**Experiment Number:** K90004     **Toxicokinetics Data Summary**     **Request Date:** 7/11/2023
**Route:** Whole Body Inhalation     **Compound:** Propylene glycol mono-t-butyl ether     **Request Time:** 10:03:16
                                     **Analyte:** Propylene glycol mono-t-butyl ether
**Species/Strain:** Mice/B6C3F1     **CAS Number:** 57018-52-7     **Lab:** Battelle

**Male**

**Treatment Group (ppm)**

| | 75 Inhalation Plasma[a] | 300 Inhalation Plasma[a] | 1200 Inhalation Plasma[b] |
|---|---|---|---|
| C_0min_pred (ug/g) | 1.69 ± 0.22 | 15.5 ± 1.8 | 547 ± 128 |
| Lambda_z (minute$^{-1}$) | | | 0.0381 ± 0.054 |
| Alpha (minute$^{-1}$) | 0.141 ± 0.021 | 0.121 ± 0.020 | |
| Alpha Half-life (minute) | 4.92 ± 0.74 | 5.72 ± 0.93 | |
| Beta (minute$^{-1}$) | 0.0111 ± 0.015 | 0.00917 ± 0.015 | |
| Beta Half-life (minute) | 62.2 ± 81 | 75.6 ± 120 | |
| AUC_0-T (ug*min/g) | 15.6 ± 0.81 | 160 ± 26 | 36333 ± 3687 |
| AUCinf_pred (ug*min/g) | 17.5 ± 3.2 | 169 ± 26 | 48266 ± 5250 |

**Toxicokinetics Data Summary**

**Compound:** Propylene glycol mono-t-butyl ether

**Analyte:** Propylene glycol mono-t-butyl ether

**CAS Number:** 57018-52-7

**Female**

| Treatment Group (ppm) | | |
|---|---|---|
| **75 Inhalation Plasma[a]** | **300 Inhalation Plasma[a]** | **1200 Inhalation Plasma[b]** |

| | 75 Inhalation Plasma[a] | 300 Inhalation Plasma[a] | 1200 Inhalation Plasma[b] |
|---|---|---|---|
| C_0min_pred (ug/g) | 1.49 ± 0.35 | 16.2 ± 3.1 | 800 ± 165 |
| Lambda_z (minute$^{-1}$) | | | 0.0623 ± 0.098 |
| Alpha (minute$^{-1}$) | 0.139 ± 0.035 | 0.148 ± 0.050 | |
| Alpha Half-life (minute) | 4.99 ± 1.3 | 4.69 ± 1.6 | |
| Beta (minute$^{-1}$) | 0.00216 ± 0.041 | 0.0294 ± 0.049 | |
| Beta Half-life (minute) | 320 ± 6015 | 23.6 ± 39 | |
| AUC_0-T (ug*min/g) | 12.9 ± 1.6 | 155 ± 27 | 53780 ± 5050 |
| AUCinf_pred (ug*min/g) | 15.4 ± 44 | 157 ± 26 | 88137 ± 10202 |

| | | |
|---|---|---|
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## LEGEND

MODELING SOFTWARE

　　PROC NLIN

MODELING METHOD & BEST FIT MODEL

[a]Fitting $C(t) = A_o e^{-\alpha t} + B_o e^{-\beta t}$ to the data using a nonlinear least-squares fitting program (SAS PROC NLIN: SAS Institute Inc.; Cary, NC) where C(t) blood concentration of PGMBE at any postexposure time (t), alpha and beta are the hybrid rate constants (min$^{-1}$) obtained from the fit, and Ao and Bo are the intercepts on the ordinate (concentration) axis of the extrapolated initial and terminal phases, respectively. Weighted fitting using [mean PGMBE blood concentration]$^{-1}$ as the weighting factor for both rats and mice. Bi-exponential blood elimination kinetics. Estimate is ± 0.5 of the 95% confidence interval AUC0-T where T =90 minutes

[b]Michaelis-Menten kinetics: $t = (C_o - PGMBE(t))/V_{max} + K_m Ln(C_o/PGMBE(t))/V_{max}$ where Co is the concentrtation of PGMBE extrapolated to time zero (t=o) which can be solved using a nonlinear least-squares fitting program (SAS PROC NLIN; SAS Institute Inc.; Cary, NC). AUC_inf = AUCt + (Cf/ke) where Cf is the concentration (ug PGMBE/g blood) measured at the final time point and ke is the rat constant for the terminal elimination phase. Model parameters were derived without weighting. PGMGE exhibited saturable Michaelis-Menten elimination kinetics. Lambda_z represents Ke, Km= 119 ± 278 ug/g and Vm = 4.54 ± 4.8 ug/g*min; Estimate is ± 0.5 of the 95% confidence interval AUC0-T where T =90 minutes

