

TABLE I

Estimates (CI 95%) for Emin, Emax, ED50 ( $\mu\text{g/kg}$ ), GSD, percentage of variance explained ( $R^2$ ) and Hill coefficient (n) for different effects in line A, B and C rats 8 days after a single oral exposure to different doses of TCDD.

| Rat line            |   | Body weight change<br>(% Initial body weight) |              | Relative thymus weight<br>(% Body weight) |                  | Liver EROD activity<br>((pmol/mg) $\times$ min) |                | Serum FFA levels<br>(nM) |                  | Serum bilirubin levels<br>( $\mu\text{M}$ ) |                 | Serum ASAT activity<br>(U/l) |               | Incisor tooth defects |                 |
|---------------------|---|---|--------------|---|------------------|---|----------------|--------------------------|------------------|---|-----------------|------------------------------|---------------|-----------------------|-----------------|
| Emin                | A | 104   | (103-105)    | 0.13                                      | (0.12 - 0.14)*   | 72  | (0 - 390)      | 0.38                     | (0.30 - 0.45) *§ | 1.6   | (1.1 - 2.1)     | 217                          | (102 - 330)   | 0.59                  | (0.33 – 0.85) § |
|                     | B | 105   | (104 - 107)  | 0.16                                      | (0.12 - 0.20)    | 85  | (0 - 250)      | 0.48                     | (0.41 - 0.55)    | 1.7   | (1.2 - 2.1)     | 175                          | (140 - 210)   | 0.20                  | (0 – 0.45)      |
|                     | C | 104   | (103 - 106)  | 0.15                                      | (0.14 - 0.16)    | 88  | (0 - 570)      | 0.54                     | (0.45 - 0.64)    | 1.9   | (0.98 - 2.8)    | 203                          | (150 - 250)   | 0.46                  | (0.2 – 0.73)    |
| Emax                | A | 95  | (93 - 96) *§ | 0.050                                     | (0.043 - 0.058)* | 1170  | (1000 - 1300)* | 0.57                     | (0.47 - 0.66) *§ | 5.0   | (0-14) *§       | 878                          | (0 - 2000)    | 2.6                   | (2.2 – 3.0)     |
|                     | B | 83  | (80 - 86) *  | 0.026                                     | (0 - 0.055)      | 1220  | (1100 - 1400)  | 1.1                      | (0.84 - 1.3)     | 12  | (11 - 14) *     | 668                          | (540 - 800) * | 2.3                   | (1.9 – 2.7)     |
|                     | C | 78  | (74 - 81)    | 0.038                                     | (0.028 - 0.047)  | 1580  | (1200 - 2000)  | 1.3                      | (1.0 - 1.5)      | 23  | (18 - 28)       | 1620                         | (840 - 2400)  | 2.7                   | (2.0 – 3.3)     |
| ED50 <sup>a</sup>   | A | 20  | (9.1 - 46) * | 1.8                                       | (0.94 - 3.3)     | 0.15  | (0.064 - 0.34) | 32                       | (0 - 3000)       | 656   | (0.0017 - 3000) | 283                          | (0.37 - 3000) | 35                    | (17 – 75) *     |
|                     | B | 21  | (14 - 33) *  | 1.9                                       | (0.44 - 8.5)     | 0.28  | (0.17 - 0.47)  | 110                      | (39 - 310) *     | 95  | (61 - 150) *    | 57                           | (25 - 130)    | 30                    | (0 - 3000)      |
|                     | C | 5.5   | (3.7 - 8.4)  | 0.83                                      | (0.54 - 1.3)     | 0.14  | (0.053 - 0.35) | 21                       | (11 - 40)        | 27  | (18 - 40)       | 33                           | (9.2 - 120)   | 9.3                   | (4.4 – 20)      |
| GSD                 | A | 5.0   | (1.7 - 15)   | 4.4                                       | (1.9 - 10)       | 3.4   | (1.1 - 11)     | 1.2                      | (0 - 50)         | 50  | (0.012 - 50)    | 15                           | (0.063 - 50)  | 2.7                   | (0.96 – 7.3)    |
|                     | B | 2.8   | (1.5 - 5.1)  | 34  | (2.5 - 50)       | 2.9   | (1.4 - 6.0)    | 3.1                      | (0.83 - 12)      | 3.6   | (2.1 - 6.2)     | 5.1                          | (1.8 - 14)    | 1.0                   | (0 - 50)        |
|                     | C | 4.2   | (2.5 - 7.2)  | 4.8                                       | (2.6 - 8.7)      | 4.0   | (0.92 - 17)    | 1.8                      | (0.90 - 3.6)     | 2.5   | (1.5 - 4.2)     | 4.9                          | (1.8 - 13)    | 2.8                   | (1.0 – 7.5)     |
| $R^2$               | A | 0.69  |              | 0.77                                      |                  | 0.65  |                | 0.13                     |                  | 0.42  |                 | 0.31                         |               | 0.57                  |                 |
|                     | B | 0.80  |              | 0.79                                      |                  | 0.81  |                | 0.51                     |                  | 0.88  |                 | 0.76                         |               | 0.59                  |                 |
|                     | C | 0.91  |              | 0.90                                      |                  | 0.70  |                | 0.48                     |                  | 0.88  |                 | 0.90                         |               | 0.61                  |                 |
| Hill n <sup>b</sup> | A | 1.1   | (0.25 – 1.9) | 1.1                                       | (0.41 – 1.8)     | 1.3   | (0 – 2.7)      | 5.0                      | (0 – 200)        | 0.31  | (0 – 1.1)       | 0.75                         | (0 – 2.1)     | 1.8                   | (0 – 3.8)       |
|                     | B | 1.5   | (0.55 – 2.5) | 0.42                                      | (0.068 – 0.78)   | 1.5   | (0.34 – 2.7)   | 5.0                      | (0 – 40)         | 1.3   | (0.71 – 1.9)    | 1.0                          | (0.33 – 1.6)  | 5.0                   | (0 – 74)        |
|                     | C | 1.1   | (0.67 – 1.6) | 1.0                                       | (0.60 – 1.5)     | 1.1   | (0 – 2.5)      | 2.8                      | (0 – 6.7)        | 1.8   | (0.82 – 2.7)    | 0.94                         | (0.40 – 1.5)  | 1.6                   | (0 – 3.36)      |

