 | 1-2<br>2 | 1-3<br>1 | 1-3<br>2 | 1-4<br>1 | 1-4<br>2 | 1-5<br>1 | 1-5<br>2 | 1-6<br>1 | 1-6<br>2 | 1-7<br>1 | 1-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 2-1<br>1                | 2-1<br>2 | 2-2<br>1 | 2-2<br>2 | 2-3<br>1 | 2-3<br>2 | 2-4<br>1 | 2-4<br>2 | 2-5<br>1 | 2-5<br>2 | 2-6<br>1 | 2-6<br>2 | 2-7<br>1 | 2-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 3-1<br>1                | 3-1<br>2 | 3-2<br>1 | 3-2<br>2 | 3-3<br>1 | 3-3<br>2 | 3-4<br>1 | 3-4<br>2 | 3-5<br>1 | 3-5<br>2 | 3-6<br>1 | 3-6<br>2 | 3-7<br>1 | 3-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 4-1<br>1                | 4-1<br>2 | 4-2<br>1 | 4-2<br>2 | 4-3<br>1 | 4-3<br>2 | 4-4<br>1 | 4-4<br>2 | 4-5<br>1 | 4-5<br>2 | 4-6<br>1 | 4-6<br>2 | 4-7<br>1 | 4-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 5-1<br>1                | 5-1<br>2 | 5-2<br>1 | 5-2<br>2 | 5-3<br>1 | 5-3<br>2 | 5-4<br>1 | 5-4<br>2 | 5-5<br>1 | 5-5<br>2 | 5-6<br>1 | 5-6<br>2 | 5-7<br>1 | 5-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 6-1<br>1                | 6-1<br>2 | 6-2<br>1 | 6-2<br>2 | 6-3<br>1 | 6-3<br>2 | 6-4<br>1 | 6-4<br>2 | 6-5<br>1 | 6-5<br>2 | 6-6<br>1 | 6-6<br>2 | 6-7<br>1 | 6-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 7-1<br>1                | 7-1<br>2 | 7-2<br>1 | 7-2<br>2 | 7-3<br>1 | 7-3<br>2 | 7-4<br>1 | 7-4<br>2 | 7-5<br>1 | 7-5<br>2 | 7-6<br>1 | 7-6<br>2 | 7-7<br>1 | 7-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 8-1<br>1                | 8-1<br>2 | 8-2<br>1 | 8-2<br>2 | 8-3<br>1 | 8-3<br>2 | 8-4<br>1 | 8-4<br>2 | 8-5<br>1 | 8-5<br>2 | 8-6<br>1 | 8-6<br>2 | 8-7<br>1 | 8-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |



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| Clinical sign       | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|---------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                     |                 | 9-1<br>1                | 9-1<br>2 | 9-2<br>1 | 9-2<br>2 | 9-3<br>1 | 9-3<br>2 | 9-4<br>1 | 9-4<br>2 | 9-5<br>1 | 9-5<br>2 | 9-6<br>1 | 9-6<br>2 | 9-7<br>1 | 9-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 0        | 0        | 0        | 0        | 1        | 1        |
| TACHYPNEA           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| DEEP BREATHING      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                     | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE      | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                     | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                     | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 24       | 24       | 24       | 24       | 24       | 23       | 23       |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 10-1<br>1               | 10-1<br>2 | 10-2<br>1 | 10-2<br>2 | 10-3<br>1 | 10-3<br>2 | 10-4<br>1 | 10-4<br>2 | 10-5<br>1 | 10-5<br>2 | 10-6<br>1 | 10-6<br>2 | 10-7<br>1 | 10-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 11-1<br>1               | 11-1<br>2 | 11-2<br>1 | 11-2<br>2 | 11-3<br>1 | 11-3<br>2 | 11-4<br>1 | 11-4<br>2 | 11-5<br>1 | 11-5<br>2 | 11-6<br>1 | 11-6<br>2 | 11-7<br>1 | 11-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 22                      | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 21        | 21        | 20        | 20        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 12-1<br>1               | 12-1<br>2 | 12-2<br>1 | 12-2<br>2 | 12-3<br>1 | 12-3<br>2 | 12-4<br>1 | 12-4<br>2 | 12-5<br>1 | 12-5<br>2 | 12-6<br>1 | 12-6<br>2 | 12-7<br>1 | 12-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 1                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 20                      | 20        | 20        | 20        | 20        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 13-1<br>1               | 13-1<br>2 | 13-2<br>1 | 13-2<br>2 | 13-3<br>1 | 13-3<br>2 | 13-4<br>1 | 13-4<br>2 | 13-5<br>1 | 13-5<br>2 | 13-6<br>1 | 13-6<br>2 | 13-7<br>1 | 13-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 17                      | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 14-1<br>1               | 14-1<br>2 | 14-2<br>1 | 14-2<br>2 | 14-3<br>1 | 14-3<br>2 | 14-4<br>1 | 14-4<br>2 | 14-5<br>1 | 14-5<br>2 | 14-6<br>1 | 14-6<br>2 | 14-7<br>1 | 14-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 17                      | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 15-1<br>1               | 15-1<br>2 | 15-2<br>1 | 15-2<br>2 | 15-3<br>1 | 15-3<br>2 | 15-4<br>1 | 15-4<br>2 | 15-5<br>1 | 15-5<br>2 | 15-6<br>1 | 15-6<br>2 | 15-7<br>1 | 15-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 17                      | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 16-1<br>1               | 16-1<br>2 | 16-2<br>1 | 16-2<br>2 | 16-3<br>1 | 16-3<br>2 | 16-4<br>1 | 16-4<br>2 | 16-5<br>1 | 16-5<br>2 | 16-6<br>1 | 16-6<br>2 | 16-7<br>1 | 16-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 17                      | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 16        | 16        |



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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 17-1<br>1               | 17-1<br>2 | 17-2<br>1 | 17-2<br>2 | 17-3<br>1 | 17-3<br>2 | 17-4<br>1 | 17-4<br>2 | 17-5<br>1 | 17-5<br>2 | 17-6<br>1 | 17-6<br>2 | 17-7<br>1 | 17-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 24        | 24        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 16                      | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 18-1<br>1               | 18-1<br>2 | 18-2<br>1 | 18-2<br>2 | 18-3<br>1 | 18-3<br>2 | 18-4<br>1 | 18-4<br>2 | 18-5<br>1 | 18-5<br>2 | 18-6<br>1 | 18-6<br>2 | 18-7<br>1 | 18-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 30 mg/kg        | 16                      | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 19-1<br>1               | 19-1<br>2 | 19-2<br>1 | 19-2<br>2 | 19-3<br>1 | 19-3<br>2 | 19-4<br>1 | 19-4<br>2 | 19-5<br>1 | 19-5<br>2 | 19-6<br>1 | 19-6<br>2 | 19-7<br>1 | 19-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 24        |
|                     | 30 mg/kg        | 16                      | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 16        | 15        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 20-1<br>1               | 20-1<br>2 | 20-2<br>1 | 20-2<br>2 | 20-3<br>1 | 20-3<br>2 | 20-4<br>1 | 20-4<br>2 | 20-5<br>1 | 20-5<br>2 | 20-6<br>1 | 20-6<br>2 | 20-7<br>1 | 20-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                     | 10 mg/kg        | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 30 mg/kg        | 15                      | 15        | 15        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 21-1<br>1               | 21-1<br>2 | 21-2<br>1 | 21-2<br>2 | 21-3<br>1 | 21-3<br>2 | 21-4<br>1 | 21-4<br>2 | 21-5<br>1 | 21-5<br>2 | 21-6<br>1 | 21-6<br>2 | 21-7<br>1 | 21-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 30 mg/kg        | 14                      | 14        | 14        | 14        | 14        | 13        | 13        | 12        | 12        | 12        | 12        | 12        | 12        | 12        |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 22-1<br>1               | 22-1<br>2 | 22-2<br>1 | 22-2<br>2 | 22-3<br>1 | 22-3<br>2 | 22-4<br>1 | 22-4<br>2 | 22-5<br>1 | 22-5<br>2 | 22-6<br>1 | 22-6<br>2 | 22-7<br>1 | 22-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 2                       | 2         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 2         | 2         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 30 mg/kg        | 11                      | 11        | 11        | 11        | 11        | 10        | 10        | 10        | 9         | 9         | 9         | 9         | 8         | 8         |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 23-1<br>1               | 23-1<br>2 | 23-2<br>1 | 23-2<br>2 | 23-3<br>1 | 23-3<br>2 | 23-4<br>1 | 23-4<br>2 | 23-5<br>1 | 23-5<br>2 | 23-6<br>1 | 23-6<br>2 | 23-7<br>1 | 23-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 2                       | 2         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 24                      | 23        | 23        | 23        | 23        | 23        | 23        | 22        | 22        | 22        | 22        | 22        | 22        | 22        |
|                     | 30 mg/kg        | 8                       | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 24-1<br>1               | 24-1<br>2 | 24-2<br>1 | 24-2<br>2 | 24-3<br>1 | 24-3<br>2 | 24-4<br>1 | 24-4<br>2 | 24-5<br>1 | 24-5<br>2 | 24-6<br>1 | 24-6<br>2 | 24-7<br>1 | 24-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 1                       | 1         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 21                      | 21        | 21        | 21        | 21        | 21        | 20        | 20        | 20        | 20        | 20        | 19        | 19        | 19        |
|                     | 30 mg/kg        | 8                       | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         |



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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 25-1<br>1               | 25-1<br>2 | 25-2<br>1 | 25-2<br>2 | 25-3<br>1 | 25-3<br>2 | 25-4<br>1 | 25-4<br>2 | 25-5<br>1 | 25-5<br>2 | 25-6<br>1 | 25-6<br>2 | 25-7<br>1 | 25-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 2         | 2         | 2         | 2         | 1         | 1         | 1         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 19                      | 19        | 19        | 19        | 19        | 19        | 19        | 18        | 18        | 18        | 18        | 18        | 18        | 18        |
|                     | 30 mg/kg        | 8                       | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         | 8         |

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| Clinical sign       | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|---------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                     |                 | 26-1<br>1               | 26-1<br>2 | 26-2<br>1 | 26-2<br>2 | 26-3<br>1 | 26-3<br>2 | 26-4<br>1 | 26-4<br>2 | 26-5<br>1 | 26-5<br>2 | 26-6<br>1 | 26-6<br>2 | 26-7<br>1 | 26-7<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 1                       | 1         | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 1                       | 1         | 1         | 1         | 0         | 0         | 0         | 4         | 4         | 4         | 4         | 4         | 4         | 4         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                     | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                     | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                     | 10 mg/kg        | 18                      | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 17        | 17        | 17        | 17        | 17        |
|                     | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 3         | 3         | 3         | 3         | 3         | 3         | 3         |

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| Clinical sign       | Group Name      | Administration Week-day |           |
|---------------------|-----------------|-------------------------|-----------|
|                     |                 | 27-1<br>1               | 27-1<br>2 |
| SWELLING            | Vehicle Control | 0                       | 0         |
|                     | 3 mg/kg         | 0                       | 0         |
|                     | 10 mg/kg        | 0                       | 0         |
|                     | 30 mg/kg        | 0                       | 0         |
| IRREGULAR BREATHING | Vehicle Control | 0                       | 0         |
|                     | 3 mg/kg         | 0                       | 0         |
|                     | 10 mg/kg        | 0                       | 0         |
|                     | 30 mg/kg        | 3                       | 2         |
| TACHYPNEA           | Vehicle Control | 0                       | 0         |
|                     | 3 mg/kg         | 0                       | 0         |
|                     | 10 mg/kg        | 0                       | 0         |
|                     | 30 mg/kg        | 0                       | 0         |
| DEEP BREATHING      | Vehicle Control | 0                       | 0         |
|                     | 3 mg/kg         | 0                       | 0         |
|                     | 10 mg/kg        | 0                       | 0         |
|                     | 30 mg/kg        | 0                       | 0         |
| NON REMARKABLE      | Vehicle Control | 23                      | 13        |
|                     | 3 mg/kg         | 24                      | 13        |
|                     | 10 mg/kg        | 17                      | 8         |
|                     | 30 mg/kg        | 3                       | 2         |

(HAN190)

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TABLE A 4

CLINICAL OBSERVATION : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 1-1<br>1                | 1-1<br>2 | 1-2<br>1 | 1-2<br>2 | 1-3<br>1 | 1-3<br>2 | 1-4<br>1 | 1-4<br>2 | 1-5<br>1 | 1-5<br>2 | 1-6<br>1 | 1-6<br>2 | 1-7<br>1 | 1-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 2-1<br>1                | 2-1<br>2 | 2-2<br>1 | 2-2<br>2 | 2-3<br>1 | 2-3<br>2 | 2-4<br>1 | 2-4<br>2 | 2-5<br>1 | 2-5<br>2 | 2-6<br>1 | 2-6<br>2 | 2-7<br>1 | 2-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 3-1<br>1                | 3-1<br>2 | 3-2<br>1 | 3-2<br>2 | 3-3<br>1 | 3-3<br>2 | 3-4<br>1 | 3-4<br>2 | 3-5<br>1 | 3-5<br>2 | 3-6<br>1 | 3-6<br>2 | 3-7<br>1 | 3-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORBUND SACRIFICE       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 4-1<br>1                | 4-1<br>2 | 4-2<br>1 | 4-2<br>2 | 4-3<br>1 | 4-3<br>2 | 4-4<br>1 | 4-4<br>2 | 4-5<br>1 | 4-5<br>2 | 4-6<br>1 | 4-6<br>2 | 4-7<br>1 | 4-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORBUND SACRIFICE       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |



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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 5-1<br>1                | 5-1<br>2 | 5-2<br>1 | 5-2<br>2 | 5-3<br>1 | 5-3<br>2 | 5-4<br>1 | 5-4<br>2 | 5-5<br>1 | 5-5<br>2 | 5-6<br>1 | 5-6<br>2 | 5-7<br>1 | 5-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 6-1<br>1                | 6-1<br>2 | 6-2<br>1 | 6-2<br>2 | 6-3<br>1 | 6-3<br>2 | 6-4<br>1 | 6-4<br>2 | 6-5<br>1 | 6-5<br>2 | 6-6<br>1 | 6-6<br>2 | 6-7<br>1 | 6-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 3 mg/kg         | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 24       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 7-1<br>1                | 7-1<br>2 | 7-2<br>1 | 7-2<br>2 | 7-3<br>1 | 7-3<br>2 | 7-4<br>1 | 7-4<br>2 | 7-5<br>1 | 7-5<br>2 | 7-6<br>1 | 7-6<br>2 | 7-7<br>1 | 7-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        |
|                         | 3 mg/kg         | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 24       |
|                         | 3 mg/kg         | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 8-1<br>1                | 8-1<br>2 | 8-2<br>1 | 8-2<br>2 | 8-3<br>1 | 8-3<br>2 | 8-4<br>1 | 8-4<br>2 | 8-5<br>1 | 8-5<br>2 | 8-6<br>1 | 8-6<br>2 | 8-7<br>1 | 8-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 3 mg/kg         | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                         | 3 mg/kg         | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|-------------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                         |                 | 9-1<br>1                | 9-1<br>2 | 9-2<br>1 | 9-2<br>2 | 9-3<br>1 | 9-3<br>2 | 9-4<br>1 | 9-4<br>2 | 9-5<br>1 | 9-5<br>2 | 9-6<br>1 | 9-6<br>2 | 9-7<br>1 | 9-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| INTERNAL MASS           | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ANEMIA                  | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| ULCER                   | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION                 | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 3 mg/kg         | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 3 mg/kg         | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 10 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                         | 30 mg/kg        | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE          | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                         | 3 mg/kg         | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                         | 10 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                         | 30 mg/kg        | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 10-1<br>1               | 10-1<br>2 | 10-2<br>1 | 10-2<br>2 | 10-3<br>1 | 10-3<br>2 | 10-4<br>1 | 10-4<br>2 | 10-5<br>1 | 10-5<br>2 | 10-6<br>1 | 10-6<br>2 | 10-7<br>1 | 10-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 2         | 2         | 2         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                         | 30 mg/kg        | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 23        | 23        | 23        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 11-1<br>1               | 11-1<br>2 | 11-2<br>1 | 11-2<br>2 | 11-3<br>1 | 11-3<br>2 | 11-4<br>1 | 11-4<br>2 | 11-5<br>1 | 11-5<br>2 | 11-6<br>1 | 11-6<br>2 | 11-7<br>1 | 11-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 2                       | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 3         | 3         | 3         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 1         | 1         | 0         | 0         | 0         | 1         | 1         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                         | 30 mg/kg        | 23                      | 23        | 23        | 23        | 22        | 22        | 22        | 22        | 22        | 21        | 21        | 21        | 21        | 21        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 12-1<br>1               | 12-1<br>2 | 12-2<br>1 | 12-2<br>2 | 12-3<br>1 | 12-3<br>2 | 12-4<br>1 | 12-4<br>2 | 12-5<br>1 | 12-5<br>2 | 12-6<br>1 | 12-6<br>2 | 12-7<br>1 | 12-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 0                       | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 0                       | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 3                       | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 4         | 4         | 4         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                         | 30 mg/kg        | 21                      | 21        | 21        | 21        | 21        | 21        | 21        | 21        | 21        | 21        | 21        | 20        | 20        | 20        |



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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 13-1<br>1               | 13-1<br>2 | 13-2<br>1 | 13-2<br>2 | 13-3<br>1 | 13-3<br>2 | 13-4<br>1 | 13-4<br>2 | 13-5<br>1 | 13-5<br>2 | 13-6<br>1 | 13-6<br>2 | 13-7<br>1 | 13-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORBUND SACRIFICE       | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 4                       | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         | 4         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                         | 30 mg/kg        | 20                      | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 19        | 19        | 19        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 14-1<br>1               | 14-1<br>2 | 14-2<br>1 | 14-2<br>2 | 14-3<br>1 | 14-3<br>2 | 14-4<br>1 | 14-4<br>2 | 14-5<br>1 | 14-5<br>2 | 14-6<br>1 | 14-6<br>2 | 14-7<br>1 | 14-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 4                       | 4         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 24        |
|                         | 30 mg/kg        | 18                      | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        | 18        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 15-1<br>1               | 15-1<br>2 | 15-2<br>1 | 15-2<br>2 | 15-3<br>1 | 15-3<br>2 | 15-4<br>1 | 15-4<br>2 | 15-5<br>1 | 15-5<br>2 | 15-6<br>1 | 15-6<br>2 | 15-7<br>1 | 15-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 6                       | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 2         | 2         | 2         | 2         | 2         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 24                      | 24        | 24        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 30 mg/kg        | 18                      | 18        | 18        | 18        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        | 17        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 16-1<br>1               | 16-1<br>2 | 16-2<br>1 | 16-2<br>2 | 16-3<br>1 | 16-3<br>2 | 16-4<br>1 | 16-4<br>2 | 16-5<br>1 | 16-5<br>2 | 16-6<br>1 | 16-6<br>2 | 16-7<br>1 | 16-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 6                       | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 6         | 7         | 7         | 7         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 10 mg/kg        | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 30 mg/kg        | 17                      | 17        | 17        | 17        | 17        | 17        | 17        | 16        | 16        | 16        | 16        | 16        | 16        | 16        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 17-1<br>1               | 17-1<br>2 | 17-2<br>1 | 17-2<br>2 | 17-3<br>1 | 17-3<br>2 | 17-4<br>1 | 17-4<br>2 | 17-5<br>1 | 17-5<br>2 | 17-6<br>1 | 17-6<br>2 | 17-7<br>1 | 17-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 7                       | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 7         | 8         | 8         | 8         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 23        | 23        |
|                         | 10 mg/kg        | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 30 mg/kg        | 16                      | 16        | 16        | 16        | 16        | 16        | 16        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 18-1<br>1               | 18-1<br>2 | 18-2<br>1 | 18-2<br>2 | 18-3<br>1 | 18-3<br>2 | 18-4<br>1 | 18-4<br>2 | 18-5<br>1 | 18-5<br>2 | 18-6<br>1 | 18-6<br>2 | 18-7<br>1 | 18-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORBUND SACRIFICE       | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 8                       | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 9         |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 10 mg/kg        | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 30 mg/kg        | 15                      | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        |

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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 19-1<br>1               | 19-1<br>2 | 19-2<br>1 | 19-2<br>2 | 19-3<br>1 | 19-3<br>2 | 19-4<br>1 | 19-4<br>2 | 19-5<br>1 | 19-5<br>2 | 19-6<br>1 | 19-6<br>2 | 19-7<br>1 | 19-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 3         | 3         | 3         |
|                         | 30 mg/kg        | 9                       | 9         | 9         | 9         | 9         | 9         | 9         | 9         | 10        | 10        | 10        | 10        | 10        | 10        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                         | 10 mg/kg        | 23                      | 23        | 23        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 21        | 21        | 21        |
|                         | 30 mg/kg        | 14                      | 14        | 14        | 14        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 20-1                    |    | 20-2 |    | 20-3 |    | 20-4 |    | 20-5 |    | 20-6 |    | 20-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 3                       | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  |
|                         | 30 mg/kg        | 10                      | 10 | 10   | 10 | 10   | 10 | 10   | 10 | 10   | 10 | 10   | 10 | 10   | 10 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 23                      | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 |
|                         | 10 mg/kg        | 21                      | 21 | 21   | 21 | 21   | 21 | 21   | 21 | 21   | 21 | 21   | 21 | 21   | 21 |
|                         | 30 mg/kg        | 13                      | 13 | 11   | 11 | 11   | 11 | 11   | 11 | 11   | 11 | 11   | 11 | 11   | 11 |



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| Clinical sign           | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|-------------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                         |                 | 21-1<br>1               | 21-1<br>2 | 21-2<br>1 | 21-2<br>2 | 21-3<br>1 | 21-3<br>2 | 21-4<br>1 | 21-4<br>2 | 21-5<br>1 | 21-5<br>2 | 21-6<br>1 | 21-6<br>2 | 21-7<br>1 | 21-7<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| MORBUND SACRIFICE       | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 3 mg/kg         | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                         | 10 mg/kg        | 3                       | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         | 3         |
|                         | 30 mg/kg        | 11                      | 11        | 11        | 11        | 11        | 11        | 11        | 11        | 11        | 11        | 12        | 12        | 12        | 12        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 30 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 2                       | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         |
|                         | 10 mg/kg        | 2                       | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 3 mg/kg         | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                         | 10 mg/kg        | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         |
|                         | 30 mg/kg        | 1                       | 1         | 1         | 1         | 3         | 3         | 3         | 3         | 3         | 3         | 2         | 2         | 2         | 2         |
| NON REMARKABLE          | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                         | 3 mg/kg         | 22                      | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        | 22        |
|                         | 10 mg/kg        | 20                      | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 20        | 19        | 19        | 19        |
|                         | 30 mg/kg        | 11                      | 11        | 11        | 11        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        | 10        |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 22-1                    |    | 22-2 |    | 22-3 |    | 22-4 |    | 22-5 |    | 22-6 |    | 22-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 3                       | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 3    | 3  | 4    | 4  |
|                         | 30 mg/kg        | 13                      | 13 | 14   | 14 | 14   | 14 | 14   | 14 | 14   | 14 | 14   | 14 | 14   | 14 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
|                         | 10 mg/kg        | 2                       | 2  | 2    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 2  | 2    | 2  | 1    | 1  |
|                         | 30 mg/kg        | 1                       | 1  | 0    | 2  | 2    | 2  | 2    | 2  | 2    | 4  | 4    | 4  | 4    | 4  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 22                      | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 |
|                         | 10 mg/kg        | 19                      | 19 | 19   | 20 | 20   | 20 | 20   | 20 | 20   | 19 | 19   | 19 | 19   | 19 |
|                         | 30 mg/kg        | 10                      | 10 | 10   | 8  | 8    | 8  | 8    | 8  | 8    | 6  | 6    | 6  | 6    | 6  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 23-1                    |    | 23-2 |    | 23-3 |    | 23-4 |    | 23-5 |    | 23-6 |    | 23-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 1                       | 1  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 4                       | 4  | 4    | 4  | 4    | 4  | 4    | 4  | 4    | 4  | 4    | 4  | 4    | 4  |
|                         | 30 mg/kg        | 14                      | 14 | 15   | 15 | 17   | 17 | 17   | 17 | 18   | 18 | 18   | 18 | 18   | 18 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 1                       | 2  | 1    | 1  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 4                       | 4  | 2    | 2  | 0    | 1  | 1    | 1  | 0    | 0  | 0    | 0  | 0    | 0  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 23                      | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 | 23   | 23 |
|                         | 10 mg/kg        | 19                      | 19 | 19   | 19 | 19   | 19 | 19   | 19 | 19   | 19 | 19   | 19 | 19   | 19 |
|                         | 30 mg/kg        | 6                       | 6  | 6    | 6  | 6    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 24-1                    |    | 24-2 |    | 24-3 |    | 24-4 |    | 24-5 |    | 24-6 |    | 24-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 4                       | 4  | 4    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  |
|                         | 30 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 22                      | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 |
|                         | 10 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 |
|                         | 30 mg/kg        | 5                       | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 25-1                    |    | 25-2 |    | 25-3 |    | 25-4 |    | 25-5 |    | 25-6 |    | 25-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 5                       | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  |
|                         | 30 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 22                      | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 |
|                         | 10 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 |
|                         | 30 mg/kg        | 5                       | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  |

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| Clinical sign           | Group Name      | Administration Week-day |    |      |    |      |    |      |    |      |    |      |    |      |    |
|-------------------------|-----------------|-------------------------|----|------|----|------|----|------|----|------|----|------|----|------|----|
|                         |                 | 26-1                    |    | 26-2 |    | 26-3 |    | 26-4 |    | 26-5 |    | 26-6 |    | 26-7 |    |
|                         |                 | 1                       | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  | 1    | 2  |
| DEATH                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 3 mg/kg         | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 10 mg/kg        | 5                       | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 6    | 6  |
|                         | 30 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| INTERNAL MASS           | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ANEMIA                  | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| ULCER                   | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| EROSION                 | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 2                       | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  | 2    | 2  |
|                         | 10 mg/kg        | 1                       | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  | 1    | 1  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 3 mg/kg         | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 10 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  |
|                         | 30 mg/kg        | 0                       | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 0    | 0  | 1    | 1  |
| NON REMARKABLE          | Vehicle Control | 24                      | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 | 24   | 24 |
|                         | 3 mg/kg         | 22                      | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 | 22   | 22 |
|                         | 10 mg/kg        | 18                      | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 18   | 18 | 17   | 17 |
|                         | 30 mg/kg        | 5                       | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 5    | 5  | 4    | 4  |

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| Clinical sign           | Group Name      | Administration Week-day |           |
|-------------------------|-----------------|-------------------------|-----------|
|                         |                 | 27-1<br>1               | 27-1<br>2 |
| DEATH                   | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 1                       | 1         |
|                         | 30 mg/kg        | 2                       | 2         |
| MORIBUND SACRIFICE      | Vehicle Control | 1                       | 1         |
|                         | 3 mg/kg         | 1                       | 1         |
|                         | 10 mg/kg        | 6                       | 6         |
|                         | 30 mg/kg        | 18                      | 18        |
| LOCOMOTOR MOVEMENT DECR | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| INTERNAL MASS           | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| ANEMIA                  | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| ULCER                   | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| EROSION                 | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 2                       | 1         |
|                         | 10 mg/kg        | 1                       | 0         |
|                         | 30 mg/kg        | 0                       | 0         |
| IRREGULAR BREATHING     | Vehicle Control | 0                       | 0         |
|                         | 3 mg/kg         | 0                       | 0         |
|                         | 10 mg/kg        | 0                       | 0         |
|                         | 30 mg/kg        | 1                       | 0         |
| NON REMARKABLE          | Vehicle Control | 24                      | 13        |
|                         | 3 mg/kg         | 22                      | 11        |
|                         | 10 mg/kg        | 17                      | 9         |
|                         | 30 mg/kg        | 4                       | 2         |

