RESULTS

ASSESSMENT OF SHOWER EXPOSURES BENZENE SOURCED FROM GROUNDWATER IMPLICATIONS FOR GUIDELINE DEVELOPMENT

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Background

- Benzene Drinking Water Guideline (DWG)
  - based on drinking water exposure (1.5 L/day consumption)

- Health Canada included showering exposures for a proposed update to the benzene DWG
  - Benzene likely causes similar effects in humans regardless of route
  - Showering contributes
    - » 1.7 & 0.88 L/day equivalent exposure via inhalation & dermal
  - Proposed change in DWG from 5 to 1 µg/L
    - » importance of benzene shower exposures supported by Lindstrom *et al.* (1994) - residence on contaminated well water
- Issues
  - HC approach used a generic screening shower model
  - may not be appropriate to assess inhalation exposures against the drinking water standard
  - Current tox data for the oral limit may not be the best

Scope

- Re-Construct published shower model developed by key researchers in the field
  - Identify sensitive model variables
  - Explore some model refinements

- Shower model calibration
  - Compare with literature values for exposure concentrations

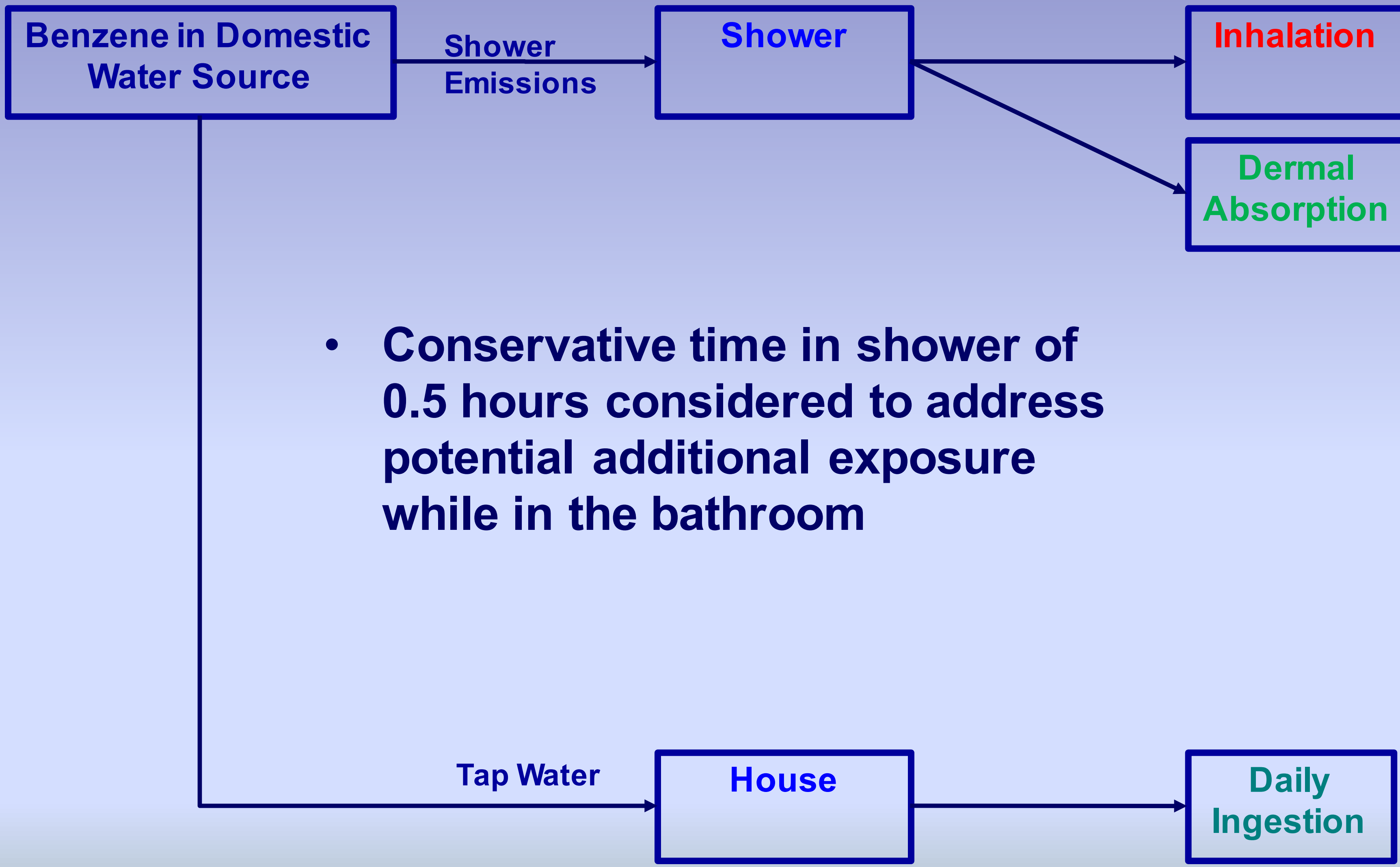
- Assess shower-related exposures associated with the benzene DWG
  - Incorporate Canada-specific exposure parameters
  - Compare with shower-related exposure assessment developed by Health Canada for guideline development
  - Generate data for input into a PB/PK model

