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## Dermal Exposure Factors: Dermal Loading of Liquids



### **EPA Modeling Approach for Assessing Dermal Exposure**

#### **Dermal Model for Finite Doses – Fractional Absorption**

#### **Model Applicability**

- "Splash-type" exposures
- Non-immersive and non-occluded scenarios
- Liquids: < 10 μL/cm<sup>2</sup>, Solids: 1 5 mg/ cm<sup>2</sup> (OECD 428 Guideline for Skin Absorption Testing)

$$D_{exp} = Q_u \times f_{abs} \times SA \times FT \times Y_{derm}$$

- $D_{exp}$  = Dermal Exposure (mg/day)
- Q<sub>u</sub> = Dermal Loading (mg/cm<sup>2</sup>-event)
- $f_{abs}$  = Fractional Absorption
- SA = Area of Contact (cm<sup>2</sup>)
- *FT* = Frequency of Contact (events/day)
- Y<sub>derm</sub> = Weight Fraction of Chemical

#### **Dermal Model for Infinite Doses – Flux-Based Permeability**

#### **Model Applicability**

- Continuous supply of chemical against skin
- Immersive or occluded scenarios
  - > Example: Material trapped under glove
- Liquids: >100 μL/cm<sup>2</sup>, Solids >10 mg/ cm<sup>2</sup> (OECD 28 Guidance Document for the Conduct of Skin Absorption Studies)

$$D_{exp} = K_{p,c} \times C \times SA \times t_{exp}$$

- $D_{exp}$  = Dermal Exposure (mg/day)
- $K_{p,c}$  = Skin Permeability Coefficent at Conc. C (cm/hr)
- *C* = Chemical Concentration (mg/cm<sup>3</sup>)
- SA = Area of Contact (cm<sup>2</sup>)
- *t<sub>exp</sub>* = Contact Time (hrs/day)

Finite Dose Model – How does it work?

# $D_{exp} = Q_u \times f_{abs} \times SA \times FT \times Y_{derm}$

EPA assumes:

 $Q_u$ 

**f**abs-

**S**A

FT

- For liquids, the applied dose is **a thin film** covering of the liquid covering one or two hands
- There is absorption of the dose over an 8-hr shift
  - Workers wash hands well at end of the 8-hr shift
  - Material remaining in the skin <u>after washing</u> <u>hands</u> is potentially absorbable
  - A certain area of skin, often equivalent to that of one or two hands, is exposed a quantity (dose) of the chemical
- A single 8-hr exposure event
- derm Based on product content

Finite Dose Model – How does it work? (2)

$$D_{exp} = Q_u \times f_{abs} \times SA \times FT \times Y_{derm}$$

#### **EPA** assumes:

- For liquids, the applied dose is a thin film covering of the liquid covering one or two hands
  - 1) Based on experimental data, e.g., IVPT, including determination of material remaining in the skin <u>after washing hands</u>
- 2) Based on diffusion modeling
- = 1 hand: 535 cm<sup>2</sup> (male), 445 cm<sup>2</sup> (female)
- = 2 hands: 1,070 cm<sup>2</sup> (male), 890 cm<sup>2</sup> (female)
- **FT** = 1 event

 $Q_{11}$ 

fabs-

**SA** 

*derm* • Based on product content

Dermal Loading – Liquids

### EPA Assumptions for Dermal Loading:

- "Routine" or Incidental Contact with Liquids:
  - > 0.7 mg/cm<sup>2</sup>-event (low-end default)
  - 1.4 mg/cm<sup>2</sup>-event (central tendency)
  - > 2.1 mg/cm<sup>2</sup>-event (high-end)
- Routine **Immersion** in Liquids:
  - 1.3 mg/cm<sup>2</sup>-event (low-end default)
  - 3.8 mg/cm<sup>2</sup>-event (central tendency)
  - 10.3 mg/cm<sup>2</sup>-event (high-end)

How does this compare?

FDA requires application of 2 mg/cm<sup>2</sup> of sunscreen in human clinical pharmacokinetic studies.



