Appendix I

Alternative Method for Estimating Dermal Absorption

APPENDIX I. ALTERNATIVE METHOD FOR ESTIMATING DERMAL ABSORPTION

This document uses the fraction absorbed approach to estimate dermal absorption, which is the method recommended in current U.S. Environmental Protection Agency guidance (U.S. EPA, 2004, 1992). This method does not accurately represent the mechanisms of dermal absorption and presents difficulties in extrapolating experimental results to actual exposure conditions. The discussion below presents an alternative approach using a more mechanistic model. This method is based on work by Dr. Annette Bunge, as published in Bunge and Parks (1998).

BASIC MODEL

Bunge and Parks (1998) present three approaches for estimating dermal dose from soil, depending on whether absorption is small, large, or based on slow soil-release kinetics (i.e., desorption from soil is slow relative to dermal permeation). The slow-release kinetics approach was selected as the best one to use because the high lipophilicity of dioxin, presence of organic carbon in the clay, and small particles associated with clay all suggest that dioxin will be tightly bound to the particles and slowly released. On this basis, the absorbed dermal dose (pg) is estimated as follows:

$$AbsDose = C_{soil,0} M_{soil} \left[1 - \exp\left(-k_{soil} \rho_{soil} f_{area} A_{\exp} t_{\exp} / M_{soil} \right) \right] \qquad \text{(I-1)}$$

where:

$C_{soil,0}$ = concentration of dioxin in soil at = 0 (pg/mg)
M_{soil} = mass of soil on exposed skin (mg)
k_{soil} = rate constant for first-order soil release kinetics (cm/s)
ρ_{soil} = soil bulk density (mg/cm^3)
f_{area} = fraction of exposed area in contact with soil
A_{exp} = exposed skin area (cm^2)
t_{exp} = exposure time (hr)

The rate constant and soil density terms can be combined into one term representing the transfer rate from soil (k) with units of mg cm^{-2} hr^{-1}. If the amount of dioxin absorbed is less than about 10% of the original amount on the skin (i.e., $C_{soil,0} \times M_{soil}$), then Eq I-1 simplifies to:

$$AbsDose = k\ f_{\mathrm{area}}\ A_{\exp}\ t_{\exp}\ C_{\mathrm{soil,0}} \qquad \text{(I-2)}$$

ESTIMATING *k*

As discussed above, Eq I-2 is based on the assumption of slow soil-release kinetics. Assuming that desorption from soil is slow relative to dermal permeation, the rate of dermal permeation can be used to estimate the rate of desorption from soil. This approach is used here.

As discussed in Section 5, this report derives the dermal absorption properties of dioxin from Roy et al. (1990), who measured dermal absorption of tetrachlorodibenzo-*p*-dioxin (TCDD) in soil with an organic carbon content of 0.45% and applied at supermonolayer coverage (monolayer estimated as 1.3 mg/cm^2 and amount applied was 6 mg/cm^2). The saturation limit for TCDD in this soil was estimated as follows:

$$C_{sat} = F_{oc}\, K_{oc}\, S_w \qquad \text{(I-3)}$$

where:

C_{sat} = saturation limit for TCDD in soil (mg/kg)
F_{oc} = fraction organic carbon in soil = 0.0045
K_{oc} = organic carbon-to-water partition coefficient = 10^7 L/kg (U.S. EPA, 2003)
S_w = solubility of TCDD in water = 2×10^{-5} mg/L (U.S. EPA, 2003)

On this basis, the soil used by Roy et al. would have a saturation limit for TCDD of 0.8 mg/kg. Roy et al. used soils with TCDD concentration of 1 mg/kg (1 ppm). Thus, the testing was conducted at levels slightly above the saturation limit, which should yield maximum flux rates through the skin.

The 24-hour average flux rate from Roy et al. was calculated as follows:

$$J = AbsDose / \left(A_{exp}\, t_{exp}\right) \qquad \text{(I-4)}$$

where:

J = flux through the skin (ng cm^{-2} hr^{-1})
AbsDose = 0.048 ng (includes amount in skin)
A_{exp} = 1.77 cm^2
t_{exp} = 24 hr

This yields a flux estimate of 0.0011 ng cm^{-2} hr^{-1}. Now, an absorption rate constant (k_a) can be calculated as follows:

$$ka = J_{SM} / C_{sat} \qquad \text{(I-5)}$$

where:

J_{SM} = maximum flux for supermonolayer coverage = 0.0011 ng cm^{-2} hr^{-1}
C_{sat} = 0.8 mg/kg = 0.8 ng/mg

On this basis, k_a is estimated to be 0.0014 mg cm^{-2} hr^{-1} and assumed equal to k.

ESTIMATING THE ABSORBED DOSE

Finally, the absorbed dose can be calculated using Eq I-2. As an example, the parameter values for Subject 2 were used:

$C_{soil,0}$ = 162 pg/g = 0.162 pg/mg
A_{exp} = 970 cm^2
t_{exp} = 4 hr
f_{area} = 1.0 (actual load exceeded monolayer)

This yields an absorbed dose of 0.88 pg. The absorbed dose calculation presented in Section 7 included an adjustment to reflect the observed difference between rat in vivo testing and rat in vitro testing. These tests indicated that the absorbed dose in vivo was about twice as high as the absorbed dose in vitro. Applying that factor to the dose estimate derived above yields an absorbed dose of 1.8 pg. This is very similar to the value reported in Table 9 (1.65 pg) based on the fraction absorbed approach. Note that the amount of dioxin in the monolayer can be estimated as 97 pg (0.162 pg/mg × 0.62 mg/cm^2 × 970 cm^2). This means that the absorbed dose is less than 10% of the applied dose and Eq I-2 is valid to use.

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