Scope

- Determine benzene and metabolite concentrations in blood from inhalation, dermal, and oral exposures associated with the DWG
  - Utilize PB/PK Modelling
  - More closely related to development of toxicity and can more properly summate exposure from multiple routes
  - Evaluate how this could influence the DWG

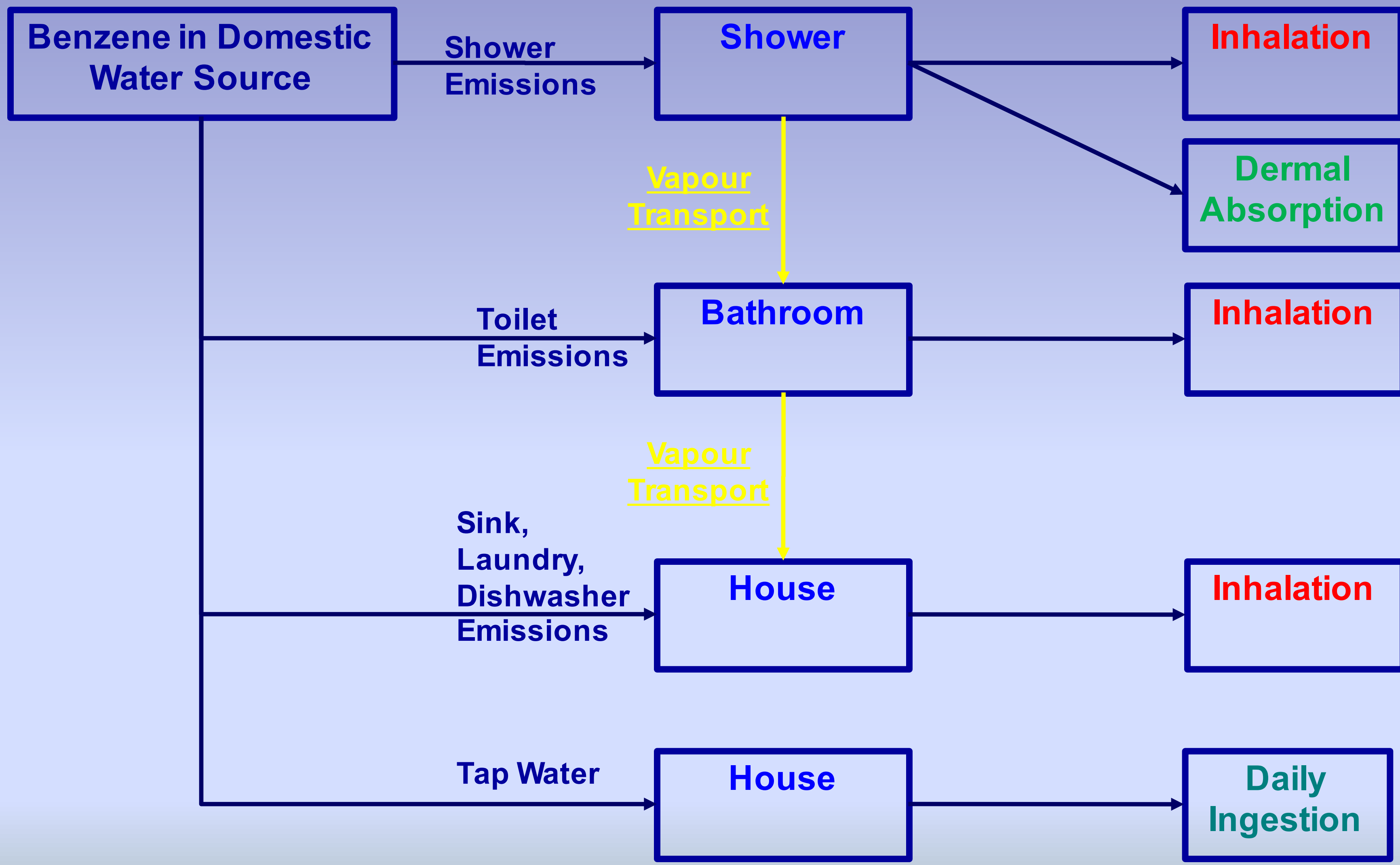
- Inhalation and oral toxicity limits are available for benzene
    - Rodent data for the oral toxicity limit
    - Human data for the inhalation toxicity limit
    - Ultimately, inhalation, dermal, and oral doses are compared with respective route-specific exposure limits
    - Complicates development of a DWG and just using an oral limit
    - Preliminary evaluation of which limit may be most appropriate for assessing cumulative oral, inhalation, and dermal exposure risks