# Dermal Loading – Liquids (2)

Where do the dermal loading defaults come from? A 1988 EPA study\* looked at retention of liquids on skin for three liquids and three exposure scenarios

### <u>Liquids</u>

- Mineral oil
- Cooking oil
- Bath oil

### <u>Scenarios</u>

- Initial wipe of hands with saturated cloth, plus wipe removal
- Secondary wipe after initial wipe, plus wipe removal
- Immersion of the hand in liquid, plus wipe removal

<sup>\*</sup> USEPA. 1988. Methods for assessing exposure to chemical substances, Volume 13, Methods for estimating retention of liquids on hands. EPA 560/5-85-017

Dermal Loading – Liquids: Incidental Contact

#### Where do the dermal loading defaults come from?

### <u>Liquids</u>

Cooking oil

- Highest liquid (oil values)
  - > 0.7 mg/cm<sup>2</sup>-event (partial removal)
  - 1.4 mg/cm<sup>2</sup>-event (average?)
  - > 2.1 mg/cm<sup>2</sup>-event (high-end)

### **Scenarios**

Initial wipe of hands with saturated cloth, plus wipe removal

# Dermal Loading – Liquids: Full Immersion

### Where do the dermal loading defaults come from?

### <u>Liquids</u>

• Mineral oil

**Scenarios** 

- Cooking oil
- Highest/high-end, lowest/low-end
  - 1.3 mg/cm<sup>2</sup>-event (Cooking oil, removal)
  - 3.8 mg/cm<sup>2</sup>-event (?? Beats me ??)
  - 10.3 mg/cm<sup>2</sup>-event (mineral oil immersion)

#### • Immersion of the hand in liquid, plus wipe removal

# Dermal Loading – Other Data

### Are other measured dermal loading data available?

- There are a few dozen studies that have measured dermal loading of liquids during real-world tasks
  - High-end values (2.3 7.5 mg/cm<sup>2</sup>) align with EPA defaults
  - Low-end values (10<sup>-2</sup> to 10<sup>-6</sup> mg/cm<sup>2</sup>) are much lower than the EPA low-end defaults 
    the same is probably true of centraltendency
- Dermal loading data from an EPA report on intermittent contact with liquid films (0.00054-0.009 mg/cm<sup>2</sup>) are consistent with the lower end of measured exposures.\*

\*Occupational Dermal Exposure Assessment. A Review of Methodologies and Field Data, Final Report. U.S. Environmental Protection Agency, Washington, DC. September 30, 1996.

Range of Measured Dermal Loading Values



## Applicability of Dermal Loading Data



The current default dermal loading parameters are appropriate for some, but not all, conditions of use.

- → Can the domain of applicability of those default parameters be better defined?
- → Are there other dermal exposure domains, i.e., a group of conditions of use, that can be defined?
- → Are there available data to characterize dermal loading for other dermal exposure domains? Do data need to be generated?

## Applicability of Dermal Loading Data, cont.



What are the characteristics of the **default data** that dictate its applicability?

- $\rightarrow$  Conditions of use
  - Handling a saturated rag (more than incidental contact)
  - Total immersion of the hand
- → Worker behavior
  - Direct dermal contact, i.e., no PPE (gloves)
  - Hands may or may not be wiped off
  - Hands are not washed off before the end of the day
- $\rightarrow$  Material properties
  - Low volatility liquid
  - High viscosity liquid

### Dermal Loading Data Needs



#### For what *domains* are data needed?

- $\rightarrow$  Conditions of use
  - True incidental contact with a liquid
- → Worker behavior
  - Hands are not wiped off or washed off
  - Hands are wiped off
  - Hands are washed off
- → Material properties
  - Aqueous solutions (lower viscosity liquids)
  - Highly volatile and semi-volatile liquids

# Path Forward



- → Domains of conditions of use need to be defined (how many? → 3 or 4?)
- → Review available data on dermal loading that could be used to characterize each domain
  - Data from the scientific literature
  - Pesticide Handlers Exposure Database?
- → Generate new data, especially for other kinds of liquids

