



Chiu et al.:

# A Tiered, Bayesian Approach to Estimating Population Variability for Regulatory Decision-Making

## Supplementary Data

### Materials and methods

**Tab. S1: Chemicals considered to have less than reliable individual EC<sub>10</sub> estimates (due to poor convergence, poor model fit, or low potency)**

| Number | CASRN      | Rationale                         |
|--------|------------|-----------------------------------|
| 7      | 50-02-2    | Low potency                       |
| 22     | 72-14-0    | Low potency                       |
| 23     | 91-53-2    | Low potency                       |
| 33     | 25152-84-5 | Not fully converged               |
| 36     | 126-98-7   | Low potency                       |
| 41     | 4376-20-9  | Low potency                       |
| 44     | 116-06-3   | Low potency                       |
| 59     | 102-36-3   | Low potency                       |
| 70     | 100-42-5   | Low potency                       |
| 71     | 110-57-6   | Low potency                       |
| 86     | 81-55-0    | Not fully converged               |
| 90     | 118-75-2   | High uncertainty in one batch     |
| 94     | 87-68-3    | Low potency                       |
| 95     | 393-75-9   | Low potency                       |
| 97     | 93-05-0    | Not fully converged               |
| 99     | 84-69-5    | Low potency                       |
| 110    | 598-91-4   | Not fully converged               |
| 113    | 117-81-7   | Low potency                       |
| 117    | 6338-41-6  | Low potency                       |
| 124    | 6112-76-1  | Some individuals high uncertainty |
| 127    | 762-75-4   | Low potency                       |
| 134    | 106-89-8   | Low potency                       |
| 138    | 101-72-4   | Not fully converged               |
| 141    | 97-32-5    | Low potency                       |
| 143    | 7779-30-8  | Low potency                       |
| 144    | 103-33-3   | Low potency                       |
| 154    | 64-86-8    | Poor fit                          |
| 158    | 137-30-4   | Poor fit                          |
| 161    | 52645-53-1 | Low potency                       |
| 163    | 23541-50-6 | Poor fit                          |
| 166    | 20830-75-5 | Poor fit                          |
| 168    | 67-97-0    | Not fully converged               |



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**Tab. S2: Chemicals considered to have reliable individual-based EC<sub>10</sub> estimates but less than reliable population-based EC<sub>10</sub> estimates (due to correlation, departure from normal distribution)**

| Number | CASRN      | Rationale   | Individual-based TDVF <sub>01</sub> estimate |
|--------|------------|-------------|----------------------------------------------|
| 17     | 396-01-0   | Correlation | 4.25                                         |
| 19     | 55-56-1    | Correlation | 7.14                                         |
| 25     | 130-26-7   | Correlation | 2.91                                         |
| 34     | 148-24-3   | Correlation | 5.45                                         |
| 39     | 127-47-9   | Multi-modal | 1.81                                         |
| 54     | 154-42-7   | Correlation | 30.4                                         |
| 76     | 548-62-9   | Multi-modal | 3.14                                         |
| 92     | 4252-78-2  | Correlation | 2.51                                         |
| 98     | 60-57-1    | Correlation | 3.76                                         |
| 100    | 117-10-2   | Multi-modal | 2.79                                         |
| 109    | 98-29-3    | Correlation | 2.06                                         |
| 119    | 137-26-8   | Correlation | 9.29                                         |
| 140    | 55-86-7    | Correlation | 7.26                                         |
| 145    | 26530-20-1 | Correlation | 5.49                                         |
| 147    | 309-00-2   | Correlation | 3.75                                         |
| 148    | 7789-12-0  | Correlation | 5.95                                         |
| 151    | 2437-29-8  | Multi-modal | 2.81                                         |
| 162    | 39025-24-6 | Correlation | 2.56                                         |
| 170    | 379-79-3   | Correlation | 5.22                                         |

**Tab. S3: Chemicals considered to have reliable individual-based EC<sub>10</sub> estimates and reliable population-based EC<sub>10</sub> estimates**