TABLE A 5

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

| Week-Day<br>on Study | Vehicle Control |                           | 3 mg/kg   |                       | 10 mg/kg          |           | 30 mg/kg              |                   |           |                       |                   |
|----------------------|-----------------|---------------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|
|                      | Av. Wt.         | No. of<br>Surviv.<br><25> | Av. Wt.   | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. Wt.   | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. Wt.   | % of<br>cont.<br><25> | No. of<br>Surviv. |
| 0-0                  | 25.1 (25)       | 25/25                     | 25.1 (25) | 100                   | 25/25             | 25.1 (25) | 100                   | 25/25             | 25.1 (25) | 100                   | 25/25             |
| 1-1                  | 24.8 (25)       | 25/25                     | 24.7 (25) | 100                   | 25/25             | 24.7 (25) | 100                   | 25/25             | 24.6 (25) | 99                    | 25/25             |
| 2-1                  | 25.6 (25)       | 25/25                     | 25.5 (25) | 100                   | 25/25             | 25.1 (25) | 98                    | 25/25             | 25.1 (25) | 98                    | 25/25             |
| 3-1                  | 26.1 (25)       | 25/25                     | 26.1 (25) | 100                   | 25/25             | 25.7 (25) | 98                    | 25/25             | 25.5 (25) | 98                    | 25/25             |
| 4-1                  | 26.7 (25)       | 25/25                     | 26.6 (25) | 100                   | 25/25             | 26.6 (25) | 100                   | 25/25             | 25.8 (25) | 97                    | 25/25             |
| 5-1                  | 27.2 (25)       | 25/25                     | 27.4 (25) | 101                   | 25/25             | 27.0 (25) | 99                    | 25/25             | 26.4 (25) | 97                    | 25/25             |
| 6-1                  | 27.7 (25)       | 25/25                     | 27.7 (25) | 100                   | 25/25             | 27.2 (25) | 98                    | 25/25             | 26.8 (25) | 97                    | 25/25             |
| 7-1                  | 28.0 (25)       | 25/25                     | 27.9 (25) | 100                   | 25/25             | 27.3 (25) | 98                    | 25/25             | 26.8 (25) | 96                    | 25/25             |
| 8-1                  | 28.5 (25)       | 25/25                     | 28.3 (25) | 99                    | 25/25             | 27.9 (25) | 98                    | 25/25             | 27.5 (25) | 96                    | 25/25             |
| 9-1                  | 28.9 (25)       | 25/25                     | 28.5 (25) | 99                    | 25/25             | 28.1 (25) | 97                    | 25/25             | 27.4 (25) | 95                    | 25/25             |
| 10-1                 | 29.2 (25)       | 25/25                     | 28.9 (25) | 99                    | 25/25             | 28.3 (25) | 97                    | 25/25             | 27.8 (23) | 95                    | 23/25             |
| 11-1                 | 29.5 (25)       | 25/25                     | 29.4 (25) | 100                   | 25/25             | 28.7 (25) | 97                    | 25/25             | 28.0 (22) | 95                    | 22/25             |
| 12-1                 | 29.5 (25)       | 25/25                     | 29.7 (25) | 101                   | 25/25             | 29.0 (25) | 98                    | 25/25             | 28.1 (20) | 95                    | 20/25             |
| 13-1                 | 29.4 (25)       | 25/25                     | 29.6 (25) | 101                   | 25/25             | 28.9 (25) | 98                    | 25/25             | 28.6 (17) | 97                    | 17/25             |
| 14-1                 | 29.7 (25)       | 25/25                     | 29.9 (25) | 101                   | 25/25             | 29.2 (25) | 98                    | 25/25             | 28.9 (17) | 97                    | 17/25             |
| 15-1                 | 29.8 (25)       | 25/25                     | 30.1 (25) | 101                   | 25/25             | 29.3 (25) | 98                    | 25/25             | 28.9 (17) | 97                    | 17/25             |
| 16-1                 | 30.0 (25)       | 25/25                     | 30.3 (25) | 101                   | 25/25             | 29.2 (25) | 97                    | 25/25             | 28.9 (17) | 96                    | 17/25             |
| 17-1                 | 30.1 (25)       | 25/25                     | 30.6 (25) | 102                   | 25/25             | 29.5 (25) | 98                    | 25/25             | 28.8 (17) | 96                    | 17/25             |
| 18-1                 | 30.4 (25)       | 25/25                     | 30.7 (25) | 101                   | 25/25             | 29.7 (25) | 98                    | 25/25             | 29.2 (16) | 96                    | 16/25             |
| 19-1                 | 30.6 (25)       | 25/25                     | 30.9 (25) | 101                   | 25/25             | 29.6 (25) | 97                    | 25/25             | 29.3 (16) | 96                    | 16/25             |
| 20-1                 | 30.9 (25)       | 25/25                     | 31.2 (25) | 101                   | 25/25             | 30.0 (24) | 97                    | 24/25             | 29.6 (15) | 96                    | 15/25             |
| 21-1                 | 31.2 (25)       | 25/25                     | 31.7 (25) | 102                   | 25/25             | 30.3 (24) | 97                    | 24/25             | 30.0 (14) | 96                    | 14/25             |
| 22-1                 | 31.4 (25)       | 25/25                     | 31.7 (25) | 101                   | 25/25             | 30.3 (24) | 96                    | 24/25             | 28.9 (14) | 92                    | 14/25             |
| 23-1                 | 31.3 (24)       | 24/25                     | 32.0 (25) | 102                   | 25/25             | 30.2 (24) | 96                    | 24/25             | 28.8 (11) | 92                    | 11/25             |
| 24-1                 | 31.5 (24)       | 24/25                     | 32.2 (25) | 102                   | 25/25             | 30.4 (23) | 97                    | 23/25             | 30.1 ( 9) | 96                    | 9/25              |
| 25-1                 | 31.6 (24)       | 24/25                     | 31.6 (25) | 100                   | 25/25             | 29.7 (21) | 94                    | 21/25             | 29.2 ( 9) | 92                    | 9/25              |
| 26-1                 | 31.8 (24)       | 24/25                     | 32.6 (25) | 103                   | 25/25             | 30.7 (20) | 97                    | 20/25             | 29.3 ( 9) | 92                    | 9/25              |
| 26-7                 | 32.2 (24)       | 24/25                     | 32.8 (25) | 102                   | 25/25             | 31.0 (18) | 96                    | 18/25             | 27.7 ( 8) | 86                    | 8/25              |

< >:No. of effective animals, ( ):No. of measured animals Av. Wt. : g

TABLE A 6

BODY WEIGHT CHANGES AND  
SURVIVAL ANIMAL NUMBERS : FEMALE  
(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

| Week-Day<br>on Study | Vehicle Control |                           | 3 mg/kg        |                       | 10 mg/kg          |                | 30 mg/kg              |                   |                |                       |                   |
|----------------------|-----------------|---------------------------|----------------|-----------------------|-------------------|----------------|-----------------------|-------------------|----------------|-----------------------|-------------------|
|                      | Av. Wt.<br>( )  | No. of<br>Surviv.<br><25> | Av. Wt.<br>( ) | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. Wt.<br>( ) | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. Wt.<br>( ) | % of<br>cont.<br><25> | No. of<br>Surviv. |
| 0-0                  | 20.8 (25)       | 25/25                     | 20.8 (25)      | 100                   | 25/25             | 20.8 (25)      | 100                   | 25/25             | 20.8 (25)      | 100                   | 25/25             |
| 1-1                  | 20.4 (25)       | 25/25                     | 20.1 (25)      | 99                    | 25/25             | 20.3 (25)      | 100                   | 25/25             | 20.0 (25)      | 98                    | 25/25             |
| 2-1                  | 21.2 (25)       | 25/25                     | 21.0 (25)      | 99                    | 25/25             | 21.3 (25)      | 100                   | 25/25             | 20.9 (25)      | 99                    | 25/25             |
| 3-1                  | 21.9 (25)       | 25/25                     | 21.5 (25)      | 98                    | 25/25             | 21.9 (25)      | 100                   | 25/25             | 21.3 (25)      | 97                    | 25/25             |
| 4-1                  | 22.1 (25)       | 25/25                     | 22.0 (25)      | 100                   | 25/25             | 22.1 (25)      | 100                   | 25/25             | 21.9 (25)      | 99                    | 25/25             |
| 5-1                  | 22.6 (25)       | 25/25                     | 22.6 (25)      | 100                   | 25/25             | 22.7 (25)      | 100                   | 25/25             | 22.3 (25)      | 99                    | 25/25             |
| 6-1                  | 23.0 (25)       | 25/25                     | 22.8 (25)      | 99                    | 25/25             | 23.2 (25)      | 101                   | 25/25             | 22.7 (25)      | 99                    | 25/25             |
| 7-1                  | 23.1 (25)       | 25/25                     | 22.7 (25)      | 98                    | 25/25             | 22.8 (25)      | 99                    | 25/25             | 22.1 (25)      | 96                    | 25/25             |
| 8-1                  | 24.0 (25)       | 25/25                     | 23.7 (25)      | 99                    | 25/25             | 24.2 (25)      | 101                   | 25/25             | 23.6 (25)      | 98                    | 25/25             |
| 9-1                  | 24.0 (25)       | 25/25                     | 23.4 (25)      | 98                    | 25/25             | 24.0 (25)      | 100                   | 25/25             | 23.3 (25)      | 97                    | 25/25             |
| 10-1                 | 24.2 (25)       | 25/25                     | 24.1 (25)      | 100                   | 25/25             | 24.1 (25)      | 100                   | 25/25             | 23.3 (24)      | 96                    | 24/25             |
| 11-1                 | 24.3 (25)       | 25/25                     | 24.3 (25)      | 100                   | 25/25             | 24.3 (25)      | 100                   | 25/25             | 23.7 (23)      | 98                    | 23/25             |
| 12-1                 | 24.2 (25)       | 25/25                     | 23.9 (25)      | 99                    | 25/25             | 24.3 (25)      | 100                   | 25/25             | 23.8 (21)      | 98                    | 21/25             |
| 13-1                 | 24.2 (24)       | 24/25                     | 24.1 (24)      | 100                   | 24/25             | 24.5 (25)      | 101                   | 25/25             | 23.6 (20)      | 98                    | 20/25             |
| 14-1                 | 24.2 (24)       | 24/25                     | 24.0 (24)      | 99                    | 24/25             | 24.0 (25)      | 99                    | 25/25             | 23.5 (20)      | 97                    | 20/25             |
| 15-1                 | 24.4 (24)       | 24/25                     | 24.0 (24)      | 98                    | 24/25             | 24.1 (25)      | 99                    | 25/25             | 23.7 (18)      | 97                    | 18/25             |
| 16-1                 | 24.4 (24)       | 24/25                     | 24.3 (24)      | 100                   | 24/25             | 24.9 (24)      | 102                   | 24/25             | 23.9 (18)      | 98                    | 18/25             |
| 17-1                 | 24.8 (24)       | 24/25                     | 24.4 (24)      | 98                    | 24/25             | 24.5 (24)      | 99                    | 24/25             | 23.9 (17)      | 96                    | 17/25             |
| 18-1                 | 25.1 (24)       | 24/25                     | 24.7 (24)      | 98                    | 24/25             | 25.1 (24)      | 100                   | 24/25             | 24.2 (15)      | 96                    | 15/25             |
| 19-1                 | 24.7 (24)       | 24/25                     | 24.6 (24)      | 100                   | 24/25             | 24.8 (24)      | 100                   | 24/25             | 23.9 (15)      | 97                    | 15/25             |
| 20-1                 | 25.2 (24)       | 24/25                     | 24.5 (24)      | 97                    | 24/25             | 25.0 (22)      | 99                    | 22/25             | 24.0 (14)      | 95                    | 14/25             |
| 21-1                 | 24.8 (24)       | 24/25                     | 25.0 (24)      | 101                   | 24/25             | 24.8 (22)      | 100                   | 22/25             | 23.8 (13)      | 96                    | 13/25             |
| 22-1                 | 25.4 (24)       | 24/25                     | 25.2 (24)      | 99                    | 24/25             | 25.1 (22)      | 99                    | 22/25             | 24.0 (11)      | 94                    | 11/25             |
| 23-1                 | 25.0 (24)       | 24/25                     | 24.9 (24)      | 100                   | 24/25             | 25.1 (21)      | 100                   | 21/25             | 22.9 (10)      | 92                    | 10/25             |
| 24-1                 | 25.3 (24)       | 24/25                     | 25.3 (24)      | 100                   | 24/25             | 25.2 (20)      | 100                   | 20/25             | 24.4 ( 5)      | 96                    | 5/25              |
| 25-1                 | 25.4 (24)       | 24/25                     | 25.3 (24)      | 100                   | 24/25             | 25.5 (19)      | 100                   | 19/25             | 24.4 ( 5)      | 96                    | 5/25              |
| 26-1                 | 25.6 (24)       | 24/25                     | 25.7 (24)      | 100                   | 24/25             | 26.1 (19)      | 102                   | 18/25             | 25.2 ( 5)      | 98                    | 5/25              |
| 26-7                 | 25.3 (24)       | 24/25                     | 25.6 (24)      | 101                   | 24/25             | 25.7 (18)      | 102                   | 18/25             | 24.6 ( 5)      | 97                    | 5/25              |

< >:No. of effective animals, ( ):No. of measured animals Av. Wt. : g

TABLE A 7

BODY WEIGHT CHANGES : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |           |           |           |           |           |
|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                 | 0-0                     | 1-1       | 2-1       | 3-1       | 4-1       | 5-1       | 6-1       |
| Vehicle Control | 25.1± 1.6               | 24.8± 1.7 | 25.6± 1.5 | 26.1± 1.5 | 26.7± 1.6 | 27.2± 1.5 | 27.7± 1.7 |
| 3 mg/kg         | 25.1± 1.6               | 24.7± 1.4 | 25.5± 1.3 | 26.1± 1.3 | 26.6± 1.4 | 27.4± 1.2 | 27.7± 1.4 |
| 10 mg/kg        | 25.1± 1.7               | 24.7± 1.7 | 25.1± 1.7 | 25.7± 1.6 | 26.6± 1.6 | 27.0± 1.6 | 27.2± 1.7 |
| 30 mg/kg        | 25.1± 1.6               | 24.6± 1.6 | 25.1± 1.9 | 25.5± 1.7 | 25.8± 1.9 | 26.4± 1.9 | 26.8± 1.8 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |             |            |             |            |           |  |
|-----------------|-------------------------|-----------|-------------|------------|-------------|------------|-----------|--|
|                 | 7-1                     | 8-1       | 9-1         | 10-1       | 11-1        | 12-1       | 13-1      |  |
| Vehicle Control | 28.0± 1.7               | 28.5± 1.7 | 28.9± 1.7   | 29.2± 1.8  | 29.5± 1.9   | 29.5± 2.1  | 29.4± 2.3 |  |
| 3 mg/kg         | 27.9± 1.3               | 28.3± 1.4 | 28.5± 1.5   | 28.9± 1.5  | 29.4± 1.4   | 29.7± 1.6  | 29.6± 1.7 |  |
| 10 mg/kg        | 27.3± 1.5               | 27.9± 1.5 | 28.1± 1.5   | 28.3± 1.5  | 28.7± 1.4   | 29.0± 1.6  | 28.9± 1.5 |  |
| 30 mg/kg        | 26.8± 1.8*              | 27.5± 1.9 | 27.4± 2.0** | 27.8± 1.7* | 28.0± 1.8** | 28.1± 2.0* | 28.6± 1.5 |  |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |           |           |           |           |           |
|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                 | 14-1                    | 15-1      | 16-1      | 17-1      | 18-1      | 19-1      | 20-1      |
| Vehicle Control | 29.7± 2.1               | 29.8± 2.0 | 30.0± 2.1 | 30.1± 2.3 | 30.4± 2.1 | 30.6± 2.2 | 30.9± 2.3 |
| 3 mg/kg         | 29.9± 1.9               | 30.1± 1.8 | 30.3± 2.1 | 30.6± 2.1 | 30.7± 2.1 | 30.9± 2.2 | 31.2± 2.3 |
| 10 mg/kg        | 29.2± 1.7               | 29.3± 1.7 | 29.2± 1.7 | 29.5± 1.8 | 29.7± 1.7 | 29.6± 1.7 | 30.0± 1.8 |
| 30 mg/kg        | 28.9± 1.6               | 28.9± 1.5 | 28.9± 1.7 | 28.8± 1.8 | 29.2± 1.7 | 29.3± 1.6 | 29.6± 1.6 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |             |            |           |            |            |             |
|-----------------|-------------------------|-------------|------------|-----------|------------|------------|-------------|
|                 | 21-1                    | 22-1        | 23-1       | 24-1      | 25-1       | 26-1       | 26-7        |
| Vehicle Control | 31.2± 2.3               | 31.4± 2.5   | 31.3± 2.4  | 31.5± 2.5 | 31.6± 2.3  | 31.8± 2.4  | 32.2± 2.4   |
| 3 mg/kg         | 31.7± 2.5               | 31.7± 2.4   | 32.0± 2.5  | 32.2± 2.4 | 31.6± 2.8  | 32.6± 2.7  | 32.8± 2.9   |
| 10 mg/kg        | 30.3± 1.8               | 30.3± 1.8   | 30.2± 2.0  | 30.4± 2.3 | 29.7± 2.7* | 30.7± 2.7  | 31.0± 2.7   |
| 30 mg/kg        | 30.0± 1.7               | 28.9± 2.4** | 28.8± 3.0* | 30.1± 1.8 | 29.2± 1.7  | 29.3± 2.2* | 27.7± 2.6** |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett



TABLE A 8

BODY WEIGHT CHANGES : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |           |           |           |           |           |
|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                 | 0-0                     | 1-1       | 2-1       | 3-1       | 4-1       | 5-1       | 6-1       |
| Vehicle Control | 20.8± 1.6               | 20.4± 1.5 | 21.2± 1.6 | 21.9± 1.7 | 22.1± 1.8 | 22.6± 1.7 | 23.0± 1.4 |
| 3 mg/kg         | 20.8± 1.4               | 20.1± 1.4 | 21.0± 1.4 | 21.5± 1.3 | 22.0± 1.2 | 22.6± 1.5 | 22.8± 1.3 |
| 10 mg/kg        | 20.8± 1.5               | 20.3± 1.5 | 21.3± 1.3 | 21.9± 1.4 | 22.1± 1.2 | 22.7± 1.6 | 23.2± 1.5 |
| 30 mg/kg        | 20.8± 1.6               | 20.0± 1.6 | 20.9± 1.6 | 21.3± 1.3 | 21.9± 1.3 | 22.3± 1.3 | 22.7± 1.3 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |           |           |           |           |           |
|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                 | 7-1                     | 8-1       | 9-1       | 10-1      | 11-1      | 12-1      | 13-1      |
| Vehicle Control | 23.1± 1.7               | 24.0± 1.6 | 24.0± 1.4 | 24.2± 1.5 | 24.3± 1.3 | 24.2± 1.6 | 24.2± 1.6 |
| 3 mg/kg         | 22.7± 1.3               | 23.7± 1.6 | 23.4± 1.7 | 24.1± 1.6 | 24.3± 1.4 | 23.9± 1.6 | 24.1± 1.3 |
| 10 mg/kg        | 22.8± 1.4               | 24.2± 1.9 | 24.0± 1.4 | 24.1± 1.4 | 24.3± 1.4 | 24.3± 1.6 | 24.5± 1.5 |
| 30 mg/kg        | 22.1± 1.4               | 23.6± 1.7 | 23.3± 1.5 | 23.3± 1.9 | 23.7± 1.8 | 23.8± 1.9 | 23.6± 1.5 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |           |           |           |           |           |
|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                 | 14-1                    | 15-1      | 16-1      | 17-1      | 18-1      | 19-1      | 20-1      |
| Vehicle Control | 24.2± 1.4               | 24.4± 1.8 | 24.4± 1.2 | 24.8± 1.7 | 25.1± 1.6 | 24.7± 1.4 | 25.2± 1.7 |
| 3 mg/kg         | 24.0± 1.5               | 24.0± 1.6 | 24.3± 1.5 | 24.4± 1.6 | 24.7± 1.6 | 24.6± 1.7 | 24.5± 1.7 |
| 10 mg/kg        | 24.0± 1.7               | 24.1± 1.6 | 24.9± 1.9 | 24.5± 1.6 | 25.1± 1.6 | 24.8± 1.4 | 25.0± 1.8 |
| 30 mg/kg        | 23.5± 1.8               | 23.7± 1.7 | 23.9± 1.4 | 23.9± 1.5 | 24.2± 1.5 | 23.9± 1.5 | 24.0± 1.7 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |           |             |           |           |           |           |
|-----------------|-------------------------|-----------|-------------|-----------|-----------|-----------|-----------|
|                 | 21-1                    | 22-1      | 23-1        | 24-1      | 25-1      | 26-1      | 26-7      |
| Vehicle Control | 24.8± 1.3               | 25.4± 1.5 | 25.0± 1.4   | 25.3± 1.5 | 25.4± 1.8 | 25.6± 1.5 | 25.3± 1.8 |
| 3 mg/kg         | 25.0± 1.6               | 25.2± 1.5 | 24.9± 1.5   | 25.3± 1.8 | 25.3± 1.6 | 25.7± 1.9 | 25.6± 2.1 |
| 10 mg/kg        | 24.8± 1.8               | 25.1± 1.9 | 25.1± 1.8   | 25.2± 1.7 | 25.5± 1.7 | 26.1± 1.8 | 25.7± 1.7 |
| 30 mg/kg        | 23.8± 1.8               | 24.0± 2.3 | 22.9± 2.2** | 24.4± 1.4 | 24.4± 0.8 | 25.2± 0.7 | 24.6± 1.4 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

TABLE A 9

FOOD CONSUMPTION CHANGES AND  
SURVIVAL ANIMAL NUMBERS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

| Week-Day<br>on Study | Vehicle Control |                           | 3 mg/kg  |                       | 10 mg/kg          |          | 30 mg/kg              |                   |          |                       |                   |
|----------------------|-----------------|---------------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|
|                      | Av. FC.         | No. of<br>Surviv.<br><25> | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. |
| 2-1                  | 3.5 (25)        | 25/25                     | 3.5 (25) | 100                   | 25/25             | 3.5 (25) | 100                   | 25/25             | 3.4 (25) | 97                    | 25/25             |
| 3-1                  | 3.2 (25)        | 25/25                     | 3.2 (25) | 100                   | 25/25             | 3.4 (25) | 106                   | 25/25             | 3.4 (25) | 106                   | 25/25             |
| 4-1                  | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.3 (25) | 100                   | 25/25             | 3.2 (25) | 97                    | 25/25             |
| 5-1                  | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.3 (25) | 100                   | 25/25             | 3.2 (25) | 97                    | 25/25             |
| 6-1                  | 3.3 (25)        | 25/25                     | 3.2 (25) | 97                    | 25/25             | 3.2 (25) | 97                    | 25/25             | 3.2 (25) | 97                    | 25/25             |
| 7-1                  | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.2 (25) | 97                    | 25/25             | 3.2 (25) | 97                    | 25/25             |
| 8-1                  | 3.4 (25)        | 25/25                     | 3.3 (25) | 97                    | 25/25             | 3.3 (25) | 97                    | 25/25             | 3.2 (25) | 94                    | 25/25             |
| 9-1                  | 3.3 (25)        | 25/25                     | 3.2 (25) | 97                    | 25/25             | 3.1 (25) | 94                    | 25/25             | 3.0 (25) | 91                    | 25/25             |
| 10-1                 | 3.3 (25)        | 25/25                     | 3.2 (25) | 97                    | 25/25             | 3.2 (25) | 97                    | 25/25             | 3.1 (23) | 94                    | 23/25             |
| 11-1                 | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.2 (25) | 97                    | 25/25             | 3.1 (22) | 94                    | 22/25             |
| 12-1                 | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.3 (25) | 100                   | 25/25             | 3.1 (20) | 94                    | 20/25             |
| 13-1                 | 3.2 (25)        | 25/25                     | 3.3 (25) | 103                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.0 (17) | 94                    | 17/25             |
| 14-1                 | 3.2 (25)        | 25/25                     | 3.3 (25) | 103                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.0 (17) | 94                    | 17/25             |
| 15-1                 | 3.1 (25)        | 25/25                     | 3.2 (25) | 103                   | 25/25             | 3.2 (25) | 103                   | 25/25             | 3.0 (17) | 97                    | 17/25             |
| 16-1                 | 3.2 (25)        | 25/25                     | 3.2 (25) | 100                   | 25/25             | 3.1 (25) | 97                    | 25/25             | 3.0 (17) | 94                    | 17/25             |
| 17-1                 | 3.2 (25)        | 25/25                     | 3.3 (25) | 103                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.0 (17) | 94                    | 17/25             |
| 18-1                 | 3.2 (25)        | 25/25                     | 3.2 (25) | 100                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.0 (16) | 94                    | 16/25             |
| 19-1                 | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.2 (25) | 97                    | 25/25             | 3.0 (16) | 91                    | 16/25             |
| 20-1                 | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.2 (24) | 97                    | 24/25             | 3.0 (15) | 91                    | 15/25             |
| 21-1                 | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.2 (24) | 97                    | 24/25             | 3.0 (14) | 91                    | 14/25             |
| 22-1                 | 3.3 (25)        | 24/25                     | 3.2 (25) | 97                    | 25/25             | 3.2 (24) | 97                    | 24/25             | 2.8 (14) | 85                    | 14/25             |
| 23-1                 | 3.3 (24)        | 24/25                     | 3.3 (25) | 100                   | 25/25             | 3.1 (24) | 94                    | 24/25             | 2.9 (11) | 88                    | 11/25             |
| 24-1                 | 3.4 (24)        | 24/25                     | 3.3 (25) | 97                    | 25/25             | 3.1 (23) | 91                    | 23/25             | 3.3 ( 9) | 97                    | 9/25              |
| 25-1                 | 3.4 (24)        | 24/25                     | 3.3 (25) | 97                    | 25/25             | 3.1 (21) | 91                    | 21/25             | 3.2 ( 9) | 94                    | 9/25              |
| 26-1                 | 3.4 (24)        | 24/25                     | 3.4 (25) | 100                   | 25/25             | 3.1 (20) | 91                    | 20/25             | 3.1 ( 9) | 91                    | 9/25              |
| 26-7                 | 3.4 (24)        | 24/25                     | 3.3 (25) | 97                    | 25/25             | 3.1 (18) | 91                    | 18/25             | 2.6 ( 8) | 76                    | 8/25              |

< >:No. of effective animals, ( ):No. of measured animals Av. FC. : g

TABLE A 10

FOOD CONSUMPTION CHANGES AND  
SURVIVAL ANIMAL NUMBERS : FEMALE  
(Vehicle control, 3, 10 and 30 mg/kg groups)