Model Construction – Health Canada



- Conservative time in shower of 0.5 hours considered to address potential additional exposure while in the bathroom

Model Construction – This Project



- Shower, bathroom, & house emissions addressed quantitatively

Sensitive Model Variables

– **Sensitive Variables**
  - **Water use levels**
  - **Emission rates from different water uses**
  - **Shower flow rate**
  - **Presence or absence of a bathroom fan**
  - **Showering time and time in bathroom**

– **Solve partial differential equations using du/dt substitutions**
  - **Shower**

$$\frac{dC_S}{dt} \cdot V_S = \left[Q_S \cdot C_W \cdot TE_S\right] - \left[Q_S (C_S(t) - C_B(t))\right]$$

  - **Bathroom**

$$\frac{dC_{BT}}{dt} \cdot V_{BT} = \left[Q_T \cdot C_W \cdot TE_T\right] - \left[Q_{BT} \cdot C_{BT}(t)\right] - \left[Q_S\left(C_{BT}(t) - C_S(t)\right)\right]$$

  - **House**

$$\frac{dC_{HT}}{dt} = \frac{Q_{HW} \cdot C_W \cdot TE_H}{V_H} + \frac{Q_{BT} \cdot C_{BT}(t)}{V_H} - \frac{Q_H}{V_H} \cdot C_H(t)$$

Model Calibration

- Lindstrom *et al.* (1994)
  - A key supporting study for shower-related benzene exposure
  - residence with benzene contaminated groundwater
    - Mean benzene water concentration – 296 µg/L ~ 60x DWG
  - No bathroom fan
  - Residence with a relatively low air exchange rate
    - (0.35 Ach/hr)
  - Shower run for 20 minutes
  - Measured transfer efficiency
    - Benzene in water: shower head – floor drain; mean of 0.88