| Number | CASRN      | Individual-based TDVF <sub>01</sub> estimate | Population-based TDVF <sub>01</sub> estimate |
|--------|------------|----------------------------------------------|----------------------------------------------|
| 1      | 66-71-7    | 1.15                                         | 1.14                                         |
| 2      | 1948-33-0  | 2.03                                         | 1.93                                         |
| 3      | 446-86-6   | 6.89                                         | 10.88                                        |
| 4      | 2016-88-8  | 2.45                                         | 2.43                                         |
| 5      | 549-18-8   | 1.48                                         | 1.55                                         |
| 6      | 106-51-4   | 4.52                                         | 3.49                                         |
| 8      | 305-03-3   | 2.79                                         | 2.87                                         |
| 9      | 120-80-9   | 3.2                                          | 2.96                                         |
| 10     | 50-28-2    | 3.13                                         | 2.47                                         |
| 11     | 51-21-8    | 11.2                                         | 10.24                                        |
| 12     | 13311-84-7 | 1.83                                         | 1.79                                         |
| 13     | 123-31-9   | 2.4                                          | 2.43                                         |
| 14     | 73-31-4    | 2.98                                         | 2.71                                         |
| 15     | 57-83-0    | 1.41                                         | 1.43                                         |
| 16     | 50-55-5    | 1.45                                         | 1.44                                         |
| 18     | 152-11-4   | 3.63                                         | 3.50                                         |
| 20     | 58-14-0    | 6.25                                         | 6.61                                         |
| 21     | 58-54-8    | 2.05                                         | 2.48                                         |
| 24     | 121-54-0   | 1.9                                          | 1.98                                         |
| 26     | 834-28-6   | 3.01                                         | 3.14                                         |
| 27     | 458-37-7   | 1.89                                         | 1.90                                         |
| 28     | 97-18-7    | 3.47                                         | 2.70                                         |
| 29     | 478-43-3   | 3.77                                         | 3.94                                         |
| 30     | 54965-24-1 | 1.45                                         | 1.47                                         |
| 31     | 1675-54-3  | 1.67                                         | 1.68                                         |
| 32     | 533-74-4   | 3.34                                         | 4.33                                         |
| 35     | 77439-76-0 | 2.2                                          | 1.98                                         |
| 37     | 34256-82-1 | 1.4                                          | 1.44                                         |
| 38     | 7778-50-9  | 5.46                                         | 4.92                                         |
| 40     | 15663-27-1 | 3.23                                         | 2.55                                         |
| 42     | 55981-09-4 | 1.98                                         | 1.81                                         |
| 43     | 142-83-6   | 1.99                                         | 2.09                                         |
| 45     | 123-30-8   | 1.69                                         | 1.62                                         |
| 46     | 472-86-6   | 1.57                                         | 1.68                                         |
| 47     | 116-31-4   | 2.29                                         | 2.02                                         |
| 48     | 879-39-0   | 1.92                                         | 1.86                                         |
| 49     | 2243-76-7  | 2.63                                         | 2.65                                         |
| 50     | 961-11-5   | 2.12                                         | 1.96                                         |



| Number | CASRN      | Individual-based<br>TDVF <sub>01</sub> estimate | Population-based<br>TDVF <sub>01</sub> estimate |
|--------|------------|-------------------------------------------------|-------------------------------------------------|
| 51     | 115-09-3   | 14.4                                            | 16.03                                           |
| 52     | 83-26-1    | 1.45                                            | 1.98                                            |
| 53     | 74-31-7    | 1.83                                            | 1.84                                            |
| 55     | 95-54-5    | 3.15                                            | 3.43                                            |
| 56     | 104-40-5   | 2.06                                            | 2.05                                            |
| 57     | 10108-64-2 | 2.03                                            | 2.22                                            |
| 58     | 65558-69-2 | 2.06                                            | 2.34                                            |
| 60     | 10563-29-8 | 3.22                                            | 3.08                                            |
| 61     | 446-35-5   | 3.06                                            | 2.98                                            |
| 62     | 62-73-7    | 1.64                                            | 1.67                                            |
| 63     | 143-50-0   | 1.55                                            | 1.56                                            |
| 64     | 538-71-6   | 2.59                                            | 2.23                                            |
| 65     | 14866-33-2 | 4.42                                            | 5.39                                            |
| 66     | 140-72-7   | 3.23                                            | 3.10                                            |
| 67     | 17831-71-9 | 2.1                                             | 1.94                                            |
| 68     | 133-06-2   | 2.57                                            | 2.04                                            |
| 69     | 62-38-4    | 8.45                                            | 71.04                                           |
| 72     | 1191-41-9  | 1.65                                            | 1.90                                            |
| 73     | 134-32-7   | 3.38                                            | 3.24                                            |
| 74     | 5153-67-3  | 2.79                                            | 2.81                                            |
| 75     | 111-30-8   | 1.58                                            | 1.64                                            |
| 77     | 485-47-2   | 2.6                                             | 2.72                                            |
| 78     | 3018-12-0  | 1.72                                            | 1.66                                            |
| 79     | 90-41-5    | 2.92                                            | 2.94                                            |
| 80     | 100-22-1   | 2.81                                            | 2.67                                            |
| 81     | 2451-62-9  | 4.4                                             | 4.50                                            |
| 82     | 95-55-6    | 4.5                                             | 4.65                                            |
| 83     | 70-30-4    | 2.59                                            | 2.47                                            |
| 84     | 532-27-4   | 1.83                                            | 1.87                                            |
| 85     | 4074-88-8  | 2.56                                            | 2.17                                            |
| 87     | 610-39-9   | 3.03                                            | 2.76                                            |
| 88     | 764-42-1   | 2.25                                            | 2.41                                            |
| 89     | 33229-34-4 | 1.49                                            | 1.42                                            |
| 91     | 13048-33-4 | 1.45                                            | 1.41                                            |
| 93     | 496-72-0   | 3.72                                            | 4.29                                            |
| 96     | 156-10-5   | 4.49                                            | 6.44                                            |
| 101    | 55-55-0    | 3.24                                            | 3.53                                            |
| 102    | 140-49-8   | 2.1                                             | 2.04                                            |