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

| Week-Day<br>on Study | Vehicle Control |                           | 3 mg/kg  |                       | 10 mg/kg          |          | 30 mg/kg              |                   |          |                       |                   |
|----------------------|-----------------|---------------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|
|                      | Av. FC.         | No. of<br>Surviv.<br><25> | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. | Av. FC.  | % of<br>cont.<br><25> | No. of<br>Surviv. |
| 2-1                  | 3.2 (25)        | 25/25                     | 3.2 (25) | 100                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.2 (25) | 100                   | 25/25             |
| 3-1                  | 3.1 (25)        | 25/25                     | 3.1 (25) | 100                   | 25/25             | 3.2 (25) | 103                   | 25/25             | 3.2 (25) | 103                   | 25/25             |
| 4-1                  | 2.9 (25)        | 25/25                     | 3.1 (25) | 107                   | 25/25             | 3.0 (25) | 103                   | 25/25             | 3.1 (25) | 107                   | 25/25             |
| 5-1                  | 2.9 (25)        | 25/25                     | 3.0 (25) | 103                   | 25/25             | 3.0 (25) | 103                   | 25/25             | 3.1 (25) | 107                   | 25/25             |
| 6-1                  | 3.2 (25)        | 25/25                     | 3.2 (25) | 100                   | 25/25             | 3.2 (25) | 100                   | 25/25             | 3.1 (25) | 97                    | 25/25             |
| 7-1                  | 3.0 (25)        | 25/25                     | 3.2 (25) | 107                   | 25/25             | 3.0 (25) | 100                   | 25/25             | 3.0 (25) | 100                   | 25/25             |
| 8-1                  | 3.3 (25)        | 25/25                     | 3.3 (25) | 100                   | 25/25             | 3.4 (25) | 103                   | 25/25             | 3.3 (25) | 100                   | 25/25             |
| 9-1                  | 3.1 (25)        | 25/25                     | 3.1 (25) | 100                   | 25/25             | 2.9 (25) | 94                    | 25/25             | 2.9 (25) | 94                    | 25/25             |
| 10-1                 | 3.1 (25)        | 25/25                     | 3.2 (25) | 103                   | 25/25             | 2.9 (25) | 94                    | 25/25             | 2.9 (24) | 94                    | 24/25             |
| 11-1                 | 3.1 (25)        | 25/25                     | 3.0 (25) | 97                    | 25/25             | 2.9 (25) | 94                    | 25/25             | 2.9 (23) | 94                    | 23/25             |
| 12-1                 | 3.0 (25)        | 25/25                     | 2.9 (25) | 97                    | 25/25             | 2.9 (25) | 97                    | 25/25             | 2.9 (21) | 97                    | 21/25             |
| 13-1                 | 2.9 (24)        | 24/25                     | 2.9 (24) | 100                   | 24/25             | 2.9 (25) | 100                   | 25/25             | 2.9 (20) | 100                   | 20/25             |
| 14-1                 | 2.9 (24)        | 24/25                     | 2.9 (24) | 100                   | 24/25             | 2.8 (25) | 97                    | 25/25             | 2.9 (20) | 100                   | 20/25             |
| 15-1                 | 3.0 (24)        | 24/25                     | 3.0 (24) | 100                   | 24/25             | 2.9 (25) | 97                    | 25/25             | 2.9 (18) | 97                    | 18/25             |
| 16-1                 | 2.9 (24)        | 24/25                     | 2.9 (24) | 100                   | 24/25             | 3.2 (24) | 110                   | 24/25             | 2.9 (18) | 100                   | 18/25             |
| 17-1                 | 3.0 (24)        | 24/25                     | 3.0 (24) | 100                   | 24/25             | 3.0 (24) | 100                   | 24/25             | 2.9 (17) | 97                    | 17/25             |
| 18-1                 | 3.1 (24)        | 24/25                     | 3.1 (24) | 100                   | 24/25             | 3.1 (24) | 100                   | 24/25             | 3.0 (15) | 97                    | 15/25             |
| 19-1                 | 2.9 (24)        | 24/25                     | 3.0 (24) | 103                   | 24/25             | 2.9 (24) | 100                   | 24/25             | 2.9 (15) | 100                   | 15/25             |
| 20-1                 | 3.0 (24)        | 24/25                     | 3.0 (24) | 100                   | 24/25             | 3.0 (22) | 100                   | 22/25             | 2.9 (14) | 97                    | 14/25             |
| 21-1                 | 2.9 (24)        | 24/25                     | 3.0 (24) | 103                   | 24/25             | 2.9 (22) | 100                   | 22/25             | 2.8 (13) | 97                    | 13/25             |
| 22-1                 | 2.9 (24)        | 24/25                     | 3.0 (24) | 103                   | 24/25             | 3.0 (22) | 103                   | 22/25             | 2.6 (11) | 90                    | 11/25             |
| 23-1                 | 2.8 (24)        | 24/25                     | 3.0 (24) | 107                   | 24/25             | 2.9 (21) | 104                   | 21/25             | 2.3 (10) | 82                    | 10/25             |
| 24-1                 | 3.0 (24)        | 24/25                     | 3.1 (24) | 103                   | 24/25             | 2.9 (20) | 97                    | 20/25             | 2.8 ( 5) | 93                    | 5/25              |
| 25-1                 | 2.8 (24)        | 24/25                     | 3.1 (24) | 111                   | 24/25             | 3.0 (19) | 107                   | 19/25             | 2.9 ( 5) | 104                   | 5/25              |
| 26-1                 | 2.9 (24)        | 24/25                     | 3.1 (24) | 107                   | 24/25             | 3.0 (19) | 103                   | 19/25             | 3.0 ( 5) | 103                   | 5/25              |
| 26-7                 | 2.8 (24)        | 24/25                     | 3.0 (24) | 107                   | 24/25             | 2.8 (18) | 100                   | 18/25             | 2.6 ( 5) | 93                    | 5/25              |

< >:No. of effective animals, ( ):No. of measured animals Av. FC. : g

TABLE A 11

FOOD CONSUMPTION CHANGES : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |          |          |          |          |          |           |
|-----------------|------------------------------------|----------|----------|----------|----------|----------|-----------|
|                 | 2-1(7)                             | 3-1(7)   | 4-1(7)   | 5-1(7)   | 6-1(7)   | 7-1(7)   | 8-1(7)    |
| Vehicle Control | 3.5± 0.3                           | 3.2± 0.3 | 3.3± 0.3 | 3.3± 0.3 | 3.3± 0.3 | 3.3± 0.2 | 3.4± 0.2  |
| 3 mg/kg         | 3.5± 0.2                           | 3.2± 0.2 | 3.3± 0.2 | 3.3± 0.2 | 3.2± 0.2 | 3.3± 0.3 | 3.3± 0.2  |
| 10 mg/kg        | 3.5± 0.2                           | 3.4± 0.2 | 3.3± 0.2 | 3.3± 0.3 | 3.2± 0.3 | 3.2± 0.3 | 3.3± 0.3  |
| 30 mg/kg        | 3.4± 0.3                           | 3.4± 0.3 | 3.2± 0.2 | 3.2± 0.2 | 3.2± 0.2 | 3.2± 0.2 | 3.2± 0.2* |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day (effective) |          |           |           |          |           |          |
|-----------------|-------------------------------------|----------|-----------|-----------|----------|-----------|----------|
|                 | 9-1 (7)                             | 10-1 (7) | 11-1 (7)  | 12-1 (7)  | 13-1 (7) | 14-1 (7)  | 15-1 (7) |
| Vehicle Control | 3.3± 0.2                            | 3.3± 0.2 | 3.3± 0.3  | 3.3± 0.3  | 3.2± 0.3 | 3.2± 0.3  | 3.1± 0.3 |
| 3 mg/kg         | 3.2± 0.3                            | 3.2± 0.3 | 3.3± 0.3  | 3.3± 0.3  | 3.3± 0.3 | 3.3± 0.3  | 3.2± 0.3 |
| 10 mg/kg        | 3.1± 0.3                            | 3.2± 0.3 | 3.2± 0.3  | 3.3± 0.3  | 3.2± 0.3 | 3.2± 0.3  | 3.2± 0.3 |
| 30 mg/kg        | 3.0± 0.3**                          | 3.1± 0.2 | 3.1± 0.3* | 3.1± 0.2* | 3.0± 0.2 | 3.0± 0.2* | 3.0± 0.2 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day (effective) |           |           |           |           |            |            |
|-----------------|-------------------------------------|-----------|-----------|-----------|-----------|------------|------------|
|                 | 16-1 (7)                            | 17-1 (7)  | 18-1 (7)  | 19-1 (7)  | 20-1 (7)  | 21-1 (7)   | 22-1 (7)   |
| Vehicle Control | 3.2± 0.3                            | 3.2± 0.3  | 3.2± 0.3  | 3.3± 0.3  | 3.3± 0.4  | 3.3± 0.3   | 3.3± 0.4   |
| 3 mg/kg         | 3.2± 0.3                            | 3.3± 0.3  | 3.2± 0.2  | 3.3± 0.3  | 3.3± 0.3  | 3.3± 0.3   | 3.2± 0.3   |
| 10 mg/kg        | 3.1± 0.3                            | 3.2± 0.4  | 3.2± 0.3  | 3.2± 0.3  | 3.2± 0.3  | 3.2± 0.3   | 3.2± 0.3   |
| 30 mg/kg        | 3.0± 0.3                            | 3.0± 0.3* | 3.0± 0.2* | 3.0± 0.3* | 3.0± 0.2* | 3.0± 0.2** | 2.8± 0.6** |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day (effective) |           |           |           |             |
|-----------------|-------------------------------------|-----------|-----------|-----------|-------------|
|                 | 23-1 (7)                            | 24-1 (7)  | 25-1 (7)  | 26-1 (7)  | 26-7 (6)    |
| Vehicle Control | 3.3 ± 0.4                           | 3.4 ± 0.6 | 3.4 ± 0.7 | 3.4 ± 0.6 | 3.4 ± 0.6   |
| 3 mg/kg         | 3.3 ± 0.3                           | 3.3 ± 0.3 | 3.3 ± 0.3 | 3.4 ± 0.3 | 3.3 ± 0.4   |
| 10 mg/kg        | 3.1 ± 0.3                           | 3.1 ± 0.4 | 3.1 ± 0.5 | 3.1 ± 0.4 | 3.1 ± 0.4   |
| 30 mg/kg        | 2.9 ± 0.7*                          | 3.3 ± 0.6 | 3.2 ± 0.6 | 3.1 ± 0.8 | 2.6 ± 1.2** |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

TABLE A 12

FOOD CONSUMPTION CHANGES : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |          |          |          |          |          |          |
|-----------------|------------------------------------|----------|----------|----------|----------|----------|----------|
|                 | 2-1(7)                             | 3-1(7)   | 4-1(7)   | 5-1(7)   | 6-1(7)   | 7-1(7)   | 8-1(7)   |
| Vehicle Control | 3.2± 0.3                           | 3.1± 0.3 | 2.9± 0.3 | 2.9± 0.3 | 3.2± 0.3 | 3.0± 0.3 | 3.3± 0.5 |
| 3 mg/kg         | 3.2± 0.3                           | 3.1± 0.3 | 3.1± 0.3 | 3.0± 0.4 | 3.2± 0.3 | 3.2± 0.3 | 3.3± 0.3 |
| 10 mg/kg        | 3.2± 0.2                           | 3.2± 0.3 | 3.0± 0.2 | 3.0± 0.3 | 3.2± 0.4 | 3.0± 0.3 | 3.4± 0.3 |
| 30 mg/kg        | 3.2± 0.4                           | 3.2± 0.3 | 3.1± 0.3 | 3.1± 0.4 | 3.1± 0.4 | 3.0± 0.5 | 3.3± 0.4 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
UNIT : g  
REPORT TYPE : A1 26  
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

| Group Name      | Administration week-day (effective) |          |          |          |          |          |          |
|-----------------|-------------------------------------|----------|----------|----------|----------|----------|----------|
|                 | 9-1 (7)                             | 10-1 (7) | 11-1 (7) | 12-1 (7) | 13-1 (7) | 14-1 (7) | 15-1 (7) |
| Vehicle Control | 3.1± 0.5                            | 3.1± 0.6 | 3.1± 0.6 | 3.0± 0.6 | 2.9± 0.3 | 2.9± 0.3 | 3.0± 0.2 |
| 3 mg/kg         | 3.1± 0.5                            | 3.2± 0.5 | 3.0± 0.5 | 2.9± 0.5 | 2.9± 0.2 | 2.9± 0.3 | 3.0± 0.3 |
| 10 mg/kg        | 2.9± 0.2                            | 2.9± 0.3 | 2.9± 0.3 | 2.9± 0.3 | 2.9± 0.3 | 2.8± 0.3 | 2.9± 0.3 |
| 30 mg/kg        | 2.9± 0.3                            | 2.9± 0.5 | 2.9± 0.4 | 2.9± 0.3 | 2.9± 0.6 | 2.9± 0.5 | 2.9± 0.4 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
UNIT : g  
REPORT TYPE : A1 26  
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

| Group Name      | Administration week-day(effective) |          |          |          |          |           |          |
|-----------------|------------------------------------|----------|----------|----------|----------|-----------|----------|
|                 | 16-1(7)                            | 17-1(7)  | 18-1(7)  | 19-1(7)  | 20-1(7)  | 21-1(7)   | 22-1(7)  |
| Vehicle Control | 2.9± 0.2                           | 3.0± 0.3 | 3.1± 0.3 | 2.9± 0.3 | 3.0± 0.3 | 2.9± 0.2  | 2.9± 0.3 |
| 3 mg/kg         | 2.9± 0.3                           | 3.0± 0.3 | 3.1± 0.4 | 3.0± 0.5 | 3.0± 0.5 | 3.0± 0.5  | 3.0± 0.6 |
| 10 mg/kg        | 3.2± 0.6                           | 3.0± 0.5 | 3.1± 0.4 | 2.9± 0.5 | 3.0± 0.4 | 2.9± 0.4  | 3.0± 0.5 |
| 30 mg/kg        | 2.9± 0.4                           | 2.9± 0.4 | 3.0± 0.5 | 2.9± 0.6 | 2.9± 0.7 | 2.8± 0.7* | 2.6± 0.5 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |          |          |          |          |
|-----------------|------------------------------------|----------|----------|----------|----------|
|                 | 23-1(7)                            | 24-1(7)  | 25-1(7)  | 26-1(7)  | 26-7(6)  |
| Vehicle Control | 2.8± 0.2                           | 3.0± 0.3 | 2.8± 0.3 | 2.9± 0.3 | 2.8± 0.3 |
| 3 mg/kg         | 3.0± 0.5                           | 3.1± 0.7 | 3.1± 0.6 | 3.1± 0.7 | 3.0± 0.7 |
| 10 mg/kg        | 2.9± 0.5                           | 2.9± 0.3 | 3.0± 0.3 | 3.0± 0.2 | 2.8± 0.3 |
| 30 mg/kg        | 2.3± 0.5*                          | 2.8± 0.2 | 2.9± 0.2 | 3.0± 0.1 | 2.6± 0.4 |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of Dunnett

TABLE A 13

URINALYSIS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

| Group Name      | NO. of Animals | pH  |     |     |     |     |     |     | CHI | Protein |   |    |    |    | CHI | Glucose |    |   |   |    | CHI | Ketone body |    |   |   |    | CHI | Occult blood |    |    |    |   | CHI |   |    |
|-----------------|----------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|----|----|----|-----|---------|----|---|---|----|-----|-------------|----|---|---|----|-----|--------------|----|----|----|---|-----|---|----|
|                 |                | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ± | +  | 2+ | 3+ |     | 4+      | -  | ± | + | 2+ |     | 3+          | 4+ | - | ± | +  |     | 2+           | 3+ | 4+ | -  | ± |     | + | 2+ |
| Vehicle Control | 18             | 0   | 3   | 3   | 5   | 2   | 0   | 5   |     | 0       | 1 | 16 | 1  | 0  | 0   |         | 18 | 0 | 0 | 0  | 0   | 0           |    | 2 | 8 | 8  | 0   | 0            | 0  |    | 18 | 0 | 0   | 0 | 0  |
| 3 mg/kg         | 21             | 0   | 1   | 4   | 4   | 5   | 4   | 3   |     | 0       | 2 | 18 | 1  | 0  | 0   |         | 21 | 0 | 0 | 0  | 0   | 0           |    | 1 | 6 | 14 | 0   | 0            | 0  |    | 21 | 0 | 0   | 0 | 0  |
| 10 mg/kg        | 14             | 0   | 6   | 1   | 2   | 1   | 3   | 1   |     | 0       | 1 | 11 | 2  | 0  | 0   |         | 14 | 0 | 0 | 0  | 0   | 0           |    | 2 | 6 | 6  | 0   | 0            | 0  |    | 14 | 0 | 0   | 0 | 0  |
| 30 mg/kg        | 6              | 0   | 0   | 2   | 1   | 2   | 0   | 1   |     | 0       | 0 | 4  | 2  | 0  | 0   |         | 6  | 0 | 0 | 0  | 0   | 0           |    | 1 | 3 | 2  | 0   | 0            | 0  |    | 6  | 0 | 0   | 0 | 0  |

Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01

Test of CHI SQUARE

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of<br>Animals | Urobilinogen |   |    |       | CHI |
|-----------------|-------------------|--------------|---|----|-------|-----|
|                 |                   | ±            | + | 2+ | 3+ 4+ |     |
| Vehicle Control | 18                | 18           | 0 | 0  | 0     | 0   |
| 3 mg/kg         | 21                | 21           | 0 | 0  | 0     | 0   |
| 10 mg/kg        | 14                | 14           | 0 | 0  | 0     | 0   |
| 30 mg/kg        | 6                 | 6            | 0 | 0  | 0     | 0   |

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Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 6

TABLE A 14

URINALYSIS : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | pH  |     |     |     |     |     |     | CHI | Protein |    |   |    |    | CHI | Glucose |   |   |   |    | CHI | Ketone body |    |   |   |   | CHI | Occult blood |    |    |   | CHI |
|-----------------|----------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|----|---|----|----|-----|---------|---|---|---|----|-----|-------------|----|---|---|---|-----|--------------|----|----|---|-----|
|                 |                | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ±  | + | 2+ | 3+ |     | 4+      | - | ± | + | 2+ |     | 3+          | 4+ | - | ± | + |     | 2+           | 3+ | 4+ | - |     |
| Vehicle Control | 24             | 0   | 7   | 4   | 3   | 1   | 8   | 1   | 1   | 11      | 11 | 1 | 0  | 0  | 24  | 0       | 0 | 0 | 0 | 0  | 1   | 11          | 10 | 2 | 0 | 0 | 24  | 0            | 0  | 0  | 0 |     |
| 3 mg/kg         | 24             | 0   | 9   | 2   | 6   | 2   | 5   | 0   | 0   | 14      | 8  | 2 | 0  | 0  | 24  | 0       | 0 | 0 | 0 | 0  | 0   | 13          | 11 | 0 | 0 | 0 | 24  | 0            | 0  | 0  | 0 |     |
| 10 mg/kg        | 17             | 0   | 3   | 3   | 1   | 4   | 5   | 1   | 0   | 8       | 8  | 1 | 0  | 0  | 17  | 0       | 0 | 0 | 0 | 0  | 2   | 7           | 4  | 4 | 0 | 0 | 17  | 0            | 0  | 0  | 0 |     |
| 30 mg/kg        | 5              | 0   | 1   | 1   | 1   | 0   | 1   | 1   | 0   | 2       | 3  | 0 | 0  | 0  | 5   | 0       | 0 | 0 | 0 | 0  | 0   | 1           | 4  | 0 | 0 | 0 | 5   | 0            | 0  | 0  | 0 |     |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS6



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of<br>Animals | Urobilinogen |   |    |       | CHI |
|-----------------|-------------------|--------------|---|----|-------|-----|
|                 |                   | ±            | + | 2+ | 3+ 4+ |     |
| Vehicle Control | 24                | 24           | 0 | 0  | 0     | 0   |
| 3 mg/kg         | 24                | 24           | 0 | 0  | 0     | 0   |
| 10 mg/kg        | 17                | 17           | 0 | 0  | 0     | 0   |
| 30 mg/kg        | 5                 | 5            | 0 | 0  | 0     | 0   |

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Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 6

TABLE A 15

HEMATOLOGY : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |        | HEMOGLOBIN<br>g/dl |       | HEMATOCRIT<br>% |       | MCV<br>fl |       | MCH<br>Pg |       | MCHC<br>g/dl |     | PLATELET<br>10 <sup>3</sup> /μl |     |
|-----------------|----------------|---------------------------------------|--------|--------------------|-------|-----------------|-------|-----------|-------|-----------|-------|--------------|-----|---------------------------------|-----|
| Vehicle Control | 24             | 10.25±                                | 0.52   | 14.6±              | 0.5   | 43.4±           | 1.8   | 42.4±     | 0.9   | 14.3±     | 0.4   | 33.7±        | 0.6 | 1489±                           | 208 |
| 3 mg/kg         | 25             | 9.92±                                 | 0.45*  | 14.3±              | 0.9   | 42.6±           | 2.5   | 42.9±     | 1.4*  | 14.4±     | 0.6   | 33.6±        | 0.6 | 1543±                           | 250 |
| 10 mg/kg        | 18             | 8.67±                                 | 1.18** | 13.4±              | 1.4** | 39.5±           | 3.8** | 45.9±     | 2.9** | 15.5±     | 0.9** | 33.9±        | 0.7 | 1564±                           | 398 |
| 30 mg/kg        | 6              | 6.89±                                 | 1.13** | 11.4±              | 1.8** | 34.4±           | 5.9** | 49.8±     | 1.4** | 16.6±     | 0.4** | 33.4±        | 1.4 | 1887±                           | 909 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

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| Group Name      | NO. of Animals | RETICULOCYTE % |       |
|-----------------|----------------|----------------|-------|
| Vehicle Control | 24             | 4.2±           | 0.6   |
| 3 mg/kg         | 25             | 4.5±           | 1.0   |
| 10 mg/kg        | 18             | 5.9±           | 2.2** |
| 30 mg/kg        | 6              | 4.1±           | 1.7   |

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Significant difference ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

| Group Name      | NO. of Animals | WBC            |      | Differential |       | WBC (%) |        | MONO  |       | EOSINO |     | BASO |     |
|-----------------|----------------|----------------|------|--------------|-------|---------|--------|-------|-------|--------|-----|------|-----|
|                 |                | $10^3/\mu\ell$ |      | NEUTRO       |       | LYMPHO  |        |       |       |        |     |      |     |
| Vehicle Control | 24             | 1.17±          | 0.82 | 18.9±        | 6.7   | 78.2±   | 6.6    | 2.4±  | 0.9   | 0.5±   | 0.7 | 0.0± | 0.0 |
| 3 mg/kg         | 25             | 1.23±          | 0.40 | 17.5±        | 8.1   | 79.2±   | 8.6    | 2.6±  | 1.0   | 0.6±   | 0.7 | 0.0± | 0.0 |
| 10 mg/kg        | 18             | 1.48±          | 1.94 | 24.6±        | 18.1  | 70.3±   | 20.8   | 4.6±  | 3.1** | 0.4±   | 0.6 | 0.0± | 0.0 |
| 30 mg/kg        | 6              | 1.42±          | 1.32 | 51.3±        | 25.9* | 38.6±   | 23.2** | 10.0± | 5.8** | 0.0±   | 0.0 | 0.1± | 0.3 |

Significant difference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

TABLE A 16

HEMATOLOGY : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |        | HEMOGLOBIN<br>g/dl |       | HEMATOCRIT<br>% |       | MCV<br>fl |       | MCH<br>Pg |       | MCHC<br>g/dl |     | PLATELET<br>10 <sup>3</sup> /μl |     |
|-----------------|----------------|---------------------------------------|--------|--------------------|-------|-----------------|-------|-----------|-------|-----------|-------|--------------|-----|---------------------------------|-----|
| Vehicle Control | 23             | 10.29±                                | 0.38   | 14.8±              | 0.3   | 43.5±           | 1.2   | 42.3±     | 0.8   | 14.4±     | 0.3   | 34.1±        | 0.5 | 1320±                           | 178 |
| 3 mg/kg         | 24             | 9.57±                                 | 0.63** | 14.2±              | 0.6** | 41.3±           | 1.8** | 43.3±     | 1.4** | 14.9±     | 0.7** | 34.4±        | 0.7 | 1295±                           | 251 |
| 10 mg/kg        | 17             | 9.10±                                 | 0.77** | 14.0±              | 0.7** | 40.7±           | 2.2** | 44.9±     | 2.4** | 15.4±     | 0.8** | 34.4±        | 0.5 | 1437±                           | 378 |
| 30 mg/kg        | 5              | 6.97±                                 | 1.36** | 11.7±              | 1.9** | 34.4±           | 5.2** | 49.8±     | 3.3** | 16.9±     | 0.9** | 34.0±        | 0.6 | 1599±                           | 405 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of Animals | RETICULOCYTE % |       |
|-----------------|----------------|----------------|-------|
| Vehicle Control | 23             | 3.9 ±          | 0.6   |
| 3 mg/kg         | 24             | 4.7 ±          | 0.8** |
| 10 mg/kg        | 17             | 4.7 ±          | 0.6** |
| 30 mg/kg        | 5              | 6.6 ±          | 2.3** |

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Significant difference ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 6



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

| Group Name      | NO. of Animals | WBC            |      | Differential |       | WBC (%) |       | MONO |       | EOSINO |     | BASO |     |
|-----------------|----------------|----------------|------|--------------|-------|---------|-------|------|-------|--------|-----|------|-----|
|                 |                | $10^3/\mu\ell$ |      | NEUTRO       |       | LYMPHO  |       |      |       |        |     |      |     |
| Vehicle Control | 23             | 1.26±          | 0.94 | 14.8±        | 5.1   | 82.7±   | 5.1   | 2.1± | 0.8   | 0.3±   | 0.5 | 0.0± | 0.0 |
| 3 mg/kg         | 24             | 1.31±          | 1.03 | 17.3±        | 7.0   | 78.8±   | 7.6   | 3.4± | 1.9** | 0.5±   | 0.7 | 0.0± | 0.0 |
| 10 mg/kg        | 17             | 0.82±          | 0.44 | 17.6±        | 6.4   | 78.5±   | 6.6   | 3.6± | 1.7** | 0.3±   | 0.6 | 0.0± | 0.0 |
| 30 mg/kg        | 5              | 0.59±          | 0.24 | 39.2±        | 8.8** | 52.0±   | 9.6** | 8.7± | 5.1** | 0.0±   | 0.0 | 0.0± | 0.0 |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Dunnett

TABLE A 17

BIOCHEMISTRY : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |     | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |    | T-CHOLESTEROL<br>mg/dl |    | TRIGLYCERIDE<br>mg/dl |    |
|-----------------|----------------|-----------------------|-----|-----------------|-----|-----------|-----|----------------------|------|------------------|----|------------------------|----|-----------------------|----|
| Vehicle Control | 24             | 5.3±                  | 0.4 | 3.1±            | 0.2 | 1.4±      | 0.1 | 0.11±                | 0.02 | 237±             | 37 | 86±                    | 22 | 31±                   | 9  |
| 3 mg/kg         | 25             | 5.3±                  | 0.3 | 3.0±            | 0.3 | 1.4±      | 0.2 | 0.11±                | 0.02 | 240±             | 48 | 90±                    | 19 | 34±                   | 9  |
| 10 mg/kg        | 18             | 5.3±                  | 0.2 | 3.1±            | 0.2 | 1.4±      | 0.2 | 0.13±                | 0.04 | 224±             | 48 | 92±                    | 19 | 33±                   | 16 |
| 30 mg/kg        | 6              | 5.2±                  | 0.2 | 3.0±            | 0.4 | 1.5±      | 0.3 | 0.12±                | 0.03 | 206±             | 56 | 107±                   | 12 | 25±                   | 15 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

(HCL074)

BAIS 6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

| Group Name      | NO. of Animals | PHOSPHOLIPID |    | AST  |     | ALT |      | LDH   |        | ALP  |     | G-GTP |     | CK   |     |
|-----------------|----------------|--------------|----|------|-----|-----|------|-------|--------|------|-----|-------|-----|------|-----|
|                 |                | mg/dl        |    | U/L  | L   | U/L | L    | U/L   | L      | U/L  | L   | U/L   | L   | U/L  | L   |
| Vehicle Control | 24             | 169±         | 41 | 54±  | 18  | 14± | 3    | 213±  | 49     | 242± | 27  | 0.4±  | 0.3 | 77±  | 24  |
| 3 mg/kg         | 25             | 177±         | 36 | 55±  | 26  | 15± | 3    | 254±  | 124    | 239± | 41  | 0.2±  | 0.3 | 134± | 281 |
| 10 mg/kg        | 18             | 183±         | 34 | 99±  | 165 | 24± | 27   | 519±  | 1029   | 256± | 49  | 0.3±  | 0.3 | 113± | 140 |
| 30 mg/kg        | 6              | 179±         | 26 | 154± | 109 | 30± | 14** | 1368± | 1553** | 394± | 340 | 0.3±  | 0.2 | 681± | 857 |

