**Experiment Number:** K10262
**Route:** Gavage, IV
**Species/Strain:** Mouse/B6C3F1

**Toxicokinetics Data Summary**
**Test Compound:** Isoeugenol
**CAS Number:** 97-54-1

**Date Report Requested:** 11/09/2016
**Time Report Requested:** 14:03:30
**Lab:** Battelle Northwest Laboratory

**Male**

| | Treatment Groups (mg/kg) | | | |
|---|---|---|---|---|
| | **35 [a]** | **70 [a]** | **140 [a]** | **35 IV [b]** |
| | **Plasma** | | | |
| $C_{0min(pred)}$ (ug/mL) | | | | 17.1 ± 3.0 |
| $C_{max}$ (ug/mL) * | 1.13 ± 0.18 | 1.27 ± 0.13 | 1.91 ± 0.14 | |
| $T_{max}$ (minute) | 20 | 10 | 20 | |
| Alpha (min^-1) | | | | 0.0872 ± 0.0068 |
| $t_{1/2(Alpha)}$ (minute) | | | | 7.95 ± 0.62 |
| Beta (min^-1) | | | | 0.00587 ± 0.00162 |
| $t_{1/2(Beta)}$ (minute) | | | | 118 ± 33 |
| Cl (mL/min/kg) | | | | 148 ± 5 |
| $Cl_{1(F)}$ (mL/min/kg) | 522 ± 24 | 595 ± 26 | 690 ± 50 | |
| $V_1$ (L/kg) | | | | 25.2 ± 7.0 |
| $AUC_{0-t}$ (ug/mL*min) | 67.0 ± 3.1 | 118 ± 5 | 203 ± 15 | 197 ± 6 |
| $AUC_{inf}$ (ug/mL*min) | | | | 208 ± 23 |
| F (percent) | 34.0 ± 4.0 | | | |

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| | Female | | | |
|---|---|---|---|---|
| | Treatment Groups (mg/kg) | | | |
| | 35 [a] | 70 [a] | 140 [a] | 35 IV [b] |
| | Plasma | | | |
| $C_{0min(pred)}$ (ug/mL) | | | | 18.0 ± 2.5 |
| $C_{max}$ (ug/mL) * | 1.94 ± 0.17 | 2.54 ± 0.17 | 3.99 ± 2.10 | |
| $T_{max}$ (minute) | 10 | 20 | 5 | |
| Alpha (min^-1) | | | | 0.0666 ± 0.0045 |
| $t_{1/2(Alpha)}$ (minute) | | | | 10.4 ± 0.7 |
| Beta (min^-1) | | | | 0.00679 ± 0.00131 |
| $t_{1/2(Beta)}$ (minute) | | | | 102 ± 20 |
| Cl (mL/min/kg) | | | | 108 ± 2 |
| $Cl_{1(F)}$ (mL/min/kg) | 348 ± 14 | 338 ± 18 | 350 ± 31 | |
| $V_1$ (L/kg) | | | | 16.0 ± 3.1 |
| $AUC_{0-t}$ (ug/mL*min) | 101 ± 4 | 207 ± 11 | 400 ± 36 | 278 ± 3 |
| $AUC_{inf}$ (ug/mL*min) | | | | 284 ± 25 |
| F (percent) | 36.0 ± 3.0 | | | |

LEGEND

Data are displayed as mean ± SEM

* Data are displayed as mean ± SD

MODELING METHOD & BEST FIT MODEL

[a] Manual; Plasma MEG concentration-versus-time profiles for both species were characterized by an early absorption phase followed by at least one secondary peak which prevented estimation of elimination rates. No modeling was done on the oral gavage data. Parameters were calculated using observed values.

[b] Nonlinear least-squares fitting program SAS PROC NLIN, SAS Institute, Inc., Cary, NC; Elimination of IEG was modeled for both species using a biphasic exponential equation C(t) = Aoe^-alpha*t + Boe^-beta*t () where C(t) is the plasma IEG concentration at any post-administration time (t), alpha and beta are the rate constants (min-1) obtained from the fit, Ao and Bo are the intercepts on the ordinate (concentration) axis of the extrapolated initial and terminal phases, respectively. weighting factor of [mean plasma IEG concentration]-2.

ANALYTE

Isoeugenol

TK PARAMETERS

$C_{0min(pred)}$ = Fitted plasma concentration at time zero (IV only)

$C_{max}$ = Observed or Predicted Maximum plasma (or tissue) concentration

$T_{max}$ = Time at which $C_{max}$ predicted or observed occurs

Alpha = Hybrid rate constant of the alpha phase

$t_{½(alpha)}$ = Half-life for the alpha phase

Beta = Hybrid rate constant of the beta phase

$t_{½(beta)}$ = Half-life for the beta phase

Cl = Clearance, includes total clearance

$Cl_{1(F)}$ = Apparent clearance of the central compartment, also $Cl_{(F)}$ for gavage groups in non-compartmental model

$V_1$ = Volume of distribution of the central compartment, includes $V_d$ and $V_{volume}$ of distribution, $V_z$ apparent volume of distribution NCA, $V_{app}$ apparent volume of distribution for intravenous studies

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

$AUC_{inf}$ = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

F = Bioavailability, absolute bioavailability

** END OF REPORT **