| Number | CASRN      | Individual-based<br>TDVF <sub>01</sub> estimate | Population-based<br>TDVF <sub>01</sub> estimate |
|--------|------------|-------------------------------------------------|-------------------------------------------------|
| 103    | 1239-45-8  | 4.73                                            | 4.69                                            |
| 104    | 3252-43-5  | 2.02                                            | 2.45                                            |
| 105    | 3524-68-3  | 4.17                                            | 4.01                                            |
| 106    | 12789-03-6 | 1.85                                            | 1.93                                            |
| 107    | 70-25-7    | 3.7                                             | 3.03                                            |
| 108    | 630-16-0   | 2.61                                            | 2.18                                            |
| 111    | 538-75-0   | 2.65                                            | 3.13                                            |
| 112    | 115-29-7   | 1.58                                            | 1.60                                            |
| 114    | 96-69-5    | 2.44                                            | 2.33                                            |
| 115    | 57-97-6    | 2.12                                            | 2.08                                            |
| 116    | 6317-18-6  | 3.01                                            | 2.93                                            |
| 118    | 793-24-8   | 1.56                                            | 1.50                                            |
| 120    | 95-85-2    | 7.86                                            | 7.43                                            |
| 121    | 7487-94-7  | 17.1                                            | 34.94                                           |
| 122    | 95-84-1    | 1.6                                             | 1.76                                            |
| 123    | 1271-19-8  | 2.42                                            | 3.24                                            |
| 125    | 100-27-6   | 2.23                                            | 2.20                                            |
| 126    | 95-83-0    | 3.63                                            | 3.84                                            |
| 128    | 138-89-6   | 7.8                                             | 4.88                                            |
| 129    | 21829-25-4 | 5.65                                            | 5.12                                            |
| 130    | 619-23-8   | 1.98                                            | 2.01                                            |
| 131    | 612-23-7   | 5.75                                            | 5.51                                            |
| 132    | 12083-48-6 | 3.67                                            | 2.45                                            |
| 133    | 933-78-8   | 1.85                                            | 2.70                                            |
| 135    | 101-90-6   | 3.74                                            | 3.42                                            |
| 136    | 101-96-2   | 2.59                                            | 2.32                                            |
| 137    | 6219-89-2  | 3.64                                            | 3.66                                            |
| 139    | 4901-51-3  | 1.26                                            | 1.31                                            |
| 142    | 1421-63-2  | 1.94                                            | 1.98                                            |
| 146    | 8001-35-2  | 1.58                                            | 1.57                                            |
| 149    | 1465-25-4  | 1.42                                            | 1.40                                            |
| 150    | 113-92-8   | 4.37                                            | 3.86                                            |
| 152    | 4/4/5743   | 2.65                                            | 2.58                                            |
| 153    | 52417-22-8 | 3.62                                            | 3.75                                            |
| 155    | 517-28-2   | 1.97                                            | 1.99                                            |
| 156    | 60207-90-1 | 1.41                                            | 1.50                                            |
| 157    | 88671-89-0 | 1.28                                            | 1.31                                            |
| 159    | 66-81-9    | 3.39                                            | 4.41                                            |



| Number | CASRN       | Individual-based TDVF <sub>01</sub> estimate | Population-based TDVF <sub>01</sub> estimate |
|--------|-------------|----------------------------------------------|----------------------------------------------|
| 160    | 1162-65-8   | 2.7                                          | 2.57                                         |
| 164    | 149845-06-7 | 1.76                                         | 1.64                                         |
| 165    | 434-07-1    | 2.29                                         | 1.99                                         |
| 167    | 105-11-3    | 1.78                                         | 1.68                                         |
| 169    | 13463-41-7  | 8.83                                         | 11.67                                        |

