

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Male

Treatment Groups (ppm)

400 a, ~, 1

400 a, #, 1

400 a, *, 1

400 a, o, 1

400 b, #, 2

400 b, o, 2

400 b, ~, 2

400 b, *, 2

400 b, ~, 3

Plasma

AUC_{0-t} (ng/mL*hr)

427 ± 17

350 ± 30

358 ± 33

3752 ± 296

143 ± 21

3422 ± 122

472 ± 15

175 ± 37

368 ± 18

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Male

Treatment Groups (ppm)

| | 400 b, *, 3 | 400 b, o, 3 | 400 b, #, 3 | 800 a, ~, 1 | 800 a, #, 1 | 800 a, *, 1 | 800 a, o, 1 | 800 b, ~, 3 | 800 b, #, 3 |
|-------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|-------------|-------------|
| <hr/> <p>Plasma</p> <hr/> | | | | | | | | | |
| AUC _{0-t} (ng/mL*hr) | 289 ± 26 | 3206 ± 368 | 224 ± 26 | 1018 ± 32 | 1566 ± 117 | 1567 ± 120 | 13728 ± 1427 | 764 ± 30 | 1237 ± 118 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Male

| | 800 b, *, 3 | 800 b, #, 2 | 800 b, o, 2 | 800 b, *, 2 | 800 b, o, 3 | 800 b, ~, 2 | 1600 a, ~, 1 | 1600 a, o, 1 | 1600 a, #, 1 |
|-------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|--------------|--------------|
| AUC _{0-t} (ng/mL*hr) | 1492 ± 144 | 635 ± 49 | 3944 ± 180 | 632 ± 46 | 7050 ± 491 | 676 ± 22 | 2069 ± 155 | 24970 ± 1357 | 4894 ± 336 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Male

| | 1600 a, *, 1 | 1600 b, #, 2 | 1600 b, ~, 3 | 1600 b, *, 2 | 1600 b, ~, 2 | 1600 b, o, 2 | 1600 b, o, 3 | 1600 b, #, 3 | 1600 b, *, 3 |
|-------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| AUC _{0-t} (ng/mL*hr) | 4958 ± 387 | 2668 ± 236 | 1449 ± 35 | 2689 ± 234 | 1429 ± 135 | 15692 ± 1883 | 13102 ± 1195 | 1681 ± 136 | 3042 ± 150 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Female

Treatment Groups (ppm)

| | 400 a, o, 1 | 400 a, #, 1 | 400 a, ~, 1 | 400 a, *, 1 | 400 b, #, 2 | 400 b, #, 3 | 400 b, o, 2 | 400 b, *, 2 | 400 b, ~, 3 |
|-------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Plasma | | | | | | | | | |
| AUC _{0-t} (ng/mL*hr) | 3638 ± 143 | 572 ± 41 | 382 ± 8 | 581 ± 35 | 368 ± 24 | 394 ± 29 | 2900 ± 87 | 395 ± 26 | 275 ± 25 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Female

Treatment Groups (ppm)

| 400 b, *, 3 | 400 b, ~, 2 | 400 b, o, 3 | 800 a, ~, 1 | 800 a, #, 1 | 800 a, *, 1 | 800 a, o, 1 | 800 b, o, 3 | 800 b, #, 2 |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|

Plasma

| | | | | | | | | | |
|-------------------------------|----------|----------|------------|----------|-----------|------------|--------------|-------------|-----------|
| AUC _{0-t} (ng/mL*hr) | 639 ± 48 | 394 ± 16 | 5084 ± 514 | 867 ± 76 | 1633 ± 90 | 1676 ± 104 | 18236 ± 1014 | 12002 ± 470 | 1319 ± 77 |
|-------------------------------|----------|----------|------------|----------|-----------|------------|--------------|-------------|-----------|

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Female

| | 800 b, o, 2 | 800 b, ~, 3 | 800 b, *, 3 | 800 b, *, 2 | 800 b, #, 3 | 800 b, ~, 2 | 1600 a, ~, 1 | 1600 a, o, 1 | 1600 a, #, 1 |
|-------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|--------------|--------------|
| AUC _{0-t} (ng/mL*hr) | 3778 ± 238 | 609 ± 27 | 1547 ± 101 | 1380 ± 84 | 985 ± 65 | 840 ± 36 | 1447 ± 97 | 22506 ± 1325 | 4820 ± 292 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

Female

| | 1600 a, *, 1 | 1600 b, ~, 3 | 1600 b, #, 2 | 1600 b, *, 2 | 1600 b, ~, 2 | 1600 b, o, 3 | 1600 b, *, 3 | 1600 b, o, 2 | 1600 b, #, 3 |
|-------------------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| AUC _{0-t} (ng/mL*hr) | 4870 ± 270 | 1079 ± 89 | 3631 ± 353 | 3727 ± 380 | 1508 ± 105 | 24254 ± 1647 | 3876 ± 395 | 13944 ± 1362 | 3350 ± 391 |

Experiment Number: C61541C

Route: Dosed Feed

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Codeine

CAS Number: 76-57-3

Date Report Requested: 12/29/2016

Time Report Requested: 15:45:42

Lab: Microbiological Associates
Inc._Burroughs Wellcome Company

LEGEND

Data are displayed as mean \pm SD

MODELING METHOD & BEST FIT MODEL

^a AUC values calculated using trapezoidal rule; Yuan JH. 1993. Modeling blood/plasma concentrations in dosed feed and dosed drinking water toxicology studies. Toxicol. Appl. Pharmacol. 119, 131-141. No parameters shown.

^b AUC values calculated using trapezoidal rule

ANALYTE

Codeine

* Total Codeine

~ Morphine

° Total Morphine

STUDY TIME

¹ 7 Day

² 21 Day

³ 90 Day

TK PARAMETERS

AUC_{0-t} = Area under the plasma concentration versus time curve, AUC, from time t_i (initial) to t_f (final), AUC_{last}

**** END OF REPORT ****