Model Calibration – Lindstrom Data

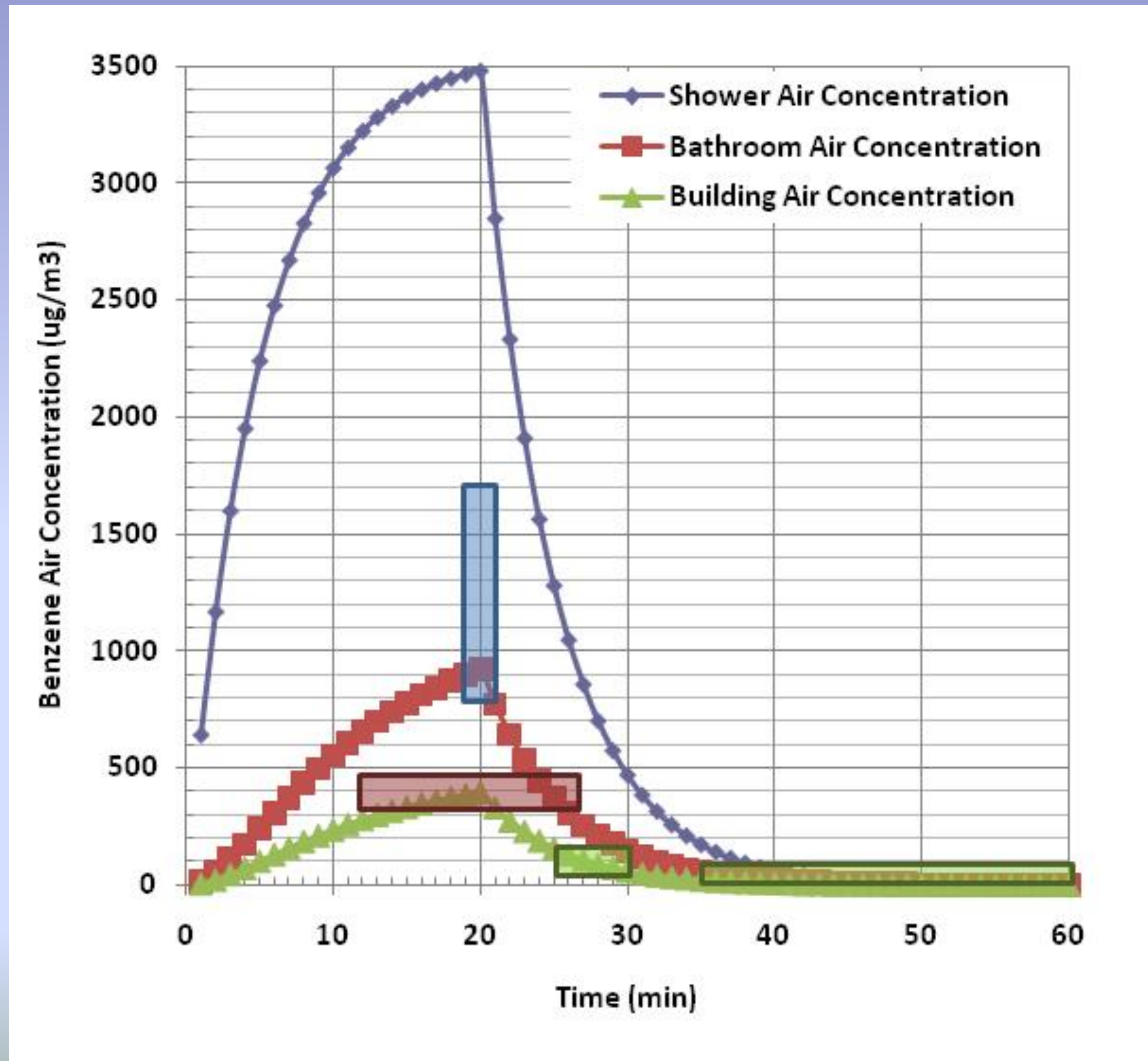
- Shower only exposure

- **Blue Bar**
- Measured Shower air concentrations over time interval

- **Red Bar**
- Measured Bathroom air concentrations over time interval

- **Green Bars**
- Measured Bedroom & House air concentrations over time interval

- Shower and bathroom
- 2x to 3x over-prediction
- Bedroom – in range
- House – 10x under-prediction