<sup>a</sup>  $\mu\text{g/kg}$  TCDD

<sup>b</sup> Hill coefficients were derived from the Hill plot model for the same data.

\* Significantly different from line C estimate.

§ Significantly different from line B estimate.

**TABLE II**

**Efficacy ((Emax-Emin)/Emin), and relative efficacy and potency (compared with line C) for different effects in line A, B and C rats 8 days after a single oral exposure to different doses of TCDD.**

|   | Rat line | Body weight change | Relative thymus weight | Liver EROD activity | Serum FFA levels | Serum bilirubin levels | Serum ASAT activity | Incisor tooth defects |
|---|----------|--------------------|------------------------|---------------------|------------------|------------------------|---------------------|-----------------------|
| Efficacy <sup>a</sup><br>((Emax – Emin)/Emin) | A        | -0.093 *§          | -0.60 *                | 15                  | 0.5 *§           | 2.2 *                  | 3.1                 | 3.31                  |
|   | B        | -0.21              | -0.84                  | 13                  | 1.3              | 6.5                    | 2.8                 | 10.62                 |
|   | C        | -0.25              | -0.74                  | 17                  | 1.4              | 11                     | 7.0                 | 4.74                  |
| Efficacy relative to line C                   | A        | 0.37               | 0.81                   | 0.90                | 0.37             | 0.19                   | 0.44                | 0.70                  |
|   | B        | 0.84               | 1.1                    | 0.78                | 0.93             | 0.57                   | 0.40                | 2.24                  |
|   | C        | 1                  | 1                      | 1                   | 1                | 1                      | 1                   | 1                     |
| Potency relative to line C                    | A        | 0.27               | 0.47                   | 0.93                | 0.66             | 0.041                  | 0.12                | 0.26                  |
|   | B        | 0.26               | 0.43                   | 0.48                | 0.19             | 0.28                   | 0.58                | 0.31                  |
|   | C        | 1                  | 1                      | 1                   | 1                | 1                      | 1                   | 1                     |

<sup>a</sup> Statistically significant ( $P < 0.05$ ) differences are shown only for efficacy.

\* Significantly different from line C estimate.

§ Significantly different from line B estimate.