ANALYTE

　　Propylene glycol mono-t-butyl ether

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TK PARAMETERS – (NOTE: All parameters use Confidence Interval instead of SD or SEM)

C_0min_pred = Fitted plasma concentration at time zero (IV only)
Lambda_z = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA ke or kelim
Alpha = Hybrid rate constant of the alpha phase
Alpha Half-life = Half-life for the alpha phase
Beta = Hybrid rate constant of the beta phase
Beta Half-life = Half-life for the beta phase
AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

TK_INHALATION PLASMA

ANALYSIS METHOD

Blood was extracted with internal standard and analyzed by validated GC/MS method incorporating selected ion monitoring. The limit of detection (LOD), limit of quantitation (LOQ), and the experimental limit of quantitation (ELOQ) were 0.00948, 0.0316, and 0.0745 ug PGMBE/g blood, respectively. The elimination half-lives for the initial and terminal phases of the concentration versus time profiles were calculated as ln2/alpha or ln2/beta, respectively. The maximum blood concentration (Co) was assumed to occur at t=0 and was calculated as Ao + Bo. The area under the curve (AUC) was estimated using the trapezoidal rule from the first to the last time point, AUC t=90, because the groups either failed to reach terminal elimination phases or there was uncertainty. The CI value is plus or minus 0.5 of the 95% confidence interval of the parameter estimate such as C_0min_pred[CI] or the (estimate plus or minus 0.5 CI).

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**Species/Strain:** Mice/B6C3F1

**CAS Number:** 57018-52-7

**Lab:** Battelle

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TK PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENOUS PLASMA

### 75 ppm, 300 ppm Male and Female

Male and female B6C3F1 mice were exposed by single administration whole body inhalation for 6 hours plus T90 (T90 = 12 minutes) of 75, 300, or 1200 ppm propylene glycol mono-t-butyl ether (PGMBE). The mice were 12 weeks old at the time of dosing with the average bodyweight of 29.3 g for the males and 23.7 g, females. Each animal was bled twice, once from each eye under anesthesia. Heparinized blood was collected at 8-9 timepoints:  for 75 ppm exposed animals at <5, 10, 20, 30, 45, 60, 90 and 120 minutes postexposure; for 300 ppm exposed animals at 5, 10, 30, 45, 60, 90, 120 and 180 minutes postexposure; and for 1200 ppm exposed animals at <5, 10, 20, 30, 60, 90, 120, 180 and 240 minutes postexposure. During exposure, animals had access to tap water, but not to food.

ANALYSIS METHOD

Blood was extracted with internal standard and analyzed by validated GC/MS method incorporating selected ion monitoring. The limit of detection (LOD), limit of quantitation (LOQ), and the experimental limit of quantitation (ELOQ) were 0.00948, 0.0316, and 0.0745 ug PGMBE/g blood, respectively. Blood concentration versus time plots from the 1200 ppm groups exhibited properties of kinetic nonlinearity, suggesting that the capacity for PGMBE elimination at this exposure concentration may be saturated. Toxicokinetic parameters for animals exposed to 1200 ppm PGMBE were derived based on Michaelis-Menten kinetics. Estimates for Co, Km, and Vmax, along with their asymptotic standard errors and approximate 95% confidence intervals, were obtained directly from the model. AUC also estimated using the trapezoidal rule. AUC t=90 because the groups either failed to reach a terminal elimination phase or there was uncertainty.

### 1200 ppm Male and Female

Male and female B6C3F1 mice were exposed by single administration whole body inhalation for 6 hours plus T90 (T90 = 12 minutes) of 75, 300, or 1200 ppm propylene glycol mono-t-butyl ether (PGMBE). The mice were 12 weeks old at the time of dosing with the average bodyweight of 29.3 g for the males and 23.7 g, females. Each animal was bled twice, once from each eye under anesthesia. Heparinized blood was collected at 8-9 timepoints:  for 75 ppm exposed animals at <5, 10, 20, 30, 45, 60, 90 and 120 minutes postexposure; for 300 ppm exposed animals at 5, 10, 30, 45, 60, 90, 120 and 180 minutes postexposure; and for 1200 ppm exposed animals at <5, 10, 20, 30, 60, 90, 120, 180 and 240 minutes postexposure. During exposure, animals had access to tap water, but not to food.