Significant difference ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

| Group Name      | NO. of Animals | UREANITROGEN<br>mg/dl |     | SODIUM<br>mEq/l |     | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |     | INORGANIC PHOSPHRUS<br>mg/dl |     |
|-----------------|----------------|-----------------------|-----|-----------------|-----|--------------------|-----|-------------------|---|------------------|-----|------------------------------|-----|
| Vehicle Control | 24             | 28.2±                 | 4.0 | 150±            | 1   | 4.2±               | 0.2 | 118±              | 2 | 9.0±             | 0.2 | 6.3±                         | 0.7 |
| 3 mg/kg         | 25             | 28.6±                 | 6.5 | 150±            | 2   | 4.2±               | 0.2 | 118±              | 2 | 9.1±             | 0.3 | 6.2±                         | 1.1 |
| 10 mg/kg        | 18             | 27.1±                 | 6.0 | 150±            | 1   | 4.2±               | 0.2 | 118±              | 1 | 9.2±             | 0.5 | 6.4±                         | 1.2 |
| 30 mg/kg        | 6              | 31.4±                 | 7.9 | 153±            | 2** | 4.1±               | 0.1 | 118±              | 3 | 9.3±             | 0.4 | 7.0±                         | 0.4 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

TABLE A 18

BIOCHEMISTRY : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |       | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |    | T-CHOLESTEROL<br>mg/dl |     | TRIGLYCERIDE<br>mg/dl |   |
|-----------------|----------------|-----------------------|-----|-----------------|-----|-----------|-------|----------------------|------|------------------|----|------------------------|-----|-----------------------|---|
| Vehicle Control | 23             | 5.3±                  | 0.2 | 3.2±            | 0.2 | 1.6±      | 0.1   | 0.12±                | 0.04 | 186±             | 29 | 63±                    | 15  | 23±                   | 7 |
| 3 mg/kg         | 23             | 5.3±                  | 0.2 | 3.2±            | 0.2 | 1.6±      | 0.2   | 0.14±                | 0.06 | 176±             | 23 | 61±                    | 13  | 20±                   | 6 |
| 10 mg/kg        | 17             | 5.3±                  | 0.2 | 3.3±            | 0.1 | 1.7±      | 0.1** | 0.13±                | 0.04 | 192±             | 24 | 71±                    | 14  | 22±                   | 6 |
| 30 mg/kg        | 5              | 5.3±                  | 0.2 | 3.3±            | 0.1 | 1.6±      | 0.1   | 0.13±                | 0.01 | 207±             | 25 | 84±                    | 12* | 18±                   | 7 |

Significant difference ; \* : P ≤ 0.05

\*\* : P ≤ 0.01

Test of Dunnett

(HCL074)

BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

| Group Name      | NO. of Animals | PHOSPHOLIPID<br>mg/dl |     | AST<br>U/L |     | ALT<br>U/L |     | LDH<br>U/L |      | ALP<br>U/L |    | G-GTP<br>U/L |     | CK<br>U/L |     |
|-----------------|----------------|-----------------------|-----|------------|-----|------------|-----|------------|------|------------|----|--------------|-----|-----------|-----|
| Vehicle Control | 23             | 129±                  | 29  | 54±        | 16  | 16±        | 6   | 208±       | 55   | 402±       | 62 | 0.1±         | 0.2 | 96±       | 71  |
| 3 mg/kg         | 23             | 120±                  | 26  | 96±        | 128 | 52±        | 119 | 323±       | 315  | 375±       | 74 | 0.2±         | 0.2 | 180±      | 275 |
| 10 mg/kg        | 17             | 142±                  | 27  | 52±        | 17  | 19±        | 11  | 207±       | 60   | 406±       | 73 | 0.2±         | 0.1 | 105±      | 68  |
| 30 mg/kg        | 5              | 162±                  | 19* | 96±        | 74  | 19±        | 6   | 887±       | 1043 | 404±       | 60 | 0.3±         | 0.1 | 328±      | 551 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

PAGE : 3

| Group Name      | NO. of Animals | UREANITROGEN<br>mg/dl |      | SODIUM<br>mEq/l |   | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |     | INORGANIC PHOSPHRUS<br>mg/dl |     |
|-----------------|----------------|-----------------------|------|-----------------|---|--------------------|-----|-------------------|---|------------------|-----|------------------------------|-----|
| Vehicle Control | 23             | 23.7±                 | 3.2  | 149±            | 1 | 3.9±               | 0.2 | 116±              | 2 | 8.9±             | 0.3 | 6.0±                         | 1.4 |
| 3 mg/kg         | 23             | 22.6±                 | 2.8  | 149±            | 2 | 4.0±               | 0.2 | 117±              | 2 | 8.9±             | 0.3 | 6.3±                         | 1.0 |
| 10 mg/kg        | 17             | 23.9±                 | 3.7  | 150±            | 1 | 3.8±               | 0.2 | 118±              | 2 | 8.9±             | 0.2 | 6.1±                         | 1.0 |
| 30 mg/kg        | 5              | 27.9±                 | 1.8* | 150±            | 1 | 3.9±               | 0.3 | 118±              | 1 | 9.1±             | 0.2 | 6.5±                         | 1.2 |

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

(HCL074)

BAIS 6

TABLE A 19

GROSS FINDINGS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0- 27W)

| Organ       | Findings       | Group Name<br>NO. of Animals | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|-------------|----------------|------------------------------|-----------------|---------|----------|----------|
|             |                |                              | 25 (%)          | 25 (%)  | 25 (%)   | 25 (%)   |
| skin/app    | ulcer          |                              | 1 ( 4)          | 0 ( 0)  | 0 ( 0)   | 0 ( 0)   |
|             | erosion        |                              | 1 ( 4)          | 1 ( 4)  | 0 ( 0)   | 1 ( 4)   |
| lung        | red zone       |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 3 ( 12)  |
| lymph node  | enlarged       |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
|             | red            |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| thymus      | enlarged       |                              | 0 ( 0)          | 0 ( 0)  | 9 ( 36)  | 15 ( 60) |
|             | red zone       |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| spleen      | enlarged       |                              | 0 ( 0)          | 0 ( 0)  | 2 ( 8)   | 9 ( 36)  |
|             | white zone     |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 1 ( 4)   |
|             | black zone     |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 3 ( 12)  |
| liver       | enlarged       |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
|             | nodule         |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
|             | deformed       |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
|             | rough          |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
| kidney      | hydronephrosis |                              | 0 ( 0)          | 1 ( 4)  | 0 ( 0)   | 0 ( 0)   |
| pituitary   | small          |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
| testis      | small          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| brain       | deformed       |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
| eye         | turbid         |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
|             | pleura         | nodule                       |                 | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
|             | thick          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| abdominal c | hemorrhage     |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0- 27W)

---

| Organ       | Findings        | Group Name<br>NO. of Animals | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|-------------|-----------------|------------------------------|-----------------|---------|----------|----------|
|             |                 |                              | 25 (%)          | 25 (%)  | 25 (%)   | 25 (%)   |
| thoracic ca | pleural fluid   |                              | 0 ( 0)          | 0 ( 0)  | 5 ( 20)  | 10 ( 40) |
| other       | thick           |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
|             | forelimb:nodule |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 0 ( 0)   |
| whole body  | anemic          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 2 ( 8)   |

---

TABLE A 20

GROSS FINDINGS : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0- 27W)

| Organ       | Findings          | Group Name<br>NO. of Animals | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|-------------|-------------------|------------------------------|-----------------|---------|----------|----------|
|             |                   |                              | 25 (%)          | 25 (%)  | 25 (%)   | 25 (%)   |
| skin/app    | erosion           |                              | 0 ( 0)          | 2 ( 8)  | 2 ( 8)   | 1 ( 4)   |
|             | scab              |                              | 1 ( 4)          | 0 ( 0)  | 0 ( 0)   | 0 ( 0)   |
| lung        | red zone          |                              | 0 ( 0)          | 0 ( 0)  | 2 ( 8)   | 5 ( 20)  |
| lymph node  | enlarged          |                              | 1 ( 4)          | 3 ( 12) | 1 ( 4)   | 1 ( 4)   |
|             | red zone          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| thymus      | enlarged          |                              | 0 ( 0)          | 1 ( 4)  | 6 ( 24)  | 16 ( 64) |
| spleen      | enlarged          |                              | 0 ( 0)          | 0 ( 0)  | 2 ( 8)   | 11 ( 44) |
|             | black zone        |                              | 1 ( 4)          | 1 ( 4)  | 0 ( 0)   | 0 ( 0)   |
| stomach     | forestomach:thick |                              | 0 ( 0)          | 0 ( 0)  | 1 ( 4)   | 1 ( 4)   |
| liver       | enlarged          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 3 ( 12)  |
|             | rough             |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| kidney      | cyst              |                              | 1 ( 4)          | 0 ( 0)  | 0 ( 0)   | 0 ( 0)   |
| adrenal     | red zone          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| brain       | red zone          |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |
| peritoneum  | red zone          |                              | 1 ( 4)          | 0 ( 0)  | 0 ( 0)   | 0 ( 0)   |
| abdominal c | hemorrhage        |                              | 1 ( 4)          | 0 ( 0)  | 0 ( 0)   | 0 ( 0)   |
| thoracic ca | pleural fluid     |                              | 0 ( 0)          | 0 ( 0)  | 6 ( 24)  | 13 ( 52) |
| whole body  | anemic            |                              | 0 ( 0)          | 0 ( 0)  | 0 ( 0)   | 1 ( 4)   |

TABLE A 21

ORGAN WEIGHT, ABSOLUTE : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight  | ADRENALS      |                 | TESTES        |               | HEART         |  | LUNGS |  | KIDNEYS |  |
|-----------------|----------------|--------------|---------------|-----------------|---------------|---------------|---------------|--|-------|--|---------|--|
| Vehicle Control | 24             | 28.7 ± 2.1   | 0.011 ± 0.002 | 0.222 ± 0.011   | 0.147 ± 0.017 | 0.143 ± 0.010 | 0.401 ± 0.042 |  |       |  |         |  |
| 3 mg/kg         | 25             | 29.4 ± 2.7   | 0.011 ± 0.003 | 0.196 ± 0.024** | 0.145 ± 0.012 | 0.146 ± 0.012 | 0.401 ± 0.044 |  |       |  |         |  |
| 10 mg/kg        | 18             | 27.8 ± 2.4   | 0.011 ± 0.003 | 0.158 ± 0.015** | 0.143 ± 0.016 | 0.150 ± 0.018 | 0.382 ± 0.037 |  |       |  |         |  |
| 30 mg/kg        | 7              | 24.9 ± 2.4** | 0.009 ± 0.001 | 0.092 ± 0.013** | 0.150 ± 0.036 | 0.148 ± 0.022 | 0.364 ± 0.046 |  |       |  |         |  |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett



STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

| Group Name      | NO. of Animals | SPLEEN |       | LIVER  |       | BRAIN  |       |
|-----------------|----------------|--------|-------|--------|-------|--------|-------|
| Vehicle Control | 24             | 0.072± | 0.012 | 1.057± | 0.136 | 0.465± | 0.014 |
| 3 mg/kg         | 25             | 0.076± | 0.027 | 1.112± | 0.162 | 0.465± | 0.016 |
| 10 mg/kg        | 18             | 0.079± | 0.029 | 1.066± | 0.145 | 0.468± | 0.018 |
| 30 mg/kg        | 7              | 0.125± | 0.068 | 1.040± | 0.174 | 0.459± | 0.007 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 6

TABLE A 22

ORGAN WEIGHT, ABSOLUTE : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
 SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight | ADRENALS |       | OVARIES |       | HEART  |       | LUNGS  |       | KIDNEYS |       |
|-----------------|----------------|-------------|----------|-------|---------|-------|--------|-------|--------|-------|---------|-------|
| Vehicle Control | 24             | 23.0± 1.5   | 0.014±   | 0.002 | 0.024±  | 0.008 | 0.119± | 0.013 | 0.137± | 0.011 | 0.309±  | 0.048 |
| 3 mg/kg         | 24             | 23.0± 1.8   | 0.013±   | 0.002 | 0.024±  | 0.006 | 0.122± | 0.014 | 0.138± | 0.014 | 0.319±  | 0.041 |
| 10 mg/kg        | 18             | 22.9± 1.5   | 0.013±   | 0.001 | 0.024±  | 0.006 | 0.121± | 0.011 | 0.136± | 0.013 | 0.306±  | 0.034 |
| 30 mg/kg        | 5              | 21.9± 1.0   | 0.012±   | 0.001 | 0.022±  | 0.005 | 0.122± | 0.015 | 0.132± | 0.010 | 0.291±  | 0.028 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

| Group Name      | NO. of Animals | SPLEEN |       | LIVER  |       | BRAIN  |       |
|-----------------|----------------|--------|-------|--------|-------|--------|-------|
| Vehicle Control | 24             | 0.077± | 0.009 | 0.898± | 0.096 | 0.469± | 0.017 |
| 3 mg/kg         | 24             | 0.083± | 0.019 | 0.881± | 0.132 | 0.476± | 0.021 |
| 10 mg/kg        | 18             | 0.074± | 0.013 | 0.928± | 0.077 | 0.473± | 0.017 |
| 30 mg/kg        | 5              | 0.124± | 0.079 | 0.955± | 0.126 | 0.464± | 0.012 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 6

TABLE A 23

ORGAN WEIGHT, RELATIVE : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight (g) | ADRENALS      | TESTES          | HEART         | LUNGS           | KIDNEYS       |
|-----------------|----------------|-----------------|---------------|-----------------|---------------|-----------------|---------------|
| Vehicle Control | 24             | 28.7 ± 2.1      | 0.037 ± 0.007 | 0.778 ± 0.060   | 0.514 ± 0.073 | 0.502 ± 0.050   | 1.403 ± 0.166 |
| 3 mg/kg         | 25             | 29.4 ± 2.7      | 0.036 ± 0.010 | 0.669 ± 0.084** | 0.495 ± 0.054 | 0.498 ± 0.050   | 1.369 ± 0.169 |
| 10 mg/kg        | 18             | 27.8 ± 2.4      | 0.041 ± 0.007 | 0.575 ± 0.086** | 0.517 ± 0.054 | 0.541 ± 0.063   | 1.379 ± 0.140 |
| 30 mg/kg        | 7              | 24.9 ± 2.4**    | 0.038 ± 0.005 | 0.370 ± 0.040** | 0.605 ± 0.145 | 0.598 ± 0.085** | 1.463 ± 0.170 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

| Group Name      | NO. of Animals | SPLEEN          | LIVER           | BRAIN           |
|-----------------|----------------|-----------------|-----------------|-----------------|
| Vehicle Control | 24             | 0.253 ± 0.044   | 3.678 ± 0.354   | 1.627 ± 0.116   |
| 3 mg/kg         | 25             | 0.262 ± 0.112   | 3.773 ± 0.377   | 1.593 ± 0.153   |
| 10 mg/kg        | 18             | 0.284 ± 0.092   | 3.834 ± 0.320   | 1.697 ± 0.141   |
| 30 mg/kg        | 7              | 0.494 ± 0.258** | 4.159 ± 0.504** | 1.855 ± 0.163** |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 6

TABLE A 24

ORGAN WEIGHT, RELATIVE : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
 SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight (g) | ADRENALS     | OVARIES      | HEART        | LUNGS        | KIDNEYS      |
|-----------------|----------------|-----------------|--------------|--------------|--------------|--------------|--------------|
| Vehicle Control | 24             | 23.0± 1.5       | 0.059± 0.009 | 0.102± 0.034 | 0.516± 0.051 | 0.594± 0.046 | 1.344± 0.205 |
| 3 mg/kg         | 24             | 23.0± 1.8       | 0.057± 0.008 | 0.105± 0.023 | 0.531± 0.058 | 0.601± 0.043 | 1.390± 0.167 |
| 10 mg/kg        | 18             | 22.9± 1.5       | 0.056± 0.007 | 0.105± 0.025 | 0.529± 0.052 | 0.594± 0.056 | 1.340± 0.152 |
| 30 mg/kg        | 5              | 21.9± 1.0       | 0.055± 0.006 | 0.099± 0.022 | 0.556± 0.051 | 0.605± 0.032 | 1.330± 0.097 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

| Group Name      | NO. of Animals | SPLEEN        | LIVER         | BRAIN         |
|-----------------|----------------|---------------|---------------|---------------|
| Vehicle Control | 24             | 0.334 ± 0.041 | 3.903 ± 0.379 | 2.043 ± 0.147 |
| 3 mg/kg         | 24             | 0.359 ± 0.071 | 3.832 ± 0.505 | 2.077 ± 0.148 |
| 10 mg/kg        | 18             | 0.325 ± 0.051 | 4.064 ± 0.322 | 2.076 ± 0.142 |
| 30 mg/kg        | 5              | 0.561 ± 0.340 | 4.358 ± 0.403 | 2.123 ± 0.075 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 6

TABLE A 25

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                            | Findings             | Group Name<br>No. of animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25   | 10 mg/kg<br>25   | 30 mg/kg<br>25    |
|----------------------------------|----------------------|---------------------------------------|-----------------------|-----------------|------------------|-------------------|
| {Hematopoietic system}           |                      |                                       |                       |                 |                  |                   |
| bone marrow                      | myelogenous leukemia |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>2 ( 8%)  | <25><br>10 ( 40%) |
| thymus                           | malignant lymphoma   |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>9 ( 36%) | <25><br>14 ( 56%) |
| {Special sense organs/appendage} |                      |                                       |                       |                 |                  |                   |
| Harder gl                        | adenoma              |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>1 ( 4%)  | <25><br>0 ( 0%)   |
| {Musculoskeletal system}         |                      |                                       |                       |                 |                  |                   |
| muscle                           | rhabdomyosarcoma     |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>1 ( 4%)  | <25><br>0 ( 0%)   |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

TABLE A 26

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                     | Group Name<br>No. of animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25   | 10 mg/kg<br>25   | 30 mg/kg<br>25    |
|------------------------|------------------------------|---------------------------------------|-----------------------|-----------------|------------------|-------------------|
| {Respiratory system}   |                              |                                       |                       |                 |                  |                   |
| lung                   | bronchiolar-alveolar adenoma |                                       | <25><br>0 ( 0%)       | <25><br>1 ( 4%) | <25><br>0 ( 0%)  | <25><br>1 ( 4%)   |
| {Hematopoietic system} |                              |                                       |                       |                 |                  |                   |
| bone marrow            | myelogenous leukemia         |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>0 ( 0%)  | <25><br>8 ( 32%)  |
| thymus                 | malignant lymphoma           |                                       | <25><br>0 ( 0%)       | <25><br>1 ( 4%) | <25><br>6 ( 24%) | <25><br>14 ( 56%) |
| {Digestive system}     |                              |                                       |                       |                 |                  |                   |
| small intes            | adenocarcinoma               |                                       | <25><br>0 ( 0%)       | <25><br>0 ( 0%) | <25><br>0 ( 0%)  | <25><br>1 ( 4%)   |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

TABLE A 27

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS : MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY No. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : MALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

| Group Name                   | Vehicle Control | 3 mg/kg     | 10 mg/kg     | 30 mg/kg      |
|------------------------------|-----------------|-------------|--------------|---------------|
| SITE : bone marrow           |                 |             |              |               |
| TUMOR : myelogenous leukemia |                 |             |              |               |
| Tumor rate                   |                 |             |              |               |
| Overall rates(a)             | 0/25 ( 0.0)     | 0/25 ( 0.0) | 2/25 ( 8.0)  | 10/25 ( 40.0) |
| Adjusted rates(b)            | 0.00            | 0.00        | 0.00         | 12.50         |
| Terminal rates(c)            | 0/24 ( 0.0)     | 0/25 ( 0.0) | 0/18 ( 0.0)  | 1/ 7 ( 14.3)  |
| Statistical analysis         |                 |             |              |               |
| Peto test                    |                 |             |              |               |
| Standard method(d)           | P < 0.0001**    |             |              |               |
| Prevalence method(d)         | P = 0.0439*     |             |              |               |
| Combined analysis(d)         | P < 0.0001**    |             |              |               |
| Cochran-Armitage test(e)     | P < 0.0001**    |             |              |               |
| Fisher Exact test(e)         |                 | P = N. C.   | P = 0.2449   | P = 0.0003**  |
| SITE : thymus                |                 |             |              |               |
| TUMOR : malignant lymphoma   |                 |             |              |               |
| Tumor rate                   |                 |             |              |               |
| Overall rates(a)             | 0/25 ( 0.0)     | 0/25 ( 0.0) | 9/25 ( 36.0) | 14/25 ( 56.0) |
| Adjusted rates(b)            | 0.00            | 0.00        | 22.22        | 62.50         |
| Terminal rates(c)            | 0/24 ( 0.0)     | 0/25 ( 0.0) | 4/18 ( 22.2) | 4/ 7 ( 57.1)  |
| Statistical analysis         |                 |             |              |               |
| Peto test                    |                 |             |              |               |
| Standard method(d)           | P < 0.0001**    |             |              |               |
| Prevalence method(d)         | P < 0.0001**    |             |              |               |
| Combined analysis(d)         | P < 0.0001**?   |             |              |               |
| Cochran-Armitage test(e)     | P < 0.0001**    |             |              |               |
| Fisher Exact test(e)         |                 | P = N. C.   | P = 0.0008** | P < 0.0001**  |

(HPT360A)

BAIS6

(a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
 Standard method : Death analysis  
 Prevalence method : Incidental tumor test  
 Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$   
 N. C. : Statistical value cannot be calculated and was not significant.



STUDY No. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : MALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

| Group Name                                       | Vehicle Control | 3 mg/kg     | 10 mg/kg      | 30 mg/kg      |
|--|-----------------|-------------|---------------|---------------|
| SITE : bone marrow, thymus                       |                 |             |               |               |
| TUMOR : myelogenous leukemia, malignant lymphoma |                 |             |               |               |
| Tumor rate                                       |                 |             |               |               |
| Overall rates(a)                                 | 0/25 ( 0.0)     | 0/25 ( 0.0) | 11/25 ( 44.0) | 23/25 ( 92.0) |
| Adjusted rates(b)                                | 0.00            | 0.00        | 22.22         | 71.43         |
| Terminal rates(c)                                | 0/24 ( 0.0)     | 0/25 ( 0.0) | 4/18 ( 22.2)  | 5/ 7 ( 71.4)  |
| Statistical analysis                             |                 |             |               |               |
| Peto test  |                 |             |               |               |
| Standard method(d)                               | P < 0.0001**?   |             |               |               |
| Prevalence method(d)                             | P < 0.0001**?   |             |               |               |
| Combined analysis(d)                             | P < 0.0001**?   |             |               |               |
| Cochran-Armitage test(e)                         | P < 0.0001**    |             |               |               |
| Fisher Exact test(e)                             |                 | P = N. C.   | P = 0.0001**  | P < 0.0001**  |

(HPT360A)

BAIS6

- (a) : Number of tumor-bearing animals/number of animals examined at the site.  
 (b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c) : Observed tumor incidence at terminal kill.  
 (d) : Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$   
 N.C. : Statistical value cannot be calculated and was not significant.

TABLE A 28

NEOPLASTIC LESIONS-INCIDENCE  
AND STATISTICAL ANALYSIS : FEMALE  
(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY No. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

| Group Name   | Vehicle Control | 3 mg/kg     | 10 mg/kg     | 30 mg/kg      |
|--|-----------------|-------------|--------------|---------------|
| SITE : bone marrow<br>TUMOR : myelogenous leukemia |                 |             |              |               |
| Tumor rate   |                 |             |              |               |
| Overall rates(a)                                   | 0/25 ( 0.0)     | 0/25 ( 0.0) | 0/25 ( 0.0)  | 8/25 ( 32.0)  |
| Adjusted rates(b)                                  | 0.00            | 0.00        | 0.00         | 0.00          |
| Terminal rates(c)                                  | 0/24 ( 0.0)     | 0/24 ( 0.0) | 0/18 ( 0.0)  | 0/ 5 ( 0.0)   |
| Statistical analysis                               |                 |             |              |               |
| Peto test  |                 |             |              |               |
| Standard method(d)                                 | P < 0.0001**?   |             |              |               |
| Prevalence method(d)                               | P = -----       |             |              |               |
| Combined analysis(d)                               | P < 0.0001**?   |             |              |               |
| Cochran-Armitage test(e)                           | P < 0.0001**    |             |              |               |
| Fisher Exact test(e)                               |                 | P = N. C.   | P = N. C.    | P = 0.0020**  |
| SITE : thymus<br>TUMOR : malignant lymphoma        |                 |             |              |               |
| Tumor rate   |                 |             |              |               |
| Overall rates(a)                                   | 0/25 ( 0.0)     | 1/25 ( 4.0) | 6/25 ( 24.0) | 14/25 ( 56.0) |
| Adjusted rates(b)                                  | 0.00            | 4.17        | 0.00         | 40.00         |
| Terminal rates(c)                                  | 0/24 ( 0.0)     | 1/24 ( 4.2) | 0/18 ( 0.0)  | 2/ 5 ( 40.0)  |
| Statistical analysis                               |                 |             |              |               |
| Peto test  |                 |             |              |               |
| Standard method(d)                                 | P < 0.0001**?   |             |              |               |
| Prevalence method(d)                               | P = 0.0042**    |             |              |               |
| Combined analysis(d)                               | P < 0.0001**?   |             |              |               |
| Cochran-Armitage test(e)                           | P < 0.0001**    |             |              |               |
| Fisher Exact test(e)                               |                 | P = 0.5000  | P = 0.0111*  | P < 0.0001**  |

(HPT360A)

BAIS6

(a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
 Standard method : Death analysis  
 Prevalence method : Incidental tumor test  
 Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$   
 N. C. : Statistical value cannot be calculated and was not significant.

STUDY No. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

| Group Name                                       | Vehicle Control | 3 mg/kg     | 10 mg/kg     | 30 mg/kg      |
|--|-----------------|-------------|--------------|---------------|
| SITE : bone marrow, thymus                       |                 |             |              |               |
| TUMOR : myelogenous leukemia, malignant lymphoma |                 |             |              |               |
| Tumor rate                                       |                 |             |              |               |
| Overall rates(a)                                 | 0/25 ( 0.0)     | 1/25 ( 4.0) | 6/25 ( 24.0) | 22/25 ( 88.0) |
| Adjusted rates(b)                                | 0.00            | 4.17        | 0.00         | 40.00         |
| Terminal rates(c)                                | 0/24 ( 0.0)     | 1/24 ( 4.2) | 0/18 ( 0.0)  | 2/ 5 ( 40.0)  |
| Statistical analysis                             |                 |             |              |               |
| Peto test  |                 |             |              |               |
| Standard method(d)                               | P < 0.0001**?   |             |              |               |
| Prevalence method(d)                             | P = 0.0042**    |             |              |               |
| Combined analysis(d)                             | P < 0.0001**?   |             |              |               |
| Cochran-Armitage test(e)                         | P < 0.0001**    |             |              |               |
| Fisher Exact test(e)                             |                 | P = 0.5000  | P = 0.0111*  | P < 0.0001**  |

(HPT360A)

BAIS6

- (a) : Number of tumor-bearing animals/number of animals examined at the site.  
 (b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c) : Observed tumor incidence at terminal kill.  
 (d) : Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$   
 N.C. : Statistical value cannot be calculated and was not significant.