### Stan (version 2.6.2) statistical model code

```

data {
  int<lower=0> Nconc;    // Number of concentrations in each dataset
  vector[Nconc] x_conc; // Chemical concentrations
  int<lower=0> Nindiv;    // Number of individuals
  int<lower=0> Nsets;     // Number of data sets
  vector[Nconc] y[Nsets]; // Responses
  int<lower=1,upper=Nindiv> indiv[Nsets]; // Which individual for each data set
  int<lower=1> Nquants;   // Number of quantiles of EC10 to calculate
  vector[Nquants] quants; // Quantiles (e.g., c(0.01,0.025,0.5,0.975,0.99))
  int<lower=1> Nbatch;   // Number of batches
  int<lower=1,upper=Nbatch> batch[Nsets]; // Which batch for each dataset
}

parameters {
  real m_0; // pop mean for beta_0
  real<lower=0> m_1; // pop mean for beta_1 (non-negative)
  real<lower=0> sd_0; // pop sd for beta_0
  real<lower=0> sd_1; // pop sd for beta_1
  real<lower=0> sigma_y[Nbatch]; // batch-specific error scale on y
  real m_theta_0;
  real<lower=0> sd_theta_0;
  real z_0[Nindiv]; // z-score for individual beta_0
  real z_1[Nindiv]; // z-score for individual beta_1
  real z_theta_0[Nsets]; // z-score for dataset theta_0
}

transformed parameters {
  real beta_0[Nindiv];
  real beta_1[Nindiv];
  real theta_0[Nsets];
  for (i in 1:Nindiv) {
    beta_0[i] <- m_0 + sd_0 * z_0[i];
    beta_1[i] <- m_1 + sd_1 * z_1[i];
  }
  for (i in 1:Nsets) {
    theta_0[i] <- m_theta_0 + sd_theta_0 * z_theta_0[i];
  }
}

model {
  // Local scope temporary variable
  vector[Nconc] eta;
  // Prior distributions
  m_0 ~ normal(-2,10);
  m_1 ~ normal(0,5); // Half-normal
  sd_0 ~ normal(0,1); // Half-normal
  sd_1 ~ normal(0,1); // Half-normal

```

```
sigma_y ~ normal(0,10); // Half-normal
m_theta_0 ~ normal(0,5);
sd_theta_0 ~ normal(0,1);
z_0 ~ normal(0,1);
z_1 ~ normal(0,1);
z_theta_0 ~ normal(0,1);
for (s in 1:Nsets) {
  for (c in 1:Nconc)
    eta[c] <- theta_0[s] + (-100-theta_0[s]) * inv_logit(beta_0[indiv[s]] + beta_1[indiv[s]] * log(x_conc[c]));
  y[s] ~ student_t(5, eta, sigma_y[batch[s]]); // Use student-t with dof=5 to address outliers
}
}
generated quantities {
  vector[Nindiv] ec10;          // Concentration at which the relative response is 10%
  real ec10_GM;                 // Geometric mean
  real ec10_GSD;                // Geometric standard deviation
  real ec10_GSD_approx;        // Approximate GSD derived from m_0,m_1,sd_0, and sd_1
  real ec10_median;            // Median
  vector[Nquants] ec10_quants; // Quantiles
  vector[Nquants] ec10_quant_ratios; // Ratios of median to quantiles

  for (i in 1:Nindiv)
    ec10[i] <- exp((log(0.1/(1-0.1)) - beta_0[i])/beta_1[i]);
  ec10_GM <- exp(mean(log(ec10)));
  ec10_GSD <- exp(sd(log(ec10)));
  ec10_GSD_approx <- exp(sqrt((sd_0 / m_1)^2 + (sd_1 / m_1)^2 * ((log(0.1/(1-0.1)) - m_0)/m_1)^2));
  {
    int ec10_indx[Nindiv];
    real p;
    real m;
    real g;
    int i;
    int itmp;
    ec10_indx <- sort_indices_asc(ec10);
    p <- 0.5;
    m <- 1-p;
    itmp <- 1;
    while (itmp < (Nindiv*p + m))
      itmp <- itmp + 1;
    i <- itmp - 1;
    g <- Nindiv*p + m - i;
    ec10_median <- (1-g)*ec10[ec10_indx[i]] + g*ec10[ec10_indx[i+1]];
    for (q in 1:Nquants) {
      p <- quants[q];
      m <- 1-p;
      itmp <- 1;
      while (itmp < (Nindiv*p + m))
        itmp <- itmp + 1;
      i <- itmp - 1;
      g <- Nindiv*p + m - i;
      ec10_quants[q] <- (1-g)*ec10[ec10_indx[i]] + g*ec10[ec10_indx[i+1]];
    }
    for (q in 1:Nquants) {
      ec10_quant_ratios[q] <- ec10_median/ec10_quants[q];
    }
  }
}
```