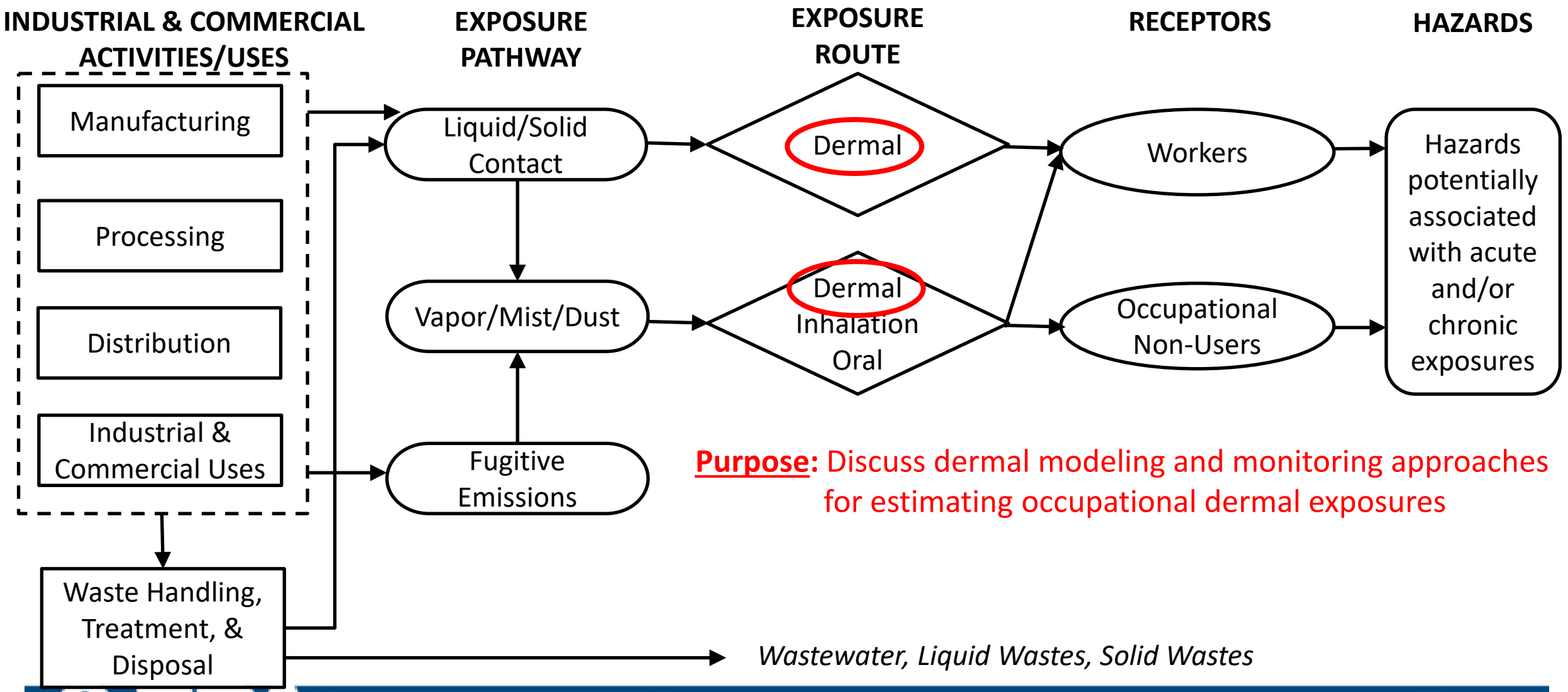
January 12, 2023

Dermal Exposure Modeling and Monitoring for Occupational Exposure Assessments

J. Aaron Murray
U.S. Environmental Protection Agency
Office of Chemical Safety and Pollution Prevention

Pathways and Routes of Exposure



Purpose: Discuss dermal modeling and monitoring approaches for estimating occupational dermal exposures

Models 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^2, Solids: 1 – 5 mg/ cm^2
  (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_u = Dermal Loading (mg/cm^2-event)
f_{abs} = Fractional Absorption
SA = Area of Contact (cm^2)
FT = Frequency of Contact (events/day)
Y_{derm} = Weight Fraction of Chemical

Challenge:
Choice of model for a given scenario is not always obvious

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^2, Solids >10 mg/ cm^2
  (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^3)
SA = Area of Contact (cm^2)
t_{exp} = Contact Time (hrs/day)

Modeling and Monitoring Parameters of Dermal Exposure

PARAMETER	MODELING APPROACH	MONITORING APPROACH
DERMAL LOADING	**Knowledge-based models**: RISKOFDERM, DREAM **Study Examples**: Cinalli 1992, Lansink 1996 **Challenge**: Models and studies may not be applicable to all representative conditions	**Interception methods**: Gauze, Charcoal pad **Removal methods**: Wiping, washing **Challenges**: • Monitoring of volatile substances • Representativeness of monitoring data
FRACTIONAL ABSORPTION	**NIOSH model**: Finite Dose Skin Permeation Calculator **AIHA model**: IH Skin Perm **Challenge**: Models may not be applicable to all representative conditions	***In vitro* absorption testing**: Human & Animal Skin ***In vivo* absorption testing**: Animal with PBPK modeling **Challenges**: • Study conditions (*e.g.*, diluents) • Utilization of data (*e.g.*, *in vitro*/*in vivo* extrapolation)
SKIN PERMEABILITY COEFFICIENT	**Statistical regression**: Model using p-chem properties (Kow, MW) and regression analysis of chemical dataset **Regression Example**: Potts & Guy 1992 **Challenge**: Models may not be applicable to all representative conditions	

Challenges and Opportunities in Occupational Dermal Exposure Assessment

Challenge 1: Selecting appropriate dermal exposure model for given exposure scenario

- ***Opportunity*** *- Development of clear decision logic for choosing appropriate dermal model*

Challenge 2: Modeling dermal exposure parameters

- ***Opportunity*** *- Development of more robust models that are applicable to broad range of conditions*

Challenge 3: Dermal monitoring in the workplace

- ***Opportunity*** *- Protocol development for dermal monitoring of volatile substances*
  - Clear decision logic for representative monitoring based on condition of use

Challenge 4: Utilization of *in vitro* and *in vivo* dermal absorption testing data

- ***Opportunity*** *- Dermal absorption testing that accounts for representative conditions*
  - Further studies to compare in vitro and in vivo absorption results

Challenge 5: Incorporation of tiered approach for occupational dermal exposure assessments

TIER 1: Conservative Assumptions, TIER 2**:** Published Literature Values, TIER 3: Condition-Specific Evaluation

- ***Opportunity*** *- Streamline dermal exposure assessments through efficient tiered approach*

THANK YOU FOR ATTENDING

QUESTIONS/COMMENTS/DISCUSSION