TABLE A 29

NUMBER OF ANIMALS WITH TUMORS AND  
NUMBER OF TUMORS - TIME RELATED: MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

| Time-related Weeks | Items                               | Group Name | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|--------------------|-------------------------------------|------------|-----------------|---------|----------|----------|
| 1 - 26             | NO. OF EXAMINED ANIMALS             |            | 1               | 0       | 7        | 17       |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0       | 7        | 17       |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0       | 7        | 16       |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 0        | 1        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0       | 0        | 0        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0       | 7        | 18       |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0       | 7        | 18       |
| 27 - 27            | NO. OF EXAMINED ANIMALS             |            | 24              | 25      | 18       | 8        |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0       | 4        | 6        |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0       | 2        | 6        |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 2        | 0        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0       | 1        | 0        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0       | 5        | 6        |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0       | 6        | 6        |
| 1 - 27             | NO. OF EXAMINED ANIMALS             |            | 25              | 25      | 25       | 25       |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0       | 11       | 23       |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0       | 9        | 22       |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 2        | 1        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0       | 1        | 0        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0       | 12       | 24       |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0       | 13       | 24       |

TABLE A 30

NUMBER OF ANIMALS WITH TUMORS AND  
NUMBER OF TUMORS - TIME RELATED: FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

| Time-related Weeks | Items                               | Group Name | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|--------------------|-------------------------------------|------------|-----------------|---------|----------|----------|
| 1 - 26             | NO. OF EXAMINED ANIMALS             |            | 1               | 1       | 7        | 20       |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0       | 6        | 20       |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0       | 6        | 20       |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 0        | 0        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0       | 0        | 0        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0       | 6        | 20       |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0       | 6        | 20       |
| 27 - 27            | NO. OF EXAMINED ANIMALS             |            | 24              | 24      | 18       | 5        |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 2       | 0        | 3        |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 2       | 0        | 2        |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 0        | 1        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 1       | 0        | 1        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 1       | 0        | 3        |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 2       | 0        | 4        |
| 1 - 27             | NO. OF EXAMINED ANIMALS             |            | 25              | 25      | 25       | 25       |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 2       | 6        | 23       |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 2       | 6        | 22       |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0       | 0        | 1        |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 1       | 0        | 1        |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 1       | 6        | 23       |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 2       | 6        | 24       |



TABLE A 31

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR: MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                   | Group Name<br>No. of Animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25 | 10 mg/kg<br>25 | 30 mg/kg<br>25 |
|------------------------|----------------------------|---------------------------------------|-----------------------|---------------|----------------|----------------|
| {Respiratory system}   |                            |                                       |                       |               |                |                |
| lung                   | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>6      | <25><br>18     |
| {Hematopoietic system} |                            |                                       |                       |               |                |                |
| bone marrow            | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>2      | <25><br>2      |
| lymph node             | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>0      |
| thymus                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
| spleen                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>5      | <25><br>11     |
| {Circulatory system}   |                            |                                       |                       |               |                |                |
| heart                  | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>2      |
| {Digestive system}     |                            |                                       |                       |               |                |                |
| liver                  | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>5      | <25><br>15     |
| {Urinary system}       |                            |                                       |                       |               |                |                |
| kidney                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>2      | <25><br>2      |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ              | Findings                   | Group Name<br>No. of Animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25 | 10 mg/kg<br>25 | 30 mg/kg<br>25 |
|--------------------|----------------------------|---------------------------------------|-----------------------|---------------|----------------|----------------|
| {Endocrine system} |                            |                                       |                       |               |                |                |
| pituitary          | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>0      |
|                    |                            |                                       |                       |               |                |                |
| adrenal            | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
|                    |                            |                                       |                       |               |                |                |
| {Nervous system}   |                            |                                       |                       |               |                |                |
| brain              | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
|                    |                            |                                       |                       |               |                |                |
| {Body cavities}    |                            |                                       |                       |               |                |                |
| pleura             | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>2      |
|                    |                            |                                       |                       |               |                |                |

< a > a : Number of animals examined at the site  
 b : Number of animals with lesion

TABLE A 32

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR: FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                   | Group Name<br>No. of Animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25 | 10 mg/kg<br>25 | 30 mg/kg<br>25 |
|------------------------|----------------------------|---------------------------------------|-----------------------|---------------|----------------|----------------|
| {Respiratory system}   |                            |                                       |                       |               |                |                |
| lung                   | leukemic cell infiltration |                                       | <25><br>0             | <25><br>1     | <25><br>6      | <25><br>20     |
| {Hematopoietic system} |                            |                                       |                       |               |                |                |
| bone marrow            | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>0      |
| lymph node             | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>3      |
| thymus                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>2      |
| spleen                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>2      | <25><br>9      |
| {Circulatory system}   |                            |                                       |                       |               |                |                |
| heart                  | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>1      |
| {Digestive system}     |                            |                                       |                       |               |                |                |
| liver                  | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>3      | <25><br>12     |
| {Urinary system}       |                            |                                       |                       |               |                |                |
| kidney                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>5      | <25><br>4      |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                 | Findings                   | Group Name<br>No. of Animals on Study | Vehicle Control<br>25 | 3 mg/kg<br>25 | 10 mg/kg<br>25 | 30 mg/kg<br>25 |
|-----------------------|----------------------------|---------------------------------------|-----------------------|---------------|----------------|----------------|
| {Endocrine system}    |                            |                                       |                       |               |                |                |
| pituitary             | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>1      | <25><br>0      |
|                       | adrenal                    | leukemic cell infiltration            | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
| {Reproductive system} |                            |                                       |                       |               |                |                |
| ovary                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
| {Nervous system}      |                            |                                       |                       |               |                |                |
| brain                 | leukemic cell infiltration |                                       | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |
|                       | spinal cord                | leukemic cell infiltration            | <25><br>0             | <25><br>0     | <25><br>0      | <25><br>1      |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

TABLE A 33

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC  
LESIONS IN JAPAN BIOASSAY RESEARCH CENTER  
: B6.129S2-Trp53 tm1Tyj/J MALE MICE

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN  
BIOASSAY RESEARCH CENTER : B6. 129S2-Trp53 tm1Tyj/J MALE MICE

| Organs<br>Tumors                    | No. of animals<br>examined | No. of animals<br>bearing tumor | Incidence<br>(%) | Min. – Max.<br>(%) |
|-------------------------------------|----------------------------|---------------------------------|------------------|--------------------|
| Bone marrow<br>Myelogenous leukemia | 50                         | 0                               | 0.0              | 0 – 0              |
| Thymus<br>Malignant lymphoma        | 50                         | 0                               | 0.0              | 0 – 0              |
| Harderian gland<br>Adenoma          | 50                         | 0                               | 0.0              | 0 – 0              |
| Muscle<br>Rhabdomyosarcoma          | 50                         | 0                               | 0.0              | 0 – 0              |

2 carcinogenicity studies examined in Japan Bioassay Research Center were used.  
Study No. : 0904, 0906



TABLE A 34

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC  
LESIONS IN JAPAN BIOASSAY RESEARCH CENTER  
: B6.129S2-Trp53 tm1Tyj/J FEMALE MICE

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN  
 BIOASSAY RESEARCH CENTER : B6. 129S2-Trp53 tm1Tyj/J FEMALE MICE

| Organs<br>Tumors                     | No. of animals<br>examined | No. of animals<br>bearing tumor | Incidence<br>(%) | Min. – Max.<br>(%) |
|--------------------------------------|----------------------------|---------------------------------|------------------|--------------------|
| Bone marrow<br>Myelogenous leukemia  | 50                         | 0                               | 0.0              | 0 – 0              |
| Thymus<br>Malignant lymphoma         | 50                         | 0                               | 0.0              | 0 – 0              |
| Lymph node<br>Malignant lymphoma     | 50                         | 1                               | 2.0              | 0 – 4              |
| Lung<br>Bronchiolar-alveolar adenoma | 50                         | 1                               | 2.0              | 0 – 4              |
| Small intestine<br>Adenocarcinoma    | 50                         | 0                               | 0.0              | 0 – 0              |

2 carcinogenicity studies examined in Japan Bioassay Research Center were used.  
 Study No. : 0904, 0907

TABLE A 35

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                            | Findings                              | Group Name<br>No. of Animals on Study<br>Grade | Vehicle Control<br>25 |           |           |           | 3 mg/kg<br>25 |           |           |           | 10 mg/kg<br>25 |           |           |           | 30 mg/kg<br>25 |           |           |           |
|----------------------------------|---------------------------------------|--|-----------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
|                                  |                                       |  | 1+<br>(%)             | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)     | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Integumentary system/appandage] |                                       |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| skin/app                         | ulcer                                 |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |                                       |  | 2<br>( 8)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 1<br>( 4) | 0<br>( 0) |           |
|                                  | erosion                               |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 1<br>( 4) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) |           |
| [Respiratory system]             |                                       |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| lung                             | inflammatory infiltration             |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |                                       |  | 1<br>( 4)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 12)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 1<br>( 4) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 1<br>( 4) | 0<br>( 0) |           |
|                                  | bronchiolar-alveolar cell hyperplasia |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)      | 0<br>( 0) |           |           |
| [Hematopoietic system]           |                                       |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| bone marrow                      | increased hematopoiesis               |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |                                       |  | 1<br>( 4)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) |           |           |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                     | Vehicle Control         |      |      |      | 3 mg/kg                 |      |      |      | 10 mg/kg                |      |      |      | 30 mg/kg                |      |      |      |
|------------------------|------------------------------|-------------------------|------|------|------|-------------------------|------|------|------|-------------------------|------|------|------|-------------------------|------|------|------|
|                        |                              | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      |
|                        |                              | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   |
|                        |                              | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  |
| {Hematopoietic system} |                              |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
| bone marrow            | myelofibrosis                | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |                              | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 1                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
| lymph node             | hemorrhage                   | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |                              | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 2                       | 0    | 0    | 0    |
|                        |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 8)                    | ( 0) | ( 0) | ( 0) |
| spleen                 | deposit of melanin           | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |                              | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 3                       | 0    | 0    | 0    |
|                        |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 12)                   | ( 0) | ( 0) | ( 0) |
|                        | extramedullary hematopoiesis | 4                       | 0    | 0    | 0    | 3                       | 0    | 0    | 0    | 7                       | 1    | 0    | 0    | 10                      | 0    | 0    | 0    |
|                        |                              | ( 16)                   | ( 0) | ( 0) | ( 0) | ( 12)                   | ( 0) | ( 0) | ( 0) | ( 28)                   | ( 4) | ( 0) | ( 0) | ( 40)                   | ( 0) | ( 0) | ( 0) |
| {Circulatory system}   |                              |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
| heart                  | arteritis                    | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |                              | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 1    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 4) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
| {Digestive system}     |                              |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
| salivary gl            | lymphocytic infiltration     | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |                              | 0                       | 0    | 0    | 0    | 1                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ              | Findings                | Vehicle Control         |       |       |       | 3 mg/kg                 |       |       |       | 10 mg/kg                |       |       |       | 30 mg/kg                |        |       |       |
|--------------------|-------------------------|-------------------------|-------|-------|-------|-------------------------|-------|-------|-------|-------------------------|-------|-------|-------|-------------------------|--------|-------|-------|
|                    |                         | No. of Animals on Study |       |       |       | No. of Animals on Study |       |       |       | No. of Animals on Study |       |       |       | No. of Animals on Study |        |       |       |
|                    |                         | 1+                      | 2+    | 3+    | 4+    | 1+                      | 2+    | 3+    | 4+    | 1+                      | 2+    | 3+    | 4+    | 1+                      | 2+     | 3+    | 4+    |
|                    |                         | (%)                     | (%)   | (%)   | (%)   | (%)                     | (%)   | (%)   | (%)   | (%)                     | (%)   | (%)   | (%)   | (%)                     | (%)    | (%)   | (%)   |
| [Digestive system] |                         |                         |       |       |       |                         |       |       |       |                         |       |       |       |                         |        |       |       |
| stomach            |                         | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |        |       |       |
|                    | karyomegaly             | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 2                       | 1      | 0     | 0     |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )                   | ( 4 )  | ( 0 ) | ( 0 ) |
|                    | hyperplasia:forestomach | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 1                       | 0      | 0     | 0     |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )                   | ( 0 )  | ( 0 ) | ( 0 ) |
| small intes        |                         | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |        |       |       |
|                    | karyomegaly             | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 6                       | 9      | 0     | 0 **  |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 24 )                  | ( 36 ) | ( 0 ) | ( 0 ) |
|                    | atypical hyperplasia    | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 6                       | 0      | 0     | 0 *   |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 24 )                  | ( 0 )  | ( 0 ) | ( 0 ) |
| liver              |                         | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |       |       |       | <25>                    |        |       |       |
|                    | malformation            | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 1                       | 0      | 0     | 0     |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )                   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | granulation             | 1                       | 0     | 0     | 0     | 1                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0      | 0     | 0     |
|                    |                         | ( 4 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | inflammatory cell nest  | 0                       | 0     | 0     | 0     | 1                       | 0     | 0     | 0     | 0                       | 0     | 0     | 0     | 0                       | 0      | 0     | 0     |
|                    |                         | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )                   | ( 0 )  | ( 0 ) | ( 0 ) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ              | Findings                            | Group Name<br>No. of Animals on Study<br>Grade | Vehicle Control<br>25 |           |           |           | 3 mg/kg<br>25 |           |           |           | 10 mg/kg<br>25 |           |           |           | 30 mg/kg<br>25 |           |           |           |
|--------------------|-------------------------------------|--|-----------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
|                    |                                     |  | 1+<br>(%)             | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)     | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Digestive system] |                                     |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| liver              | acidophilic cell focus              |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                    |                                     |  | 1                     | 0         | 0         | 0         | 0             | 0         | 0         | 0         | 1              | 0         | 0         | 0         | 0              | 0         | 0         | 0         |
|                    |                                     |  | ( 4)                  | ( 0)      | ( 0)      | ( 0)      | ( 0)          | ( 0)      | ( 0)      | ( 0)      | ( 4)           | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      |
| [Urinary system]   |                                     |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| kidney             | hydronephrosis                      |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                    |                                     |  | 0                     | 0         | 0         | 0         | 0             | 1         | 0         | 0         | 0              | 0         | 0         | 0         | 0              | 0         | 0         | 0         |
|                    |                                     |  | ( 0)                  | ( 0)      | ( 0)      | ( 0)      | ( 0)          | ( 4)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      |
|                    | nuclear enlargement:proximal tubule |  | 0                     | 0         | 0         | 0         | 0             | 0         | 0         | 0         | 3              | 0         | 0         | 0         | 7              | 0         | 0         | 0 *       |
|                    |                                     |  | ( 0)                  | ( 0)      | ( 0)      | ( 0)      | ( 0)          | ( 0)      | ( 0)      | ( 0)      | ( 12)          | ( 0)      | ( 0)      | ( 0)      | ( 28)          | ( 0)      | ( 0)      | ( 0)      |
| [Endocrine system] |                                     |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| pituitary          | cyst                                |  | <25>                  |           |           |           | <25>          |           |           |           | <24>           |           |           |           | <25>           |           |           |           |
|                    |                                     |  | 1                     | 0         | 0         | 0         | 2             | 0         | 0         | 0         | 0              | 0         | 0         | 0         | 0              | 0         | 0         | 0         |
|                    |                                     |  | ( 4)                  | ( 0)      | ( 0)      | ( 0)      | ( 8)          | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      |
|                    | Rathke pouch                        |  | 1                     | 0         | 0         | 0         | 0             | 0         | 0         | 0         | 0              | 0         | 0         | 0         | 0              | 0         | 0         | 0         |
|                    |                                     |  | ( 4)                  | ( 0)      | ( 0)      | ( 0)      | ( 0)          | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      | ( 0)           | ( 0)      | ( 0)      | ( 0)      |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                 | Findings                     | Vehicle Control         |      |      |      | 3 mg/kg                 |      |      |      | 10 mg/kg                |       |      |      | 30 mg/kg                |       |      |      |
|-----------------------|------------------------------|-------------------------|------|------|------|-------------------------|------|------|------|-------------------------|-------|------|------|-------------------------|-------|------|------|
|                       |                              | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      | No. of Animals on Study |       |      |      | No. of Animals on Study |       |      |      |
|                       |                              | Grade                   |      |      |      | Grade                   |      |      |      | Grade                   |       |      |      | Grade                   |       |      |      |
|                       |                              | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+    | 3+   | 4+   | 1+                      | 2+    | 3+   | 4+   |
|                       |                              | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)   | (%)  | (%)  | (%)                     | (%)   | (%)  | (%)  |
| [Endocrine system]    |                              |                         |      |      |      |                         |      |      |      |                         |       |      |      |                         |       |      |      |
| adrenal               | hyperplasia:cortical cell    | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |       |      |      | <25>                    |       |      |      |
|                       |                              | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 1                       | 0     | 0    | 0    | 0                       | 0     | 0    | 0    |
|                       |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0)  | ( 0) | ( 0) | ( 0)                    | ( 0)  | ( 0) | ( 0) |
| [Reproductive system] |                              |                         |      |      |      |                         |      |      |      |                         |       |      |      |                         |       |      |      |
| testis                | tubular atrophy              | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |       |      |      | <25>                    |       |      |      |
|                       |                              | 1                       | 0    | 0    | 0    | 3                       | 2    | 0    | 0    | 20                      | 5     | 0    | 0    | 2                       | 23    | 0    | 0    |
|                       |                              | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 12)                   | ( 8) | ( 0) | ( 0) | ( 80)                   | ( 20) | ( 0) | ( 0) | ( 8)                    | ( 92) | ( 0) | ( 0) |
| epididymis            | decreased:sperma             | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |       |      |      | <25>                    |       |      |      |
|                       |                              | 0                       | 0    | 0    | 0    | 1                       | 0    | 0    | 0    | 0                       | 0     | 0    | 0    | 3                       | 0     | 0    | 0    |
|                       |                              | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0)  | ( 0) | ( 0) | ( 12)                   | ( 0)  | ( 0) | ( 0) |
|                       | debris of spermatic elements | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |       |      |      | <25>                    |       |      |      |
|                       |                              | 2                       | 0    | 0    | 0    | 3                       | 0    | 0    | 0    | 14                      | 0     | 0    | 0    | 23                      | 0     | 0    | 0    |
|                       |                              | ( 8)                    | ( 0) | ( 0) | ( 0) | ( 12)                   | ( 0) | ( 0) | ( 0) | ( 56)                   | ( 0)  | ( 0) | ( 0) | ( 92)                   | ( 0)  | ( 0) | ( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



TABLE A 36

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                            | Findings                                   | Group Name<br>No. of Animals on Study<br>Grade | Vehicle Control<br>25 |           |           |           | 3 mg/kg<br>25 |           |           |           | 10 mg/kg<br>25 |           |           |           | 30 mg/kg<br>25 |           |           |           |
|----------------------------------|--|--|-----------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
|                                  |  |  | 1+<br>(%)             | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)     | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Integumentary system/appandage] |  |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| skin/app                         | ulcer                                      |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |  |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 8)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                                  | erosion                                    |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 1<br>( 4) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                                  | scab                                       |  | 1<br>( 4)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| [Respiratory system]             |  |  |                       |           |           |           |               |           |           |           |                |           |           |           |                |           |           |           |
| nasal cavit                      | eosinophilic change:olfactory epithelium   |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |  |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                                  | eosinophilic change:respiratory epithelium |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 8)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| lung                             | inflammatory infiltration                  |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |           |           |           | <25>           |           |           |           |
|                                  |  |  | 1<br>( 4)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 8)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 8)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                                     | Vehicle Control         |      |      |      | 3 mg/kg                 |      |      |      | 10 mg/kg                |      |      |      | 30 mg/kg                |      |      |      |
|------------------------|--|-------------------------|------|------|------|-------------------------|------|------|------|-------------------------|------|------|------|-------------------------|------|------|------|
|                        |  | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      | No. of Animals on Study |      |      |      |
|                        |  | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   | 1+                      | 2+   | 3+   | 4+   |
|                        |  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  | (%)                     | (%)  | (%)  | (%)  |
| {Hematopoietic system} |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
| bone marrow            |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
|                        | increased hematopoiesis                      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |  | 1                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |  | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
|                        | increased hemotopoiesis:granulocyte/monocyte | 0                       | 0    | 0    | 0    | 0                       | 1    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |  | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 4) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
| spleen                 |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
|                        | deposit of melanin                           | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |  | 1                       | 0    | 0    | 0    | 1                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |  | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
|                        | extramedullary hematopoiesis                 | 8                       | 0    | 0    | 0    | 12                      | 0    | 0    | 0    | 13                      | 1    | 0    | 0    | 15                      | 0    | 0    | 0    |
|                        |  | ( 32)                   | ( 0) | ( 0) | ( 0) | ( 48)                   | ( 0) | ( 0) | ( 0) | ( 52)                   | ( 4) | ( 0) | ( 0) | ( 60)                   | ( 0) | ( 0) | ( 0) |
| {Digestive system}     |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
| salivary gl            |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
|                        | inflammatory infiltration                    | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |  | 1                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    |
|                        |  | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) |
| stomach                |  |                         |      |      |      |                         |      |      |      |                         |      |      |      |                         |      |      |      |
|                        | karyomegaly                                  | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      | <25>                    |      |      |      |
|                        |  | 0                       | 0    | 0    | 0    | 0                       | 0    | 0    | 0    | 1                       | 0    | 0    | 0    | 16                      | 0    | 0    | 0    |
|                        |  | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 64)                   | ( 0) | ( 0) | ( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ              | Findings                  | Vehicle Control         |      |      |      | 3 mg/kg |      |      |      | 10 mg/kg |      |      |      | 30 mg/kg |       |      |      |
|--------------------|---------------------------|-------------------------|------|------|------|---------|------|------|------|----------|------|------|------|----------|-------|------|------|
|                    |                           | No. of Animals on Study |      |      |      | 25      |      |      |      | 25       |      |      |      | 25       |       |      |      |
|                    |                           | 1+                      | 2+   | 3+   | 4+   | 1+      | 2+   | 3+   | 4+   | 1+       | 2+   | 3+   | 4+   | 1+       | 2+    | 3+   | 4+   |
|                    |                           | (%)                     | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)      | (%)  | (%)  | (%)  | (%)      | (%)   | (%)  | (%)  |
| [Digestive system] |                           |                         |      |      |      |         |      |      |      |          |      |      |      |          |       |      |      |
| stomach            |                           | <25>                    |      |      |      | <25>    |      |      |      | <25>     |      |      |      | <25>     |       |      |      |
|                    | hyperplasia:forestomach   | 0                       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 2        | 0    | 0    | 0    | 1        | 0     | 0    | 0    |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 8)     | ( 0) | ( 0) | ( 0) | ( 4)     | ( 0)  | ( 0) | ( 0) |
|                    | erosion:glandular stomach | 0                       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 1        | 0     | 0    | 0    |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)     | ( 0) | ( 0) | ( 0) | ( 4)     | ( 0)  | ( 0) | ( 0) |
| small intes        |                           | <25>                    |      |      |      | <25>    |      |      |      | <25>     |      |      |      | <25>     |       |      |      |
|                    | karyomegaly               | 0                       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0        | 1    | 0    | 0    | 5        | 13    | 0    | 0 ** |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)     | ( 4) | ( 0) | ( 0) | ( 20)    | ( 52) | ( 0) | ( 0) |
|                    | desquamation:epithelium   | 0                       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 2        | 1     | 0    | 0    |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)     | ( 0) | ( 0) | ( 0) | ( 8)     | ( 4)  | ( 0) | ( 0) |
|                    | atypical hyperplasia      | 0                       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 1        | 1    | 0    | 0    | 12       | 0     | 0    | 0 ** |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 4)     | ( 4) | ( 0) | ( 0) | ( 48)    | ( 0)  | ( 0) | ( 0) |
| liver              |                           | <25>                    |      |      |      | <25>    |      |      |      | <25>     |      |      |      | <25>     |       |      |      |
|                    | degeneration:centeral     | 0                       | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0        | 0     | 0    | 0    |
|                    |                           | ( 0)                    | ( 0) | ( 0) | ( 0) | ( 4)    | ( 0) | ( 0) | ( 0) | ( 0)     | ( 0) | ( 0) | ( 0) | ( 0)     | ( 0)  | ( 0) | ( 0) |
|                    | inflammatory infiltration | 1                       | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 1        | 0    | 0    | 0    | 0        | 0     | 0    | 0    |
|                    |                           | ( 4)                    | ( 0) | ( 0) | ( 0) | ( 4)    | ( 0) | ( 0) | ( 0) | ( 4)     | ( 0) | ( 0) | ( 0) | ( 0)     | ( 0)  | ( 0) | ( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ              | Findings                 | Vehicle Control<br>25               |           |           |           | 3 mg/kg<br>25                       |           |           |           | 10 mg/kg<br>25                      |           |           |           | 30 mg/kg<br>25                      |           |           |           |
|--------------------|--------------------------|-------------------------------------|-----------|-----------|-----------|-------------------------------------|-----------|-----------|-----------|-------------------------------------|-----------|-----------|-----------|-------------------------------------|-----------|-----------|-----------|
|                    |                          | 1+<br>(%)                           | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)                           | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)                           | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)                           | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Digestive system] |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
| liver              |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
|                    | lymphocytic infiltration | <25><br>2 ( 8) 0 ( 0) 0 ( 0) 0 ( 0) |           |           |           | <25><br>3 (12) 0 ( 0) 0 ( 0) 0 ( 0) |           |           |           | <25><br>0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0) |           |           |           | <25><br>0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0) |           |           |           |
|                    | granulation              | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 2 ( 8) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |
|                    | acidophilic cell focus   | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |
| [Urinary system]   |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
| kidney             |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
|                    | cyst                     | 0 ( 0) 1 ( 4) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |
|                    | hyaline cast             | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |
|                    | scar                     | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |
| [Endocrine system] |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
| pituitary          |                          |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |                                     |           |           |           |
|                    | cyst                     | 4 (16) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 0 ( 0) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           | 1 ( 4) 0 ( 0) 0 ( 0) 0 ( 0)         |           |           |           |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                    | Findings                       | Group Name<br>No. of Animals on Study<br>Grade | Vehicle Control<br>25 |           |           |           | 3 mg/kg<br>25 |           |           |           | 10 mg/kg<br>25 |            |           |           | 30 mg/kg<br>25 |           |            |           |           |           |           |           |
|--------------------------|--------------------------------|--|-----------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|----------------|------------|-----------|-----------|----------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|
|                          |                                |  | 1+<br>(%)             | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)     | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%)  | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)      | 2+<br>(%) | 3+<br>(%)  | 4+<br>(%) |           |           |           |           |
| [Endocrine system]       |                                |  |                       |           |           |           |               |           |           |           |                |            |           |           |                |           |            |           |           |           |           |           |
| parathyroid              | cyst                           |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |            |           |           | <25>           |           |            |           |           |           |           |           |
|                          |                                |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0)  | 2<br>( 8) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) |           |           |           |           |
| [Reproductive system]    |                                |  |                       |           |           |           |               |           |           |           |                |            |           |           |                |           |            |           |           |           |           |           |
| ovary                    | vacuolation:interstitial cell  |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |            |           |           | <25>           |           |            |           |           |           |           |           |
|                          |                                |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 9<br>( 36) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | **        |
| uterus                   | cystic endometrial hyperplasia |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |            |           |           | <25>           |           |            |           |           |           |           |           |
|                          |                                |  | 13<br>( 52)           | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 8<br>( 32)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 7<br>( 28) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 2<br>( 8)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | **        |
| [Musculoskeletal system] |                                |  |                       |           |           |           |               |           |           |           |                |            |           |           |                |           |            |           |           |           |           |           |
| bone                     | osteosclerosis                 |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |            |           |           | <25>           |           |            |           |           |           |           |           |
|                          |                                |  | 1<br>( 4)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| [Body cavities]          |                                |  |                       |           |           |           |               |           |           |           |                |            |           |           |                |           |            |           |           |           |           |           |
| pleura                   | hyperplasia                    |  | <25>                  |           |           |           | <25>          |           |           |           | <25>           |            |           |           | <25>           |           |            |           |           |           |           |           |
|                          |                                |  | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)      | 0<br>( 0) | 2<br>( 8)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ | Findings | Vehicle Control         |     |     |     | 3 mg/kg                 |     |     |     | 10 mg/kg                |     |     |     | 30 mg/kg                |     |     |     |
|-------|----------|-------------------------|-----|-----|-----|-------------------------|-----|-----|-----|-------------------------|-----|-----|-----|-------------------------|-----|-----|-----|
|       |          | No. of Animals on Study |     |     |     | No. of Animals on Study |     |     |     | No. of Animals on Study |     |     |     | No. of Animals on Study |     |     |     |
|       |          | 25                      |     |     |     | 25                      |     |     |     | 25                      |     |     |     | 25                      |     |     |     |
|       |          | 1+                      | 2+  | 3+  | 4+  | 1+                      | 2+  | 3+  | 4+  | 1+                      | 2+  | 3+  | 4+  | 1+                      | 2+  | 3+  | 4+  |
|       |          | (%)                     | (%) | (%) | (%) | (%)                     | (%) | (%) | (%) | (%)                     | (%) | (%) | (%) | (%)                     | (%) | (%) | (%) |

{Body cavities}

|            |            |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------|------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| peritoneum | hemorrhage | <25> |      |      |      | <25> |      |      |      | <25> |      |      |      | <25> |      |      |      |
|            |            | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|            |            | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

TABLE A 37

CAUSE OF DEATH: MALE

(Vehicle control, 3, 10 and 30 mg/kg groups)



STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
SEX : MALE

COUSE OF DEATH (SUMMARY)  
(0- 27W)

PAGE : 1

| Group Name                             | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|--|-----------------|---------|----------|----------|
| Number of Dead and Moribund Animal     | 1               | 0       | 7        | 18       |
| no microscop confirm tumor d: leukemia | 1<br>0          | 0<br>0  | 0<br>7   | 0<br>18  |

(BI0120)

BAIS6

TABLE A 38

CAUSE OF DEATH: FEMALE

(Vehicle control, 3, 10 and 30 mg/kg groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
SEX : FEMALE

COUSE OF DEATH (SUMMARY)  
(0- 27W)

| Group Name                             | Vehicle Control | 3 mg/kg | 10 mg/kg | 30 mg/kg |
|--|-----------------|---------|----------|----------|
| Number of Dead and Moribund Animal     | 1               | 1       | 7        | 20       |
| no microscop confirm tumor d: leukemia | 1<br>0          | 1<br>0  | 1<br>6   | 0<br>20  |

(BI0120)

BAIS6

TABLE B 1

SURVIVAL ANIMAL NUMBERS : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 0-0   | 1-1            | 1-2            | 1-3            | 1-4            | 1-5            | 1-6            | 1-7            | 2-1            | 2-2            | 2-3            | 2-4            | 2-5            | 2-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

(HAN360)

BAIS6

STUDY NO. : 0923

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : MALE

SURVIVAL ANIMAL NUMBERS

PAGE : 2

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 2-7   | 3-1            | 3-2            | 3-3            | 3-4            | 3-5            | 3-6            | 3-7            | 4-1            | 4-2            | 4-3            | 4-4            | 4-5            | 4-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

(HAN360)

BAIS6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 4-7   | 5-1            | 5-2            | 5-3            | 5-4            | 5-5            | 5-6            | 5-7            | 6-1            | 6-2            | 6-3            | 6-4            | 6-5            | 6-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 6-7   | 7-1            | 7-2            | 7-3            | 7-4            | 7-5            | 7-6            | 7-7            | 8-1            | 8-2            | 8-3            | 8-4            | 8-5            | 8-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 8-7   | 9-1            | 9-2            | 9-3            | 9-4            | 9-5            | 9-6            | 9-7            | 10-1           | 10-2           | 10-3           | 10-4           | 10-5           | 10-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 10-7  | 11-1           | 11-2           | 11-3           | 11-4           | 11-5           | 11-6           | 11-7           | 12-1           | 12-2           | 12-3           | 12-4           | 12-5           | 12-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 12-7  | 13-1           | 13-2           | 13-3           | 13-4           | 13-5           | 13-6           | 13-7           | 14-1           | 14-2           | 14-3           | 14-4           | 14-5           | 14-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0923

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 14-7  | 15-1           | 15-2           | 15-3           | 15-4           | 15-5           | 15-6           | 15-7           | 16-1           | 16-2           | 16-3           | 16-4           | 16-5           | 16-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 16-7  | 17-1           | 17-2           | 17-3           | 17-4           | 17-5           | 17-6           | 17-7           | 18-1           | 18-2           | 18-3           | 18-4           | 18-5           | 18-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 18-7  | 19-1           | 19-2           | 19-3           | 19-4           | 19-5           | 19-6           | 19-7           | 20-1           | 20-2           | 20-3           | 20-4           | 20-5           | 20-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

(HAN360)

BAIS6

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 20-7  | 21-1           | 21-2           | 21-3           | 21-4           | 21-5           | 21-6           | 21-7           | 22-1           | 22-2           | 22-3           | 22-4           | 22-5           | 22-6           |                |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 22-7  | 23-1           | 23-2           | 23-3           | 23-4           | 23-5           | 23-6           | 23-7           | 24-1           | 24-2           | 24-3           | 24-4           | 24-5           | 24-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 24-7  | 25-1           | 25-2           | 25-3           | 25-4           | 25-5           | 25-6           | 25-7           | 26-1           | 26-2           | 26-3           | 26-4           | 26-5           | 26-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days) |                |
|-----------------|---------------------|-----------------------|----------------|
|                 |                     | 26-7                  | 27-1           |
| Vehicle Control | 25                  | 24/25<br>96.0         | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0        | 15/15<br>100.0 |

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Number of survival/ Number of effective animals  
Survival rate(%)

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TABLE B 2

SURVIVAL ANIMAL NUMBERS : FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 0-0   | 1-1            | 1-2            | 1-3            | 1-4            | 1-5            | 1-6            | 1-7            | 2-1            | 2-2            | 2-3            | 2-4            | 2-5            | 2-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 2-7   | 3-1            | 3-2            | 3-3            | 3-4            | 3-5            | 3-6            | 3-7            | 4-1            | 4-2            | 4-3            | 4-4            | 4-5            | 4-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 3

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 4-7   | 5-1            | 5-2            | 5-3            | 5-4            | 5-5            | 5-6            | 5-7            | 6-1            | 6-2            | 6-3            | 6-4            | 6-5            | 6-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

(HAN360)

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 6-7   | 7-1            | 7-2            | 7-3            | 7-4            | 7-5            | 7-6            | 7-7            | 8-1            | 8-2            | 8-3            | 8-4            | 8-5            | 8-6            |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 8-7   | 9-1            | 9-2            | 9-3            | 9-4            | 9-5            | 9-6            | 9-7            | 10-1           | 10-2           | 10-3           | 10-4           | 10-5           | 10-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 10-7  | 11-1           | 11-2           | 11-3           | 11-4           | 11-5           | 11-6           | 11-7           | 12-1           | 12-2           | 12-3           | 12-4           | 12-5           | 12-6           |
| Vehicle Control | 25                  | 25/25<br>100.0  | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 25/25<br>100.0 | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi.Control    | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 12-7  | 13-1           | 13-2           | 13-3           | 13-4           | 13-5           | 13-6           | 13-7           | 14-1           | 14-2           | 14-3           | 14-4           | 14-5           | 14-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 14-7  | 15-1           | 15-2           | 15-3           | 15-4           | 15-5           | 15-6           | 15-7           | 16-1           | 16-2           | 16-3           | 16-4           | 16-5           | 16-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 16-7  | 17-1           | 17-2           | 17-3           | 17-4           | 17-5           | 17-6           | 17-7           | 18-1           | 18-2           | 18-3           | 18-4           | 18-5           | 18-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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STUDY NO. : 0924

ANIMAL : B6.129S2-Trp53tm1Tyj/J

REPORT TYPE : A1 27

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 18-7  | 19-1           | 19-2           | 19-3           | 19-4           | 19-5           | 19-6           | 19-7           | 20-1           | 20-2           | 20-3           | 20-4           | 20-5           | 20-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

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BAIS6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 20-7  | 21-1           | 21-2           | 21-3           | 21-4           | 21-5           | 21-6           | 21-7           | 22-1           | 22-2           | 22-3           | 22-4           | 22-5           | 22-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27  
 SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 22-7  | 23-1           | 23-2           | 23-3           | 23-4           | 23-5           | 23-6           | 23-7           | 24-1           | 24-2           | 24-3           | 24-4           | 24-5           | 24-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

| Group Name      | Animals<br>At start | Administration (Days)   |                |                |                |                |                |                |                |                |                |                |                |                |                |
|-----------------|---------------------|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                 |                     | 24-7  | 25-1           | 25-2           | 25-3           | 25-4           | 25-5           | 25-6           | 25-7           | 26-1           | 26-2           | 26-3           | 26-4           | 26-5           | 26-6           |
| Vehicle Control | 25                  | 24/25<br>96.0   | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  | 24/25<br>96.0  |
| Posi.Control    | 15                  | 15/15<br>100.0  | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 | 15/15<br>100.0 |
|                 |                     | Number of survival/ Number of effective animals<br>Survival rate(%) |                |                |                |                |                |                |                |                |                |                |                |                |                |



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

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| Group Name      | Animals<br>At start | Administration (Days) |                |
|-----------------|---------------------|-----------------------|----------------|
|                 |                     | 26-7                  | 27-1           |
| Vehicle Control | 25                  | 24/25<br>96.0         | 24/25<br>96.0  |
| Posi. Control   | 15                  | 15/15<br>100.0        | 15/15<br>100.0 |

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Number of survival/ Number of effective animals  
Survival rate(%)

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TABLE B 3

CLINICAL OBSERVATION : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 1

| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 1-1<br>1                | 1-1<br>2 | 1-2<br>1 | 1-2<br>2 | 1-3<br>1 | 1-3<br>2 | 1-4<br>1 | 1-4<br>2 | 1-5<br>1 | 1-5<br>2 | 1-6<br>1 | 1-6<br>2 | 1-7<br>1 | 1-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 2-1<br>1                | 2-1<br>2 | 2-2<br>1 | 2-2<br>2 | 2-3<br>1 | 2-3<br>2 | 2-4<br>1 | 2-4<br>2 | 2-5<br>1 | 2-5<br>2 | 2-6<br>1 | 2-6<br>2 | 2-7<br>1 | 2-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 3-1<br>1                | 3-1<br>2 | 3-2<br>1 | 3-2<br>2 | 3-3<br>1 | 3-3<br>2 | 3-4<br>1 | 3-4<br>2 | 3-5<br>1 | 3-5<br>2 | 3-6<br>1 | 3-6<br>2 | 3-7<br>1 | 3-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 4-1<br>1                | 4-1<br>2 | 4-2<br>1 | 4-2<br>2 | 4-3<br>1 | 4-3<br>2 | 4-4<br>1 | 4-4<br>2 | 4-5<br>1 | 4-5<br>2 | 4-6<br>1 | 4-6<br>2 | 4-7<br>1 | 4-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 5-1<br>1                | 5-1<br>2 | 5-2<br>1 | 5-2<br>2 | 5-3<br>1 | 5-3<br>2 | 5-4<br>1 | 5-4<br>2 | 5-5<br>1 | 5-5<br>2 | 5-6<br>1 | 5-6<br>2 | 5-7<br>1 | 5-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCCLUSION      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 6-1<br>1                | 6-1<br>2 | 6-2<br>1 | 6-2<br>2 | 6-3<br>1 | 6-3<br>2 | 6-4<br>1 | 6-4<br>2 | 6-5<br>1 | 6-5<br>2 | 6-6<br>1 | 6-6<br>2 | 6-7<br>1 | 6-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 7-1<br>1                | 7-1<br>2 | 7-2<br>1 | 7-2<br>2 | 7-3<br>1 | 7-3<br>2 | 7-4<br>1 | 7-4<br>2 | 7-5<br>1 | 7-5<br>2 | 7-6<br>1 | 7-6<br>2 | 7-7<br>1 | 7-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 8-1<br>1                | 8-1<br>2 | 8-2<br>1 | 8-2<br>2 | 8-3<br>1 | 8-3<br>2 | 8-4<br>1 | 8-4<br>2 | 8-5<br>1 | 8-5<br>2 | 8-6<br>1 | 8-6<br>2 | 8-7<br>1 | 8-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCLUSION       | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 9-1<br>1                | 9-1<br>2 | 9-2<br>1 | 9-2<br>2 | 9-3<br>1 | 9-3<br>2 | 9-4<br>1 | 9-4<br>2 | 9-5<br>1 | 9-5<br>2 | 9-6<br>1 | 9-6<br>2 | 9-7<br>1 | 9-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| TRAUMA             | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| MALOCCCLUSION      | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 10-1<br>1               | 10-1<br>2 | 10-2<br>1 | 10-2<br>2 | 10-3<br>1 | 10-3<br>2 | 10-4<br>1 | 10-4<br>2 | 10-5<br>1 | 10-5<br>2 | 10-6<br>1 | 10-6<br>2 | 10-7<br>1 | 10-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 11-1<br>1               | 11-1<br>2 | 11-2<br>1 | 11-2<br>2 | 11-3<br>1 | 11-3<br>2 | 11-4<br>1 | 11-4<br>2 | 11-5<br>1 | 11-5<br>2 | 11-6<br>1 | 11-6<br>2 | 11-7<br>1 | 11-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 1                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 12-1<br>1               | 12-1<br>2 | 12-2<br>1 | 12-2<br>2 | 12-3<br>1 | 12-3<br>2 | 12-4<br>1 | 12-4<br>2 | 12-5<br>1 | 12-5<br>2 | 12-6<br>1 | 12-6<br>2 | 12-7<br>1 | 12-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 13-1<br>1               | 13-1<br>2 | 13-2<br>1 | 13-2<br>2 | 13-3<br>1 | 13-3<br>2 | 13-4<br>1 | 13-4<br>2 | 13-5<br>1 | 13-5<br>2 | 13-6<br>1 | 13-6<br>2 | 13-7<br>1 | 13-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 14-1<br>1               | 14-1<br>2 | 14-2<br>1 | 14-2<br>2 | 14-3<br>1 | 14-3<br>2 | 14-4<br>1 | 14-4<br>2 | 14-5<br>1 | 14-5<br>2 | 14-6<br>1 | 14-6<br>2 | 14-7<br>1 | 14-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 15-1<br>1               | 15-1<br>2 | 15-2<br>1 | 15-2<br>2 | 15-3<br>1 | 15-3<br>2 | 15-4<br>1 | 15-4<br>2 | 15-5<br>1 | 15-5<br>2 | 15-6<br>1 | 15-6<br>2 | 15-7<br>1 | 15-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 16-1<br>1               | 16-1<br>2 | 16-2<br>1 | 16-2<br>2 | 16-3<br>1 | 16-3<br>2 | 16-4<br>1 | 16-4<br>2 | 16-5<br>1 | 16-5<br>2 | 16-6<br>1 | 16-6<br>2 | 16-7<br>1 | 16-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 17-1<br>1               | 17-1<br>2 | 17-2<br>1 | 17-2<br>2 | 17-3<br>1 | 17-3<br>2 | 17-4<br>1 | 17-4<br>2 | 17-5<br>1 | 17-5<br>2 | 17-6<br>1 | 17-6<br>2 | 17-7<br>1 | 17-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 25                      | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 25        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 18-1<br>1               | 18-1<br>2 | 18-2<br>1 | 18-2<br>2 | 18-3<br>1 | 18-3<br>2 | 18-4<br>1 | 18-4<br>2 | 18-5<br>1 | 18-5<br>2 | 18-6<br>1 | 18-6<br>2 | 18-7<br>1 | 18-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 19-1<br>1               | 19-1<br>2 | 19-2<br>1 | 19-2<br>2 | 19-3<br>1 | 19-3<br>2 | 19-4<br>1 | 19-4<br>2 | 19-5<br>1 | 19-5<br>2 | 19-6<br>1 | 19-6<br>2 | 19-7<br>1 | 19-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 20-1<br>1               | 20-1<br>2 | 20-2<br>1 | 20-2<br>2 | 20-3<br>1 | 20-3<br>2 | 20-4<br>1 | 20-4<br>2 | 20-5<br>1 | 20-5<br>2 | 20-6<br>1 | 20-6<br>2 | 20-7<br>1 | 20-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 21-1<br>1               | 21-1<br>2 | 21-2<br>1 | 21-2<br>2 | 21-3<br>1 | 21-3<br>2 | 21-4<br>1 | 21-4<br>2 | 21-5<br>1 | 21-5<br>2 | 21-6<br>1 | 21-6<br>2 | 21-7<br>1 | 21-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 2         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |    |    |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----|----|
|                    |                 | 22-1<br>1               | 22-1<br>2 | 22-2<br>1 | 22-2<br>2 | 22-3<br>1 | 22-3<br>2 | 22-4<br>1 | 22-4<br>2 | 22-5<br>1 | 22-5<br>2 | 22-6<br>1 | 22-6<br>2 | 22-7<br>1 | 22-7<br>2 |    |    |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 1         | 1         | 1         | 1         | 1  | 1  |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0  | 0  |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0  | 0  |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0  | 0  |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0  | 0  |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1  | 1  |
| EROSION            | Vehicle Control | 2                       | 2         | 2         | 2         | 2         | 2         | 2         | 2         | 1         | 1         | 1         | 1         | 1         | 1         | 1  | 1  |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0  | 0  |
| NON REMARKABLE     | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23 | 23 |
|                    | Posi. Control   | 14                      | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14 | 14 |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 23-1<br>1               | 23-1<br>2 | 23-2<br>1 | 23-2<br>2 | 23-3<br>1 | 23-3<br>2 | 23-4<br>1 | 23-4<br>2 | 23-5<br>1 | 23-5<br>2 | 23-6<br>1 | 23-6<br>2 | 23-7<br>1 | 23-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                    | Posi. Control   | 14                      | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        | 14        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 24-1<br>1               | 24-1<br>2 | 24-2<br>1 | 24-2<br>2 | 24-3<br>1 | 24-3<br>2 | 24-4<br>1 | 24-4<br>2 | 24-5<br>1 | 24-5<br>2 | 24-6<br>1 | 24-6<br>2 | 24-7<br>1 | 24-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| NON REMARKABLE     | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                    | Posi. Control   | 13                      | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 25-1<br>1               | 25-1<br>2 | 25-2<br>1 | 25-2<br>2 | 25-3<br>1 | 25-3<br>2 | 25-4<br>1 | 25-4<br>2 | 25-5<br>1 | 25-5<br>2 | 25-6<br>1 | 25-6<br>2 | 25-7<br>1 | 25-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| NON REMARKABLE     | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                    | Posi. Control   | 13                      | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 26-1<br>1               | 26-1<br>2 | 26-2<br>1 | 26-2<br>2 | 26-3<br>1 | 26-3<br>2 | 26-4<br>1 | 26-4<br>2 | 26-5<br>1 | 26-5<br>2 | 26-6<br>1 | 26-6<br>2 | 26-7<br>1 | 26-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
| NON REMARKABLE     | Vehicle Control | 23                      | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        | 23        |
|                    | Posi. Control   | 13                      | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        | 13        |

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| Clinical sign      | Group Name      | Administration Week-day |           |
|--------------------|-----------------|-------------------------|-----------|
|                    |                 | 27-1<br>1               | 27-1<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         |
|                    | Posi. Control   | 0                       | 0         |
| TRAUMA             | Vehicle Control | 0                       | 0         |
|                    | Posi. Control   | 0                       | 0         |
| MALOCCLUSION       | Vehicle Control | 0                       | 0         |
|                    | Posi. Control   | 1                       | 1         |
| EROSION            | Vehicle Control | 1                       | 0         |
|                    | Posi. Control   | 1                       | 0         |
| NON REMARKABLE     | Vehicle Control | 23                      | 13        |
|                    | Posi. Control   | 13                      | 6         |

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**TABLE B 4**

**CLINICAL OBSERVATION : FEMALE**

(Vehicle control and Positive control groups)

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 1-1<br>1                | 1-1<br>2 | 1-2<br>1 | 1-2<br>2 | 1-3<br>1 | 1-3<br>2 | 1-4<br>1 | 1-4<br>2 | 1-5<br>1 | 1-5<br>2 | 1-6<br>1 | 1-6<br>2 | 1-7<br>1 | 1-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 2-1<br>1                | 2-1<br>2 | 2-2<br>1 | 2-2<br>2 | 2-3<br>1 | 2-3<br>2 | 2-4<br>1 | 2-4<br>2 | 2-5<br>1 | 2-5<br>2 | 2-6<br>1 | 2-6<br>2 | 2-7<br>1 | 2-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 3-1<br>1                | 3-1<br>2 | 3-2<br>1 | 3-2<br>2 | 3-3<br>1 | 3-3<br>2 | 3-4<br>1 | 3-4<br>2 | 3-5<br>1 | 3-5<br>2 | 3-6<br>1 | 3-6<br>2 | 3-7<br>1 | 3-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 4-1<br>1                | 4-1<br>2 | 4-2<br>1 | 4-2<br>2 | 4-3<br>1 | 4-3<br>2 | 4-4<br>1 | 4-4<br>2 | 4-5<br>1 | 4-5<br>2 | 4-6<br>1 | 4-6<br>2 | 4-7<br>1 | 4-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 5-1<br>1                | 5-1<br>2 | 5-2<br>1 | 5-2<br>2 | 5-3<br>1 | 5-3<br>2 | 5-4<br>1 | 5-4<br>2 | 5-5<br>1 | 5-5<br>2 | 5-6<br>1 | 5-6<br>2 | 5-7<br>1 | 5-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 6-1<br>1                | 6-1<br>2 | 6-2<br>1 | 6-2<br>2 | 6-3<br>1 | 6-3<br>2 | 6-4<br>1 | 6-4<br>2 | 6-5<br>1 | 6-5<br>2 | 6-6<br>1 | 6-6<br>2 | 6-7<br>1 | 6-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 7-1<br>1                | 7-1<br>2 | 7-2<br>1 | 7-2<br>2 | 7-3<br>1 | 7-3<br>2 | 7-4<br>1 | 7-4<br>2 | 7-5<br>1 | 7-5<br>2 | 7-6<br>1 | 7-6<br>2 | 7-7<br>1 | 7-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 1        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 25                      | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 25       | 24       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 8-1<br>1                | 8-1<br>2 | 8-2<br>1 | 8-2<br>2 | 8-3<br>1 | 8-3<br>2 | 8-4<br>1 | 8-4<br>2 | 8-5<br>1 | 8-5<br>2 | 8-6<br>1 | 8-6<br>2 | 8-7<br>1 | 8-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|-----------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    |                 | 9-1<br>1                | 9-1<br>2 | 9-2<br>1 | 9-2<br>2 | 9-3<br>1 | 9-3<br>2 | 9-4<br>1 | 9-4<br>2 | 9-5<br>1 | 9-5<br>2 | 9-6<br>1 | 9-6<br>2 | 9-7<br>1 | 9-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| EROSION            | Vehicle Control | 1                       | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
|                    | Posi. Control   | 0                       | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        |
| NON REMARKABLE     | Vehicle Control | 24                      | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       | 24       |
|                    | Posi. Control   | 15                      | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       | 15       |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 10-1<br>1               | 10-1<br>2 | 10-2<br>1 | 10-2<br>2 | 10-3<br>1 | 10-3<br>2 | 10-4<br>1 | 10-4<br>2 | 10-5<br>1 | 10-5<br>2 | 10-6<br>1 | 10-6<br>2 | 10-7<br>1 | 10-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 11-1<br>1               | 11-1<br>2 | 11-2<br>1 | 11-2<br>2 | 11-3<br>1 | 11-3<br>2 | 11-4<br>1 | 11-4<br>2 | 11-5<br>1 | 11-5<br>2 | 11-6<br>1 | 11-6<br>2 | 11-7<br>1 | 11-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 12-1<br>1               | 12-1<br>2 | 12-2<br>1 | 12-2<br>2 | 12-3<br>1 | 12-3<br>2 | 12-4<br>1 | 12-4<br>2 | 12-5<br>1 | 12-5<br>2 | 12-6<br>1 | 12-6<br>2 | 12-7<br>1 | 12-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 0                       | 0         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 1                       | 1         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 13-1<br>1               | 13-1<br>2 | 13-2<br>1 | 13-2<br>2 | 13-3<br>1 | 13-3<br>2 | 13-4<br>1 | 13-4<br>2 | 13-5<br>1 | 13-5<br>2 | 13-6<br>1 | 13-6<br>2 | 13-7<br>1 | 13-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 14-1<br>1               | 14-1<br>2 | 14-2<br>1 | 14-2<br>2 | 14-3<br>1 | 14-3<br>2 | 14-4<br>1 | 14-4<br>2 | 14-5<br>1 | 14-5<br>2 | 14-6<br>1 | 14-6<br>2 | 14-7<br>1 | 14-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 15-1<br>1               | 15-1<br>2 | 15-2<br>1 | 15-2<br>2 | 15-3<br>1 | 15-3<br>2 | 15-4<br>1 | 15-4<br>2 | 15-5<br>1 | 15-5<br>2 | 15-6<br>1 | 15-6<br>2 | 15-7<br>1 | 15-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 16-1<br>1               | 16-1<br>2 | 16-2<br>1 | 16-2<br>2 | 16-3<br>1 | 16-3<br>2 | 16-4<br>1 | 16-4<br>2 | 16-5<br>1 | 16-5<br>2 | 16-6<br>1 | 16-6<br>2 | 16-7<br>1 | 16-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 17-1<br>1               | 17-1<br>2 | 17-2<br>1 | 17-2<br>2 | 17-3<br>1 | 17-3<br>2 | 17-4<br>1 | 17-4<br>2 | 17-5<br>1 | 17-5<br>2 | 17-6<br>1 | 17-6<br>2 | 17-7<br>1 | 17-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 18-1<br>1               | 18-1<br>2 | 18-2<br>1 | 18-2<br>2 | 18-3<br>1 | 18-3<br>2 | 18-4<br>1 | 18-4<br>2 | 18-5<br>1 | 18-5<br>2 | 18-6<br>1 | 18-6<br>2 | 18-7<br>1 | 18-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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BAIS 6



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 19-1<br>1               | 19-1<br>2 | 19-2<br>1 | 19-2<br>2 | 19-3<br>1 | 19-3<br>2 | 19-4<br>1 | 19-4<br>2 | 19-5<br>1 | 19-5<br>2 | 19-6<br>1 | 19-6<br>2 | 19-7<br>1 | 19-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 20-1<br>1               | 20-1<br>2 | 20-2<br>1 | 20-2<br>2 | 20-3<br>1 | 20-3<br>2 | 20-4<br>1 | 20-4<br>2 | 20-5<br>1 | 20-5<br>2 | 20-6<br>1 | 20-6<br>2 | 20-7<br>1 | 20-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 21-1<br>1               | 21-1<br>2 | 21-2<br>1 | 21-2<br>2 | 21-3<br>1 | 21-3<br>2 | 21-4<br>1 | 21-4<br>2 | 21-5<br>1 | 21-5<br>2 | 21-6<br>1 | 21-6<br>2 | 21-7<br>1 | 21-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

PAGE : 22

| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 22-1<br>1               | 22-1<br>2 | 22-2<br>1 | 22-2<br>2 | 22-3<br>1 | 22-3<br>2 | 22-4<br>1 | 22-4<br>2 | 22-5<br>1 | 22-5<br>2 | 22-6<br>1 | 22-6<br>2 | 22-7<br>1 | 22-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 23-1<br>1               | 23-1<br>2 | 23-2<br>1 | 23-2<br>2 | 23-3<br>1 | 23-3<br>2 | 23-4<br>1 | 23-4<br>2 | 23-5<br>1 | 23-5<br>2 | 23-6<br>1 | 23-6<br>2 | 23-7<br>1 | 23-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

PAGE : 24

| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 24-1<br>1               | 24-1<br>2 | 24-2<br>1 | 24-2<br>2 | 24-3<br>1 | 24-3<br>2 | 24-4<br>1 | 24-4<br>2 | 24-5<br>1 | 24-5<br>2 | 24-6<br>1 | 24-6<br>2 | 24-7<br>1 | 24-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 25-1<br>1               | 25-1<br>2 | 25-2<br>1 | 25-2<br>2 | 25-3<br>1 | 25-3<br>2 | 25-4<br>1 | 25-4<br>2 | 25-5<br>1 | 25-5<br>2 | 25-6<br>1 | 25-6<br>2 | 25-7<br>1 | 25-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

PAGE : 26

| Clinical sign      | Group Name      | Administration Week-day |           |           |           |           |           |           |           |           |           |           |           |           |           |
|--------------------|-----------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                    |                 | 26-1<br>1               | 26-1<br>2 | 26-2<br>1 | 26-2<br>2 | 26-3<br>1 | 26-3<br>2 | 26-4<br>1 | 26-4<br>2 | 26-5<br>1 | 26-5<br>2 | 26-6<br>1 | 26-6<br>2 | 26-7<br>1 | 26-7<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         | 1         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| EROSION            | Vehicle Control | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
|                    | Posi. Control   | 0                       | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        | 24        |
|                    | Posi. Control   | 15                      | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        | 15        |

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BAIS 6



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1 27

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 27

| Clinical sign      | Group Name      | Administration Week-day |           |
|--------------------|-----------------|-------------------------|-----------|
|                    |                 | 27-1<br>1               | 27-1<br>2 |
| MORIBUND SACRIFICE | Vehicle Control | 1                       | 1         |
|                    | Posi. Control   | 0                       | 0         |
| EROSION            | Vehicle Control | 0                       | 0         |
|                    | Posi. Control   | 0                       | 0         |
| NON REMARKABLE     | Vehicle Control | 24                      | 13        |
|                    | Posi. Control   | 15                      | 7         |

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TABLE B 5

BODY WEIGHT CHANGES : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |            |            |            |            |            |             |
|-----------------|-------------------------|------------|------------|------------|------------|------------|-------------|
|                 | 0-0                     | 1-1        | 2-1        | 3-1        | 4-1        | 5-1        | 6-1         |
| Vehicle Control | 25.1 ± 1.6              | 24.8 ± 1.7 | 25.6 ± 1.5 | 26.1 ± 1.5 | 26.7 ± 1.6 | 27.2 ± 1.5 | 27.7 ± 1.7  |
| Posi. Control   | 25.2 ± 1.8              | 24.9 ± 1.8 | 26.0 ± 1.6 | 26.1 ± 1.3 | 26.2 ± 1.5 | 26.5 ± 1.5 | 26.5 ± 1.5* |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |       | 7-1   | 8-1   | 9-1   | 10-1  | 11-1  | 12-1  | 13-1  |       |       |       |       |       |
|-----------------|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                 | 7-1                     | 8-1   |       |       |       |       |       |       |       |       |       |       |       |       |
| Vehicle Control | 28.0±                   | 1.7   | 28.5± | 1.7   | 28.9± | 1.7   | 29.2± | 1.8   | 29.5± | 1.9   | 29.5± | 2.1   | 29.4± | 2.3   |
| Posi. Control   | 26.3±                   | 1.4** | 26.5± | 1.5** | 26.6± | 1.6** | 26.4± | 1.6** | 26.7± | 1.5** | 27.1± | 1.6** | 26.8± | 1.5** |

Significant difference ; \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |              | 16-1         | 17-1         | 18-1         | 19-1         | 20-1         |
|-----------------|-------------------------|--------------|--------------|--------------|--------------|--------------|--------------|
|                 | 14-1                    | 15-1         |              |              |              |              |              |
| Vehicle Control | 29.7 ± 2.1              | 29.8 ± 2.0   | 30.0 ± 2.1   | 30.1 ± 2.3   | 30.4 ± 2.1   | 30.6 ± 2.2   | 30.9 ± 2.3   |
| Posi. Control   | 27.1 ± 1.6**            | 27.0 ± 1.7** | 26.6 ± 1.8** | 26.9 ± 1.7** | 26.7 ± 1.8** | 26.9 ± 1.9** | 26.9 ± 1.6** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |             |             |             |             |             |             |
|-----------------|-------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                 | 21-1                    | 22-1        | 23-1        | 24-1        | 25-1        | 26-1        | 26-7        |
| Vehicle Control | 31.2± 2.3               | 31.4± 2.5   | 31.3± 2.4   | 31.5± 2.5   | 31.6± 2.3   | 31.8± 2.4   | 32.2± 2.4   |
| Posi. Control   | 27.0± 1.8**             | 26.8± 1.9** | 26.8± 1.9** | 26.7± 2.0** | 26.3± 2.2** | 26.5± 2.1** | 27.1± 2.1** |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of t

**TABLE B 6**

**BODY WEIGHT CHANGES : FEMALE**

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |            |            |            |            |            |             |
|-----------------|-------------------------|------------|------------|------------|------------|------------|-------------|
|                 | 0-0                     | 1-1        | 2-1        | 3-1        | 4-1        | 5-1        | 6-1         |
| Vehicle Control | 20.8 ± 1.6              | 20.4 ± 1.5 | 21.2 ± 1.6 | 21.9 ± 1.7 | 22.1 ± 1.8 | 22.6 ± 1.7 | 23.0 ± 1.4  |
| Posi. Control   | 20.8 ± 1.6              | 19.9 ± 1.5 | 21.0 ± 1.0 | 21.6 ± 1.0 | 21.9 ± 1.0 | 22.3 ± 1.2 | 22.1 ± 1.1* |

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |              |              |             |              |             |            |
|-----------------|-------------------------|--------------|--------------|-------------|--------------|-------------|------------|
|                 | 7-1                     | 8-1          | 9-1          | 10-1        | 11-1         | 12-1        | 13-1       |
| Vehicle Control | 23.1 ± 1.7              | 24.0 ± 1.6   | 24.0 ± 1.4   | 24.2 ± 1.5  | 24.3 ± 1.3   | 24.2 ± 1.6  | 24.2 ± 1.6 |
| Posi. Control   | 22.2 ± 1.3              | 22.7 ± 1.1** | 22.7 ± 1.1** | 23.1 ± 1.0* | 23.1 ± 1.2** | 23.1 ± 1.2* | 23.3 ± 1.4 |

Significant difference ; \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |             |              |              |              |              |              |
|-----------------|-------------------------|-------------|--------------|--------------|--------------|--------------|--------------|
|                 | 14-1                    | 15-1        | 16-1         | 17-1         | 18-1         | 19-1         | 20-1         |
| Vehicle Control | 24.2 ± 1.4              | 24.4 ± 1.8  | 24.4 ± 1.2   | 24.8 ± 1.7   | 25.1 ± 1.6   | 24.7 ± 1.4   | 25.2 ± 1.7   |
| Posi. Control   | 23.3 ± 1.4*             | 23.3 ± 1.3* | 22.9 ± 1.1** | 23.1 ± 1.0** | 23.4 ± 1.1** | 23.0 ± 1.2** | 23.1 ± 1.0** |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day |              | 23-1         | 24-1         | 25-1         | 26-1         | 26-7         |
|-----------------|-------------------------|--------------|--------------|--------------|--------------|--------------|--------------|
|                 | 21-1                    | 22-1         |              |              |              |              |              |
| Vehicle Control | 24.8 ± 1.3              | 25.4 ± 1.5   | 25.0 ± 1.4   | 25.3 ± 1.5   | 25.4 ± 1.8   | 25.6 ± 1.5   | 25.3 ± 1.8   |
| Posi. Control   | 23.3 ± 1.2**            | 23.3 ± 1.2** | 23.3 ± 1.1** | 23.4 ± 1.3** | 23.3 ± 1.1** | 23.4 ± 1.1** | 23.3 ± 1.6** |

Significant difference ; \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

TABLE B 7

FOOD CONSUMPTION CHANGES : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|------------|------------|
|                 | 2-1(7)                             | 3-1(7)     | 4-1(7)     | 5-1(7)     | 6-1(7)     | 7-1(7)     | 8-1(7)     |
| Vehicle Control | 3.5± 0.3                           | 3.2± 0.3   | 3.3± 0.3   | 3.3± 0.3   | 3.3± 0.3   | 3.3± 0.2   | 3.4± 0.2   |
| Posi. Control   | 3.2± 0.3**                         | 3.0± 0.2** | 2.9± 0.2** | 2.9± 0.3** | 2.8± 0.3** | 2.8± 0.2** | 2.9± 0.2** |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|------------|------------|
|                 | 9-1(7)                             | 10-1(7)    | 11-1(7)    | 12-1(7)    | 13-1(7)    | 14-1(7)    | 15-1(7)    |
| Vehicle Control | 3.3± 0.2                           | 3.3± 0.2   | 3.3± 0.3   | 3.3± 0.3   | 3.2± 0.3   | 3.2± 0.3   | 3.1± 0.3   |
| Posi. Control   | 2.8± 0.2**                         | 2.7± 0.3** | 2.7± 0.2** | 2.9± 0.2** | 2.7± 0.2** | 2.7± 0.2** | 2.7± 0.2** |

Significant difference ; \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|------------|------------|
|                 | 16-1(7)                            | 17-1(7)    | 18-1(7)    | 19-1(7)    | 20-1(7)    | 21-1(7)    | 22-1(7)    |
| Vehicle Control | 3.2± 0.3                           | 3.2± 0.3   | 3.2± 0.3   | 3.3± 0.3   | 3.3± 0.4   | 3.3± 0.3   | 3.3± 0.4   |
| Posi. Control   | 2.6± 0.2**                         | 2.7± 0.2** | 2.5± 0.1** | 2.7± 0.2** | 2.6± 0.2** | 2.7± 0.3** | 2.6± 0.4** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |             |             |             |             |
|-----------------|------------------------------------|-------------|-------------|-------------|-------------|
|                 | 23-1(7)                            | 24-1(7)     | 25-1(7)     | 26-1(7)     | 26-7(6)     |
| Vehicle Control | 3.3 ± 0.4                          | 3.4 ± 0.6   | 3.4 ± 0.7   | 3.4 ± 0.6   | 3.4 ± 0.6   |
| Posi. Control   | 2.7 ± 0.4**                        | 2.7 ± 0.5** | 2.7 ± 0.4** | 2.7 ± 0.4** | 2.7 ± 0.5** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t



TABLE B 8

FOOD CONSUMPTION CHANGES : FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |           |          |          |            |           |            |
|-----------------|------------------------------------|-----------|----------|----------|------------|-----------|------------|
|                 | 2-1(7)                             | 3-1(7)    | 4-1(7)   | 5-1(7)   | 6-1(7)     | 7-1(7)    | 8-1(7)     |
| Vehicle Control | 3.2± 0.3                           | 3.1± 0.3  | 2.9± 0.3 | 2.9± 0.3 | 3.2± 0.3   | 3.0± 0.3  | 3.3± 0.5   |
| Posi. Control   | 2.8± 0.3**                         | 2.8± 0.3* | 2.8± 0.2 | 2.8± 0.3 | 2.7± 0.2** | 2.8± 0.3* | 2.8± 0.2** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|------------|------------|
|                 | 9-1(7)                             | 10-1(7)    | 11-1(7)    | 12-1(7)    | 13-1(7)    | 14-1(7)    | 15-1(7)    |
| Vehicle Control | 3.1± 0.5                           | 3.1± 0.6   | 3.1± 0.6   | 3.0± 0.6   | 2.9± 0.3   | 2.9± 0.3   | 3.0± 0.2   |
| Posi. Control   | 2.7± 0.3**                         | 2.7± 0.2** | 2.6± 0.3** | 2.6± 0.2** | 2.6± 0.2** | 2.5± 0.1** | 2.6± 0.2** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|------------|------------|
|                 | 16-1(7)                            | 17-1(7)    | 18-1(7)    | 19-1(7)    | 20-1(7)    | 21-1(7)    | 22-1(7)    |
| Vehicle Control | 2.9± 0.2                           | 3.0± 0.3   | 3.1± 0.3   | 2.9± 0.3   | 3.0± 0.3   | 2.9± 0.2   | 2.9± 0.3   |
| Posi. Control   | 2.4± 0.2**                         | 2.7± 0.2** | 2.7± 0.2** | 2.5± 0.1** | 2.6± 0.2** | 2.5± 0.2** | 2.5± 0.2** |

Significant difference ; \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 UNIT : g  
 REPORT TYPE : A1 26  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

| Group Name      | Administration week-day(effective) |            |            |            |            |
|-----------------|------------------------------------|------------|------------|------------|------------|
|                 | 23-1(7)                            | 24-1(7)    | 25-1(7)    | 26-1(7)    | 26-7(6)    |
| Vehicle Control | 2.8± 0.2                           | 3.0± 0.3   | 2.8± 0.3   | 2.9± 0.3   | 2.8± 0.3   |
| Posi. Control   | 2.5± 0.2**                         | 2.6± 0.2** | 2.5± 0.2** | 2.5± 0.2** | 2.5± 0.3** |

Significant difference ; \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

TABLE B 9

URINALYSIS : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | pH  |     |     |     |     |     |     | CHI | Protein |   |    |    |    | CHI | Glucose |    |   |   |    | CHI | Ketone body |    |    |   |   | CHI | Occult blood |    |    | CHI |   |   |   |    |
|-----------------|----------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|----|----|----|-----|---------|----|---|---|----|-----|-------------|----|----|---|---|-----|--------------|----|----|-----|---|---|---|----|
|                 |                | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ± | +  | 2+ | 3+ |     | 4+      | -  | ± | + | 2+ |     | 3+          | 4+ | -  | ± | + |     | 2+           | 3+ | 4+ |     | - | ± | + | 2+ |
| Vehicle Control | 18             | 0   | 3   | 3   | 5   | 2   | 0   | 5   |     | 0       | 1 | 16 | 1  | 0  | 0   |         | 18 | 0 | 0 | 0  | 0   | 0           |    | 2  | 8 | 8 | 0   | 0            | 0  |    | 18  | 0 | 0 | 0 | 0  |
| Posi. Control   | 14             | 0   | 12  | 2   | 0   | 0   | 0   | 0   | **  | 10      | 4 | 0  | 0  | 0  | 0   | **      | 14 | 0 | 0 | 0  | 0   | 0           |    | 14 | 0 | 0 | 0   | 0            | 0  | ** | 14  | 0 | 0 | 0 | 0  |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of CHI SQUARE

(HCL101)

BAIS 6

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of<br>Animals | Urobilinogen |   |    |    | CHI |    |
|-----------------|-------------------|--------------|---|----|----|-----|----|
|                 |                   | ±            | + | 2+ | 3+ |     | 4+ |
| Vehicle Control | 18                | 18           | 0 | 0  | 0  | 0   |    |
| Posi. Control   | 14                | 14           | 0 | 0  | 0  | 0   |    |

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Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 6



**TABLE B 10**

**URINALYSIS : FEMALE**

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE REPORT TYPE : A1

URINALYSIS

| Group Name      | NO. of Animals | pH  |     |     |     |     |     |     | CHI | Protein |    |   |    |    | CHI | Glucose |   |   |   |    | CHI | Ketone body |    |   |   |   | CHI | Occult blood |    |    | CHI |
|-----------------|----------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|----|---|----|----|-----|---------|---|---|---|----|-----|-------------|----|---|---|---|-----|--------------|----|----|-----|
|                 |                | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ±  | + | 2+ | 3+ |     | 4+      | - | ± | + | 2+ |     | 3+          | 4+ | - | ± | + |     | 2+           | 3+ | 4+ |     |
| Vehicle Control | 24             | 0   | 7   | 4   | 3   | 1   | 8   | 1   | 1   | 11      | 11 | 1 | 0  | 0  | 24  | 0       | 0 | 0 | 0 | 0  | 1   | 11          | 10 | 2 | 0 | 0 | 24  | 0            | 0  | 0  | 0   |
| Posi. Control   | 15             | 0   | 10  | 2   | 1   | 1   | 1   | 0   | 6   | 8       | 1  | 0 | 0  | 0  | **  | 15      | 0 | 0 | 0 | 0  | 4   | 10          | 1  | 0 | 0 | * | 15  | 0            | 0  | 0  | 0   |

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01

Test of CHI SQUARE

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of<br>Animals | Urobilinogen |   |    |    | CHI |
|-----------------|-------------------|--------------|---|----|----|-----|
|                 |                   | ±            | + | 2+ | 3+ |     |
| Vehicle Control | 24                | 24           | 0 | 0  | 0  | 0   |
| Posi. Control   | 15                | 15           | 0 | 0  | 0  | 0   |

---

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 6

TABLE B 11

HEMATOLOGY : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

| Group Name      | NO. of Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |        | HEMOGLOBIN<br>g/dl |       | HEMATOCRIT<br>% |       | MCV<br>fl |       | MCH<br>Pg |       | MCHC<br>g/dl |       | PLATELET<br>10 <sup>3</sup> /μl |       |
|-----------------|----------------|---------------------------------------|--------|--------------------|-------|-----------------|-------|-----------|-------|-----------|-------|--------------|-------|---------------------------------|-------|
| Vehicle Control | 24             | 10.25±                                | 0.52   | 14.6±              | 0.5   | 43.4±           | 1.8   | 42.4±     | 0.9   | 14.3±     | 0.4   | 33.7±        | 0.6   | 1489±                           | 208   |
| Posi. Control   | 14             | 8.94±                                 | 0.51** | 12.0±              | 0.7** | 36.7±           | 1.6** | 41.0±     | 1.2** | 13.5±     | 0.5** | 32.8±        | 0.8** | 1760±                           | 293** |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01      Test of t

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

---

| Group Name      | NO. of Animals | RETICULOCYTE % |       |
|-----------------|----------------|----------------|-------|
| Vehicle Control | 24             | 4.2±           | 0.6   |
| Posi. Control   | 14             | 14.3±          | 2.2** |

---

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL070)

BAIS 6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

| Group Name      | NO. of Animals | WBC            |        | Differential |       | WBC (%) |       | MONO |     | EOSINO |     | BASO |     |
|-----------------|----------------|----------------|--------|--------------|-------|---------|-------|------|-----|--------|-----|------|-----|
|                 |                | $10^3/\mu\ell$ |        | NEUTRO       |       | LYMPHO  |       |      |     |        |     |      |     |
| Vehicle Control | 24             | 1.17±          | 0.82   | 18.9±        | 6.7   | 78.2±   | 6.6   | 2.4± | 0.9 | 0.5±   | 0.7 | 0.0± | 0.0 |
| Posi. Control   | 14             | 2.41±          | 1.28** | 27.8±        | 11.9* | 69.9±   | 11.8* | 2.0± | 0.7 | 0.3±   | 0.3 | 0.1± | 0.2 |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$       Test of t

TABLE B 12

HEMATOLOGY : FEMALE

(Vehicle control and Positive control groups)



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |        | HEMOGLOBIN<br>g/dl |       | HEMATOCRIT<br>% |       | MCV<br>fl |     | MCH<br>Pg |       | MCHC<br>g/dl |       | PLATELET<br>10 <sup>3</sup> /μl |     |
|-----------------|----------------|---------------------------------------|--------|--------------------|-------|-----------------|-------|-----------|-----|-----------|-------|--------------|-------|---------------------------------|-----|
| Vehicle Control | 23             | 10.29±                                | 0.38   | 14.8±              | 0.3   | 43.5±           | 1.2   | 42.3±     | 0.8 | 14.4±     | 0.3   | 34.1±        | 0.5   | 1320±                           | 178 |
| Posi. Control   | 15             | 9.09±                                 | 0.33** | 12.5±              | 0.5** | 38.1±           | 1.7** | 41.9±     | 1.5 | 13.8±     | 0.7** | 32.8±        | 0.9** | 1422±                           | 92* |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01      Test of t

(HCL070)

BAIS 6

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
MEASURE. TIME : 1  
SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 27W)

PAGE : 2

---

| Group Name      | NO. of Animals | RETICULOCYTE % |  |
|-----------------|----------------|----------------|--|
| Vehicle Control | 23             | 3.9 ± 0.6      |  |
| Posi. Control   | 15             | 10.8 ± 2.1**   |  |

---

Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$

Test of t

(HCL070)

BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 27W)

| Group Name      | NO. of Animals | WBC          |       | Differential |     | WBC (%) |     | MONO |      | EOSINO |     | BASO |     |
|-----------------|----------------|--------------|-------|--------------|-----|---------|-----|------|------|--------|-----|------|-----|
|                 |                | $10^3/\mu l$ |       | NEUTRO       |     | LYMPHO  |     |      |      |        |     |      |     |
| Vehicle Control | 23             | 1.26±        | 0.94  | 14.8±        | 5.1 | 82.7±   | 5.1 | 2.1± | 0.8  | 0.3±   | 0.5 | 0.0± | 0.0 |
| Posi. Control   | 15             | 2.14±        | 1.17* | 18.9±        | 9.8 | 77.7±   | 9.2 | 2.7± | 0.9* | 0.7±   | 0.7 | 0.0± | 0.0 |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of t

TABLE B 13

BIOCHEMISTRY : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |      | A/G RATIO |     | T-BILIRUBIN<br>mg/dl |       | GLUCOSE<br>mg/dl |      | T-CHOLESTEROL<br>mg/dl |      | TRIGLYCERIDE<br>mg/dl |      |
|-----------------|----------------|-----------------------|-----|-----------------|------|-----------|-----|----------------------|-------|------------------|------|------------------------|------|-----------------------|------|
| Vehicle Control | 24             | 5.3±                  | 0.4 | 3.1±            | 0.2  | 1.4±      | 0.1 | 0.11±                | 0.02  | 237±             | 37   | 86±                    | 22   | 31±                   | 9    |
| Posi. Control   | 15             | 5.5±                  | 0.3 | 3.2±            | 0.2* | 1.4±      | 0.1 | 0.14±                | 0.04* | 203±             | 30** | 110±                   | 21** | 44±                   | 12** |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL074)

BAIS 6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

| Group Name      | NO. of Animals | PHOSPHOLIPID<br>mg/dl |      | AST<br>U/L |     | ALT<br>U/L |      | LDH<br>U/L |       | ALP<br>U/L |      | G-GTP<br>U/L |     | CK<br>U/L |     |
|-----------------|----------------|-----------------------|------|------------|-----|------------|------|------------|-------|------------|------|--------------|-----|-----------|-----|
| Vehicle Control | 24             | 169±                  | 41   | 54±        | 18  | 14±        | 3    | 213±       | 49    | 242±       | 27   | 0.4±         | 0.3 | 77±       | 24  |
| Posi. Control   | 15             | 218±                  | 47** | 113±       | 86* | 82±        | 40** | 337±       | 122** | 306±       | 51** | 0.5±         | 0.4 | 100±      | 33* |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL074)

BAIS 6

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

PAGE : 3

| Group Name      | NO. of Animals | UREANITROGEN<br>mg/dl |        | SODIUM<br>mEq/l |    | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |     | CALCIUM<br>mg/dl |       | INORGANIC PHOSPHRUS<br>mg/dl |     |
|-----------------|----------------|-----------------------|--------|-----------------|----|--------------------|-----|-------------------|-----|------------------|-------|------------------------------|-----|
| Vehicle Control | 24             | 28.2±                 | 4.0    | 150±            | 1  | 4.2±               | 0.2 | 118±              | 2   | 9.0±             | 0.2   | 6.3±                         | 0.7 |
| Posi. Control   | 15             | 53.7±                 | 14.8** | 149±            | 2* | 4.2±               | 0.2 | 115±              | 2** | 9.5±             | 0.5** | 6.5±                         | 0.8 |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL074)

BAIS 6

**TABLE B 14**

**BIOCHEMISTRY : FEMALE**

(Vehicle control and Positive control groups)



STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 1

| Group Name      | NO. of Animals | TOTAL PROTEIN<br>g/dl |       | ALBUMIN<br>g/dl |       | A/G RATIO |     | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |      | T-CHOLESTEROL<br>mg/dl |      | TRIGLYCERIDE<br>mg/dl |      |
|-----------------|----------------|-----------------------|-------|-----------------|-------|-----------|-----|----------------------|------|------------------|------|------------------------|------|-----------------------|------|
| Vehicle Control | 23             | 5.3±                  | 0.2   | 3.2±            | 0.2   | 1.6±      | 0.1 | 0.12±                | 0.04 | 186±             | 29   | 63±                    | 15   | 23±                   | 7    |
| Posi. Control   | 15             | 5.6±                  | 0.2** | 3.4±            | 0.1** | 1.5±      | 0.1 | 0.13±                | 0.03 | 215±             | 22** | 107±                   | 21** | 35±                   | 12** |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL074)

BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

REPORT TYPE : A1

PAGE : 2

| Group Name      | NO. of Animals | PHOSPHOLIPID<br>mg/dl |      | AST<br>U/L |    | ALT<br>U/L |     | LDH<br>U/L |    | ALP<br>U/L |    | G-GTP<br>U/L |       | CK<br>U/L |     |
|-----------------|----------------|-----------------------|------|------------|----|------------|-----|------------|----|------------|----|--------------|-------|-----------|-----|
| Vehicle Control | 23             | 129±                  | 29   | 54±        | 16 | 16±        | 6   | 208±       | 55 | 402±       | 62 | 0.1±         | 0.2   | 96±       | 71  |
| Posi. Control   | 15             | 208±                  | 40** | 57±        | 27 | 36±        | 8** | 194±       | 50 | 375±       | 35 | 0.4±         | 0.2** | 61±       | 11* |

Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL074)

BAIS 6

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 MEASURE. TIME : 1  
 SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 27W)

| Group Name      | NO. of Animals | UREANITROGEN<br>mg/dl |        | SODIUM<br>mEq/l |    | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |    | CALCIUM<br>mg/dl |       | INORGANIC PHOSPHRUS<br>mg/dl |     |
|-----------------|----------------|-----------------------|--------|-----------------|----|--------------------|-----|-------------------|----|------------------|-------|------------------------------|-----|
| Vehicle Control | 23             | 23.7±                 | 3.2    | 149±            | 1  | 3.9±               | 0.2 | 116±              | 2  | 8.9±             | 0.3   | 6.0±                         | 1.4 |
| Posi. Control   | 15             | 44.7±                 | 13.5** | 147±            | 3* | 4.0±               | 0.2 | 113±              | 4* | 9.4±             | 0.2** | 6.0±                         | 1.0 |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01      Test of t

TABLE B 15

GROSS FINDINGS : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0- 27W)

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| Organ    | Findings                   | Group Name<br>NO. of Animals | Vehicle Control<br>25 (%) | Posi. Control<br>15 (%) |
|----------|----------------------------|------------------------------|---------------------------|-------------------------|
| skin/app | ulcer                      |                              | 1 ( 4)                    | 0 ( 0)                  |
|          | erosion                    |                              | 1 ( 4)                    | 1 ( 7)                  |
| stomach  | glandular stomach:red zone |                              | 0 ( 0)                    | 1 ( 7)                  |
| kidney   | deformed                   |                              | 0 ( 0)                    | 5 ( 33)                 |
|          | hydronephrosis             |                              | 0 ( 0)                    | 1 ( 7)                  |

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**TABLE B 16**

**GROSS FINDINGS : FEMALE**

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0- 27W)

PAGE : 1

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| Organ       | Findings   | Group Name<br>NO. of Animals | Vehicle Control<br>25 (%) | Posi. Control<br>15 (%) |
|-------------|------------|------------------------------|---------------------------|-------------------------|
| skin/app    | scab       |                              | 1 ( 4)                    | 0 ( 0)                  |
| lymph node  | enlarged   |                              | 1 ( 4)                    | 0 ( 0)                  |
| spleen      | black zone |                              | 1 ( 4)                    | 0 ( 0)                  |
| kidney      | cyst       |                              | 1 ( 4)                    | 0 ( 0)                  |
| peritoneum  | red zone   |                              | 1 ( 4)                    | 0 ( 0)                  |
| abdominal c | hemorrhage |                              | 1 ( 4)                    | 0 ( 0)                  |

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(HPT080)

BAIS 6

TABLE B 17

ORGAN WEIGHT, ABSOLUTE : MALE

(Vehicle control and Positive control groups)



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE  
 UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
 SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight  | ADRENALS      |  | TESTES        |  | HEART          |  | LUNGS         |  | KIDNEYS       |  |
|-----------------|----------------|--------------|---------------|--|---------------|--|----------------|--|---------------|--|---------------|--|
| Vehicle Control | 24             | 28.7 ± 2.1   | 0.011 ± 0.002 |  | 0.222 ± 0.011 |  | 0.147 ± 0.017  |  | 0.143 ± 0.010 |  | 0.401 ± 0.042 |  |
| Posi. Control   | 15             | 23.8 ± 1.9** | 0.012 ± 0.003 |  | 0.213 ± 0.030 |  | 0.133 ± 0.016* |  | 0.153 ± 0.020 |  | 0.436 ± 0.366 |  |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of t



TABLE B 18

ORGAN WEIGHT, ABSOLUTE : FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
 SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight | ADRENALS |       | OVARIES |       | HEART  |       | LUNGS  |       | KIDNEYS |       |
|-----------------|----------------|-------------|----------|-------|---------|-------|--------|-------|--------|-------|---------|-------|
| Vehicle Control | 24             | 23.0± 1.5   | 0.014±   | 0.002 | 0.024±  | 0.008 | 0.119± | 0.013 | 0.137± | 0.011 | 0.309±  | 0.048 |
| Posi. Control   | 15             | 21.0± 1.4** | 0.013±   | 0.002 | 0.023±  | 0.005 | 0.114± | 0.010 | 0.135± | 0.011 | 0.302±  | 0.015 |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of t

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

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| Group Name      | NO. of Animals | SPLEEN |         | LIVER  |         | BRAIN  |       |
|-----------------|----------------|--------|---------|--------|---------|--------|-------|
| Vehicle Control | 24             | 0.077± | 0.009   | 0.898± | 0.096   | 0.469± | 0.017 |
| Posi. Control   | 15             | 0.111± | 0.009** | 1.023± | 0.081** | 0.460± | 0.013 |

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Significant difference : \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of t

(HCL040)

BAIS 6

TABLE B 19

ORGAN WEIGHT, RELATIVE : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight (g) | ADRENALS        | TESTES          | HEART          | LUNGS           | KIDNEYS       |
|-----------------|----------------|-----------------|-----------------|-----------------|----------------|-----------------|---------------|
| Vehicle Control | 24             | 28.7 ± 2.1      | 0.037 ± 0.007   | 0.778 ± 0.060   | 0.514 ± 0.073  | 0.502 ± 0.050   | 1.403 ± 0.166 |
| Posi. Control   | 15             | 23.8 ± 1.9**    | 0.051 ± 0.011** | 0.901 ± 0.142** | 0.560 ± 0.051* | 0.644 ± 0.078** | 1.791 ± 1.317 |

Significant difference : \* : P ≤ 0.05    \*\* : P ≤ 0.01

Test of t

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE  
UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

| Group Name      | NO. of Animals | SPLEEN          | LIVER           | BRAIN           |
|-----------------|----------------|-----------------|-----------------|-----------------|
| Vehicle Control | 24             | 0.253 ± 0.044   | 3.678 ± 0.354   | 1.627 ± 0.116   |
| Posi. Control   | 15             | 0.446 ± 0.079** | 4.678 ± 0.376** | 1.936 ± 0.138** |

Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of t

(HCL042)

BAIS 6



TABLE B 20

ORGAN WEIGHT, RELATIVE : FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

| Group Name      | NO. of Animals | Body Weight (g) | ADRENALS     | OVARIES      | HEART        | LUNGS          | KIDNEYS       |
|-----------------|----------------|-----------------|--------------|--------------|--------------|----------------|---------------|
| Vehicle Control | 24             | 23.0± 1.5       | 0.059± 0.009 | 0.102± 0.034 | 0.516± 0.051 | 0.594± 0.046   | 1.344± 0.205  |
| Posi. Control   | 15             | 21.0± 1.4**     | 0.062± 0.008 | 0.111± 0.023 | 0.545± 0.041 | 0.644± 0.056** | 1.445± 0.089* |

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of t

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 27W)

PAGE : 2

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| Group Name      | NO. of Animals | SPLEEN          | LIVER           | BRAIN           |
|-----------------|----------------|-----------------|-----------------|-----------------|
| Vehicle Control | 24             | 0.334 ± 0.041   | 3.903 ± 0.379   | 2.043 ± 0.147   |
| Posi. Control   | 15             | 0.531 ± 0.043** | 4.880 ± 0.309** | 2.202 ± 0.137** |

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Significant difference : \* : P ≤ 0.05      \*\* : P ≤ 0.01      Test of t

(HCL042)

BAIS 6

TABLE B 21

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : MALE

(Vehicle control and Positive control groups)

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                | Findings                     | Group Name<br>No. of animals on Study | Vehicle Control<br>25 | Posi. Control<br>15 |
|----------------------|------------------------------|---------------------------------------|-----------------------|---------------------|
| {Respiratory system} |                              |                                       |                       |                     |
| lung                 | bronchiolar-alveolar adenoma |                                       | <25><br>0 ( 0%)       | <15><br>1 ( 7%)     |
| {Urinary system}     |                              |                                       |                       |                     |
| urin bladd           | transitional cell papilloma  |                                       | <25><br>0 ( 0%)       | <15><br>2 ( 13%)    |
|                      | transitional cell carcinoma  |                                       | 0 ( 0%)               | 1 ( 7%)             |
|                      | leiomyosarcoma               |                                       | 0 ( 0%)               | 1 ( 7%)             |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

TABLE B 22

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 27W)

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| Organ                | Findings                    | Group Name<br>No. of animals on Study | Vehicle Control<br>25 | Posi. Control<br>15 |
|----------------------|-----------------------------|---------------------------------------|-----------------------|---------------------|
| {Respiratory system} |                             |                                       |                       |                     |
| nasal cavit          | adenoma                     |                                       | <25><br>0 ( 0%)       | <15><br>1 ( 7%)     |
| {Urinary system}     |                             |                                       |                       |                     |
| urin bladd           | squamous cell papilloma     |                                       | <25><br>0 ( 0%)       | <15><br>1 ( 7%)     |
|                      | transitional cell papilloma |                                       | 0 ( 0%)               | 1 ( 7%)             |

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< a > a : Number of animals examined at the site  
b ( c ) b : Number of animals with neoplasm c : b / a \* 100

TABLE B 23

NEOPLASTIC LESIONS-INCIDENCE  
AND STATISTICAL ANALYSIS : MALE  
(Vehicle control and Positive control groups)



NEOPLASTIC LESIONS – INCIDENCE AND STATISTICAL ANALYSIS

STUDY NO.: 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : MALE

PAGE: 1

| Group Name            | Vehicle Control  | Posi. Control |
|-----------------------|--|---------------|
|                       | SITE : urinary bladder   |               |
|                       | TUMOR : transitional cell papilloma                              |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 2/15 ( 13.3 ) |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.1346    |
|                       | SITE : urinary bladder   |               |
|                       | TUMOR : transitional cell carcinoma                              |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 1/15 ( 6.7 )  |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.3750    |
|                       | SITE : urinary bladder   |               |
|                       | TUMOR : transitional cell papilloma, transitional cell carcinoma |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 3/15 ( 20.0 ) |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.0461*   |

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Fisher exact test compare directly the overall incidence rates.

Significant difference: \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

TABLE B 24

NEOPLASTIC LESIONS-INCIDENCE  
AND STATISTICAL ANALYSIS : FEMALE  
(Vehicle control and Positive control groups)

NEOPLASTIC LESIONS – INCIDENCE AND STATISTICAL ANALYSIS

STUDY NO.: 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 SEX : FEMALE

PAGE: 1

| Group Name            | Vehicle Control  | Posi. Control |
|-----------------------|--|---------------|
|                       | SITE : urinary bladder                                       |               |
|                       | TUMOR : squamous cell papilloma                              |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 1/15 ( 6.7 )  |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.3750    |
|                       | SITE : urinary bladder                                       |               |
|                       | TUMOR : transitional cell papilloma                          |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 1/15 ( 6.7 )  |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.3750    |
|                       | SITE : urinary bladder                                       |               |
|                       | TUMOR : squamous cell papilloma, transitional cell papilloma |               |
| Tumor rate (a)        | 0/25 ( 0.0 )   | 2/15 ( 13.3 ) |
| Statistical analysis  |  |               |
| Fisher Exact test (b) |  | P = 0.1346    |

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Fisher exact test compare directly the overall incidence rates.

Significant difference: \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

TABLE B 25

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF  
TUMORS - TIME RELATED: MALE  
(Vehicle control and Positive control groups)

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

| Time-related Weeks | Items                               | Group Name | Vehicle Control | Posi. Control |
|--------------------|-------------------------------------|------------|-----------------|---------------|
| 1 - 26             | NO. OF EXAMINED ANIMALS             |            | 1               | 0             |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0             |
| 27 - 27            | NO. OF EXAMINED ANIMALS             |            | 24              | 15            |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 5             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 5             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 3             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 2             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 5             |
| 1 - 27             | NO. OF EXAMINED ANIMALS             |            | 25              | 15            |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 5             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 5             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 3             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 2             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 5             |

TABLE B 26

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF  
TUMORS - TIME RELATED: FEMALE  
(Vehicle control and Positive control groups)

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

| Time-related Weeks | Items                               | Group Name | Vehicle Control | Posi. Control |
|--------------------|-------------------------------------|------------|-----------------|---------------|
| 1 - 26             | NO. OF EXAMINED ANIMALS             |            | 1               | 0             |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 0             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 0             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 0             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 0             |
| 27 - 27            | NO. OF EXAMINED ANIMALS             |            | 24              | 15            |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 3             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 3             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 3             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 3             |
| 1 - 27             | NO. OF EXAMINED ANIMALS             |            | 25              | 15            |
|                    | NO. OF ANIMALS WITH TUMORS          |            | 0               | 3             |
|                    | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0               | 3             |
|                    | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0               | 0             |
|                    | NO. OF BENIGN TUMORS                |            | 0               | 3             |
|                    | NO. OF MALIGNANT TUMORS             |            | 0               | 0             |
|                    | NO. OF TOTAL TUMORS                 |            | 0               | 3             |

TABLE B 27

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: MALE

(Vehicle control and Positive control groups)



STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                            | Findings                                    | Vehicle Control<br>No. of Animals on Study 25 |           |           |           | Posi. Control<br>15 |            |            |              |
|----------------------------------|---|---|-----------|-----------|-----------|---------------------|------------|------------|--------------|
|                                  |   | Grade<br>1+<br>(%)                            | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)           | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)    |
| [Integumentary system/appandage] |   |   |           |           |           |                     |            |            |              |
| skin/app                         | ulcer                                       | <25>  |           |           |           | <15>                |            |            |              |
|                                  |   | 2<br>( 8)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 7)           | 0<br>( 0)  | 0<br>( 0)  | 0<br>( 0)    |
| [Respiratory system]             |   |   |           |           |           |                     |            |            |              |
| nasal cavit                      | eosinophilic change:olfactory epithelium    | <25>  |           |           |           | <15>                |            |            |              |
|                                  |   | 0<br>( 0)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 15<br>(100)         | 0<br>( 0)  | 0<br>( 0)  | 0<br>( 0) ** |
|                                  | respiratory metaplasia:olfactory epithelium | 0<br>( 0)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 9<br>( 60)          | 1<br>( 7)  | 3<br>( 20) | 0<br>( 0) ** |
|                                  | respiratory metaplasia:gland                | 0<br>( 0)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)           | 1<br>( 7)  | 3<br>( 20) | 0<br>( 0) *  |
|                                  | atrophy:olfactory epithelium                | 0<br>( 0)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 11<br>( 73)         | 3<br>( 20) | 1<br>( 7)  | 0<br>( 0) ** |
| lung                             | inflammatory infiltration                   | <25>  |           |           |           | <15>                |            |            |              |
|                                  |   | 1<br>( 4)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)           | 0<br>( 0)  | 0<br>( 0)  | 0<br>( 0)    |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 27W)

| Organ                  | Findings                       | Vehicle Control<br>No. of Animals on Study 25 |           |           |           | Posi. Control<br>15                         |           |           |           |
|------------------------|--------------------------------|---|-----------|-----------|-----------|---|-----------|-----------|-----------|
|                        |                                | Grade<br>1+<br>(%)                            | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)                                   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| {Hematopoietic system} |                                |   |           |           |           |   |           |           |           |
| bone marrow            | increased hematopoiesis        | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)        |           |           |           | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |           |           |           |
| spleen                 | extramedullary hematopoiesis   | <25><br>4 0 0 0<br>( 16) ( 0) ( 0) ( 0)       |           |           |           | <15><br>15 0 0 0 **<br>(100) ( 0) ( 0) ( 0) |           |           |           |
| {Digestive system}     |                                |   |           |           |           |   |           |           |           |
| liver                  | necrosis:focal                 | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |           |           |           | <15><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0)      |           |           |           |
|                        | granulation                    | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                |           |           |           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |           |           |           |
|                        | acidophilic cell focus         | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                |           |           |           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |           |           |           |
|                        | degeneration/necrosis:midzonal | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |           |           |           | 8 7 0 0 **<br>( 53) ( 47) ( 0) ( 0)         |           |           |           |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
< a > a : Number of animals examined at the site  
b : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ            | Findings                                   | Group Name<br>No. of Animals on Study |           |           |           | Vehicle Control<br>25 |           |           |           | Posi. Control<br>15 |      |  |  |
|------------------|--|---------------------------------------|-----------|-----------|-----------|-----------------------|-----------|-----------|-----------|---------------------|------|--|--|
|                  |  | Grade                                 | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)             | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)           |      |  |  |
| {Urinary system} |  |                                       |           |           |           |                       |           |           |           |                     |      |  |  |
| kidney           |  |                                       |           |           |           |                       |           |           |           |                     |      |  |  |
|                  | regeneration                               |                                       | <25>      |           |           |                       | <15>      |           |           |                     |      |  |  |
|                  |  |                                       | 0         | 0         | 0         | 0                     | 12        | 0         | 0         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 80)     | ( 0)      | ( 0)      | ( 0)                | ( 0) |  |  |
|                  | scar                                       |                                       | 0         | 0         | 0         | 0                     | 2         | 1         | 4         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 13)     | ( 7)      | ( 27)     | ( 0)                | ( 0) |  |  |
|                  | hydronephrosis                             |                                       | 0         | 0         | 0         | 0                     | 0         | 0         | 1         | 0                   | 0    |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 0)      | ( 0)      | ( 7)      | ( 0)                | ( 0) |  |  |
|                  | papillary necrosis                         |                                       | 0         | 0         | 0         | 0                     | 8         | 3         | 0         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 53)     | ( 20)     | ( 0)      | ( 0)                | ( 0) |  |  |
| urin bladd       |  |                                       |           |           |           |                       |           |           |           |                     |      |  |  |
|                  | erosion                                    |                                       | <25>      |           |           |                       | <15>      |           |           |                     |      |  |  |
|                  |  |                                       | 0         | 0         | 0         | 0                     | 3         | 0         | 0         | 0                   | 0    |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 20)     | ( 0)      | ( 0)      | ( 0)                | ( 0) |  |  |
|                  | squamous cell metaplasia                   |                                       | 0         | 0         | 0         | 0                     | 9         | 0         | 0         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 60)     | ( 0)      | ( 0)      | ( 0)                | ( 0) |  |  |
|                  | simple hyperplasia:transitional epithelium |                                       | 0         | 0         | 0         | 0                     | 1         | 14        | 0         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 7)      | ( 93)     | ( 0)      | ( 0)                | ( 0) |  |  |
|                  | papillary and/or nodular hyperplasia       |                                       | 0         | 0         | 0         | 0                     | 10        | 0         | 0         | 0                   | 0 ** |  |  |
|                  |  |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 67)     | ( 0)      | ( 0)      | ( 0)                | ( 0) |  |  |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0923  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                 | Findings                     | Group Name<br>No. of Animals on Study<br>Grade |           |           |           | Vehicle Control<br>25 |            |           |           | Posi. Control<br>15 |  |  |  |
|-----------------------|------------------------------|--|-----------|-----------|-----------|-----------------------|------------|-----------|-----------|---------------------|--|--|--|
|                       |                              | 1+<br>(%)                                      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)             | 2+<br>(%)  | 3+<br>(%) | 4+<br>(%) |                     |  |  |  |
| [Endocrine system]    |                              |  |           |           |           |                       |            |           |           |                     |  |  |  |
| pituitary             | cyst                         | <25>   |           |           |           | <15>                  |            |           |           |                     |  |  |  |
|                       |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 7)             | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) |                     |  |  |  |
|                       | Rathke pouch                 | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)             | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) |                     |  |  |  |
| [Reproductive system] |                              |  |           |           |           |                       |            |           |           |                     |  |  |  |
| testis                | tubular atrophy              | <25>   |           |           |           | <15>                  |            |           |           |                     |  |  |  |
|                       |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 7)             | 2<br>( 13) | 0<br>( 0) | 0<br>( 0) |                     |  |  |  |
| epididymis            | debris of spermatic elements | <25>   |           |           |           | <15>                  |            |           |           |                     |  |  |  |
|                       |                              | 2<br>( 8)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 4<br>( 27)            | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) |                     |  |  |  |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

TABLE B 28

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: FEMALE

(Vehicle control and Positive control groups)

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                            | Findings                                    | Group Name<br>No. of Animals on Study |           |           |           | Vehicle Control<br>25 |           |           |           | Posi. Control<br>15 |      |  |  |
|----------------------------------|---|---------------------------------------|-----------|-----------|-----------|-----------------------|-----------|-----------|-----------|---------------------|------|--|--|
|                                  |   | Grade                                 | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)             | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)           |      |  |  |
| [Integumentary system/appandage] |   |                                       |           |           |           |                       |           |           |           |                     |      |  |  |
| skin/app                         | scab  |                                       | <25>      |           |           |                       | <15>      |           |           |                     |      |  |  |
|                                  |   |                                       | 1         | 0         | 0         | 0                     | 0         | 0         | 0         | 0                   | 0    |  |  |
|                                  |   |                                       | ( 4)      | ( 0)      | ( 0)      | ( 0)                  | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 0) |  |  |
| [Respiratory system]             |   |                                       |           |           |           |                       |           |           |           |                     |      |  |  |
| nasal cavit                      | eosinophilic change:olfactory epithelium    |                                       | <25>      |           |           |                       | <15>      |           |           |                     |      |  |  |
|                                  |   |                                       | 0         | 0         | 0         | 0                     | 11        | 3         | 0         | 0                   | **   |  |  |
|                                  |   |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 73)     | ( 20)     | ( 0)      | ( 0)                |      |  |  |
|                                  | respiratory metaplasia:olfactory epithelium |                                       | 0         | 0         | 0         | 0                     | 3         | 2         | 0         | 0                   | **   |  |  |
|                                  |   |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 20)     | ( 13)     | ( 0)      | ( 0)                |      |  |  |
|                                  | respiratory metaplasia:gland                |                                       | 0         | 0         | 0         | 0                     | 1         | 0         | 2         | 0                   |      |  |  |
|                                  |   |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 7)      | ( 0)      | ( 13)     | ( 0)                |      |  |  |
|                                  | atrophy:olfactory epithelium                |                                       | 0         | 0         | 0         | 0                     | 3         | 1         | 0         | 0                   | *    |  |  |
|                                  |   |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 20)     | ( 7)      | ( 0)      | ( 0)                |      |  |  |
| nasopharynx                      | eosinophilic change:olfactory epithelium    |                                       | <25>      |           |           |                       | <15>      |           |           |                     |      |  |  |
|                                  |   |                                       | 0         | 0         | 0         | 0                     | 1         | 0         | 0         | 0                   |      |  |  |
|                                  |   |                                       | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 7)      | ( 0)      | ( 0)      | ( 0)                |      |  |  |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                  | Findings                     | Group Name<br>No. of Animals on Study<br>Grade |           |           |           | Vehicle Control<br>25 |           |           |              | Posi. Control<br>15 |  |  |  |
|------------------------|------------------------------|--|-----------|-----------|-----------|-----------------------|-----------|-----------|--------------|---------------------|--|--|--|
|                        |                              | 1+<br>(%)                                      | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)             | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)    |                     |  |  |  |
| [Respiratory system]   |                              |  |           |           |           |                       |           |           |              |                     |  |  |  |
| lung                   | inflammatory infiltration    | <25>   |           |           |           | <15>                  |           |           |              |                     |  |  |  |
|                        |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |                     |  |  |  |
| [Hematopoietic system] |                              |  |           |           |           |                       |           |           |              |                     |  |  |  |
| bone marrow            | increased hematopoiesis      | <25>   |           |           |           | <15>                  |           |           |              |                     |  |  |  |
|                        |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |                     |  |  |  |
| spleen                 | deposit of melanin           | <25>   |           |           |           | <15>                  |           |           |              |                     |  |  |  |
|                        |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |                     |  |  |  |
|                        | extramedullary hematopoiesis | 8<br>( 32)                                     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 15<br>(100)           | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) ** |                     |  |  |  |
| [Digestive system]     |                              |  |           |           |           |                       |           |           |              |                     |  |  |  |
| salivary gl            | inflammatory infiltration    | <25>   |           |           |           | <15>                  |           |           |              |                     |  |  |  |
|                        |                              | 1<br>( 4)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 4<br>( 27)            | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |                     |  |  |  |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 27W)

| Organ                          | Findings                  | Vehicle Control<br>No. of Animals on Study 25 |           |           |           | Posi. Control<br>15 |           |           |           |           |
|--------------------------------|---------------------------|---|-----------|-----------|-----------|---------------------|-----------|-----------|-----------|-----------|
|                                |                           | Grade   | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)           | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Digestive system]             |                           |   |           |           |           |                     |           |           |           |           |
| liver                          | inflammatory infiltration |   | <25>      |           |           |                     | <15>      |           |           |           |
|                                |                           | 1   | 0         | 0         | 0         | 0                   | 0         | 0         | 0         |           |
|                                |                           | ( 4)  | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      |           |
|                                | lymphocytic infiltration  | 2   | 0         | 0         | 0         | 0                   | 0         | 0         | 0         |           |
|                                |                           | ( 8)  | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      |           |
| granulation                    |                           | 1   | 0         | 0         | 0         | 0                   | 0         | 0         | 0         |           |
|                                |                           | ( 4)  | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      |           |
| acidophilic cell focus         |                           | 1   | 0         | 0         | 0         | 0                   | 0         | 0         | 0         |           |
|                                |                           | ( 4)  | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      |           |
| degeneration/necrosis:midzonal |                           | 0   | 0         | 0         | 0         | 14                  | 0         | 0         | 0 **      |           |
|                                |                           | ( 0)  | ( 0)      | ( 0)      | ( 0)      | ( 93)               | ( 0)      | ( 0)      | ( 0)      |           |
| [Urinary system]               |                           |   |           |           |           |                     |           |           |           |           |
| kidney                         | cyst                      |   | <25>      |           |           |                     | <15>      |           |           |           |
|                                |                           | 0   | 1         | 0         | 0         | 0                   | 0         | 0         | 0         |           |
|                                |                           | ( 0)  | ( 4)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      |           |
| hyaline cast                   |                           | 1   | 0         | 0         | 0         | 1                   | 0         | 0         | 0         |           |
|                                |                           | ( 4)  | ( 0)      | ( 0)      | ( 0)      | ( 7)                | ( 0)      | ( 0)      | ( 0)      |           |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
< a > a : Number of animals examined at the site  
b : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



STUDY NO. : 0924  
ANIMAL : B6.129S2-Trp53tm1Tyj/J  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 27W)

| Organ              | Findings   | Group Name<br>No. of Animals on Study |           |           |           | Vehicle Control<br>25 |           |           |           | Posi. Control<br>15 |  |  |  |
|--------------------|--|---------------------------------------|-----------|-----------|-----------|-----------------------|-----------|-----------|-----------|---------------------|--|--|--|
|                    |  | Grade                                 | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)             | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)           |  |  |  |
| {Urinary system}   |  |                                       |           |           |           |                       |           |           |           |                     |  |  |  |
| kidney             | scar   |                                       | <25>      |           |           |                       | <15>      |           |           |                     |  |  |  |
|                    |  | 0                                     | 0         | 0         | 0         | 1                     | 0         | 0         | 0         |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 7)                  | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |
|                    | papillary necrosis                               | 0                                     | 0         | 0         | 0         | 5                     | 0         | 0         | 0 **      |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 33)                 | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |
|                    | regeneration:renal tubule                        | 0                                     | 0         | 0         | 0         | 6                     | 0         | 0         | 0 **      |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 40)                 | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |
| urin bladd         | squamous cell metaplasia:transitional epithelium |                                       | <25>      |           |           |                       | <15>      |           |           |                     |  |  |  |
|                    |  | 0                                     | 0         | 0         | 0         | 4                     | 0         | 0         | 0 *       |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 27)                 | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |
|                    | simple hyperplasia:transitional epithelium       | 0                                     | 0         | 0         | 0         | 1                     | 14        | 0         | 0 **      |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 7)                  | ( 93)     | ( 0)      | ( 0)      |                     |  |  |  |
|                    | papillary and/or nodular hyperplasia             | 0                                     | 0         | 0         | 0         | 4                     | 0         | 0         | 0 *       |                     |  |  |  |
|                    |  | ( 0)                                  | ( 0)      | ( 0)      | ( 0)      | ( 27)                 | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |
| {Endocrine system} |  |                                       |           |           |           |                       |           |           |           |                     |  |  |  |
| pituitary          | cyst   |                                       | <25>      |           |           |                       | <15>      |           |           |                     |  |  |  |
|                    |  | 4                                     | 0         | 0         | 0         | 0                     | 0         | 0         | 0         |                     |  |  |  |
|                    |  | ( 16)                                 | ( 0)      | ( 0)      | ( 0)      | ( 0)                  | ( 0)      | ( 0)      | ( 0)      |                     |  |  |  |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
< a > a : Number of animals examined at the site  
b b : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0924  
 ANIMAL : B6.129S2-Trp53tm1Tyj/J  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 27W)

| Organ                    | Findings                       | Vehicle Control<br>No. of Animals on Study 25 |           |           |           | Posi. Control<br>15 |           |           |           |           |
|--------------------------|--------------------------------|---|-----------|-----------|-----------|---------------------|-----------|-----------|-----------|-----------|
|                          |                                | Grade   | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%)           | 1+<br>(%) | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Reproductive system]    |                                |   |           |           |           |                     |           |           |           |           |
| ovary                    | cyst                           |   | <25>      |           |           |                     | <15>      |           |           |           |
|                          |                                |   | 0         | 0         | 0         | 0                   | 1         | 0         | 0         | 0         |
|                          |                                |   | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 7)      | ( 0)      | ( 0)      | ( 0)      |
|                          | vacuolation:interstitial cell  |   | 0         | 0         | 0         | 0                   | 4         | 0         | 0         | 0 *       |
|                          |                                |   | ( 0)      | ( 0)      | ( 0)      | ( 0)                | ( 27)     | ( 0)      | ( 0)      | ( 0)      |
| uterus                   | cystic endometrial hyperplasia |   | <25>      |           |           |                     | <15>      |           |           |           |
|                          |                                |   | 13        | 0         | 0         | 0                   | 0         | 0         | 0         | 0 **      |
|                          |                                |   | ( 52)     | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      | ( 0)      |
| [Musculoskeletal system] |                                |   |           |           |           |                     |           |           |           |           |
| bone                     | osteosclerosis                 |   | <25>      |           |           |                     | <15>      |           |           |           |
|                          |                                |   | 1         | 0         | 0         | 0                   | 0         | 0         | 0         | 0         |
|                          |                                |   | ( 4)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      | ( 0)      |
| [Body cavities]          |                                |   |           |           |           |                     |           |           |           |           |
| peritoneum               | hemorrhage                     |   | <25>      |           |           |                     | <15>      |           |           |           |
|                          |                                |   | 1         | 0         | 0         | 0                   | 0         | 0         | 0         | 0         |
|                          |                                |   | ( 4)      | ( 0)      | ( 0)      | ( 0)                | ( 0)      | ( 0)      | ( 0)      | ( 0)      |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square