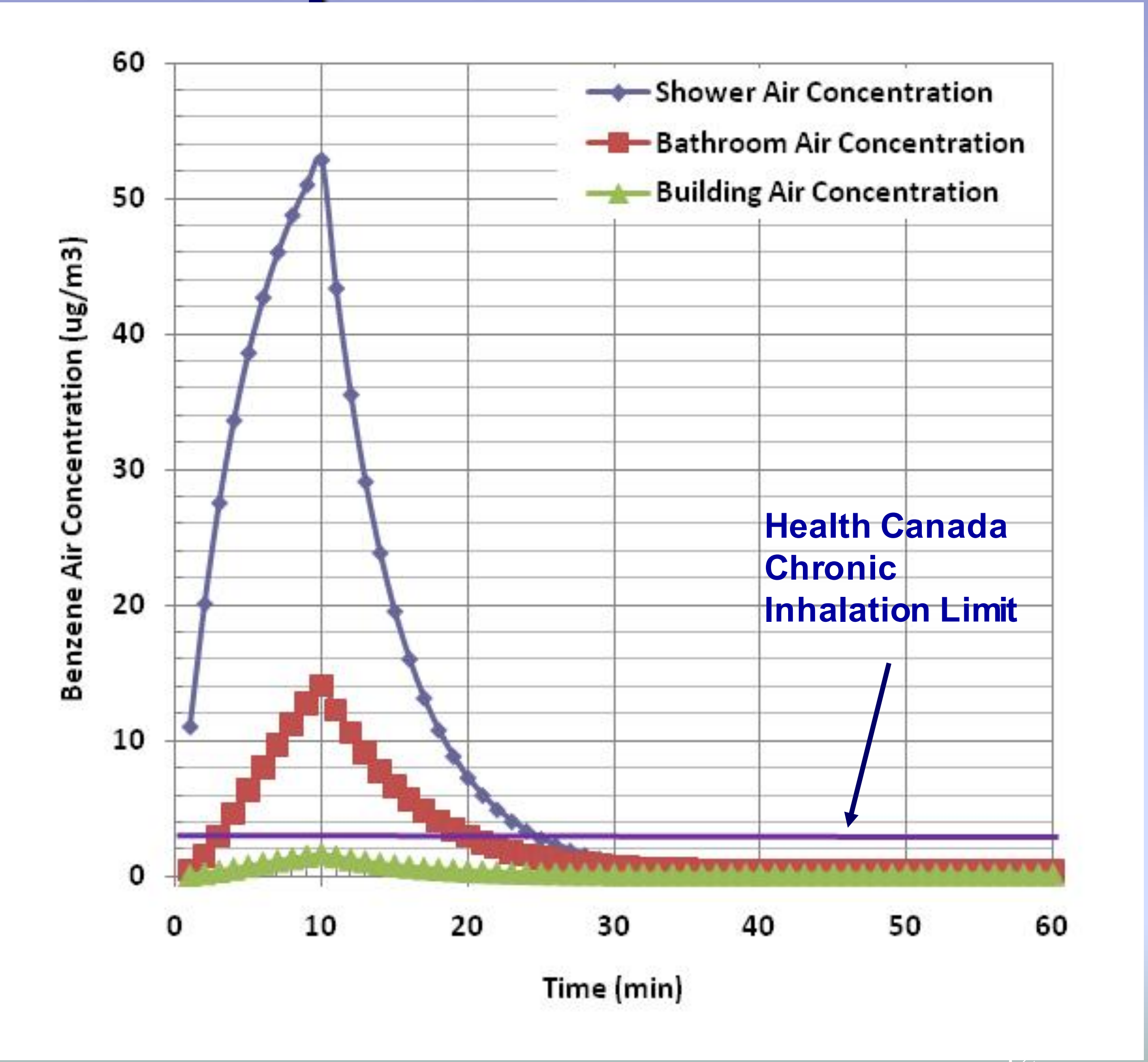
Modeling for Guideline Development

- Model parameters developed
- Key differences include:
- 10 versus 20 min shower
- More specific building parameters
- Hold and cold water temperature for different uses
- Shower frequency
- Household water use for a family of 4
- Water flow rate

Parameter Name	Units	Value min	Value MLE	Value Max	Reference
Shower water flow	L/min	8.7	10	11.4	Jo et al 1990 a,b; in Chowd 2009
	L/min	4.9	8	12.9	US EPA, 1997
Shower stall volume	m^3	1.67	2	2.25	Jo et al 1990 a,b; in Chowd 2009
Bathroom volume	m^3	5	10	50	McKone, 1989 (estimated)
Building volume	m^3		535.8		AENV, 2008 (12.2 x 12.2 x 3.6)
Shower air exchange rate	Ach/hr		12		
Bathroom air exchange rate	Ach/hr		3		
Building ventilation rate	Ach/hr		0.5		(AENV, 2008)
Shower time	min/shwr	5	10	20	McKone, 1987
	min/shwr		10.4		US EPA, 1997
Time in bathroom after shower	Min		20		McKone and Knezovich, 1991
Hot water temperature	C	35	40	45	Chowdhury (in press); in Chowd 2009
Cold water temperature	C	15	20	25	Chowdhury (in press); in Chowd 2009
Shower frequency	shwr/day	0.72	0.74	0.76	US EPA (1997)
Area of exposed skin to shower water	m^2	1.69	1.82	1.94	Health Canada, 1997
Toilet water use (n=family of 4)	L/day		68.4 x 4		US EPA (1997)
Dishwasher & Laundry (n=family of 4)	L/day		72.2 x 4		US EPA (1997)
Kitchen sink and cleaning use (n=4)	L/day		19 x 4		US EPA (1997)

Modeling for Guideline Development

- **Water Concentration**
  - **0.005 mg/L (5 µg/L)**
- **Chronic inhalation limit not exceeded for times in the house after showering and in the bathroom**



Preliminary Inhalation Doses

Exposure	Amortized Air Conc.	Absorbed Dose	Dose Ratio	HC Ratio
	mg/cu.m	mg/kg-d	Inh/Oral	
Shower - Inhalation	1.5E-04	1.6E-05	0.16	--
Bathroom - Inhalation	1.1E-05	1.1E-06	0.01	--
House - Inhalation	1.5E-04	1.6E-05	0.15	--
Sum - Inhalation	**3.1E-04**	**3.2E-05**	**0.32**	**1.75**

- **Assumptions – Inhalation**
  - Amortized concentrations
    - shower = 0 to 10 min; bathroom 10 to 20 min; house – rest of day
  - 0.74 showers/day
  - Inhalation bioavailability – 50%; oral bioavailability – 90%
    - Based on literature data
  - Inhalation to oral dose ratio was 0.32
    - Approximately 5- to 6-fold lower than HC's ratio of 1.75
  - Rationale for differences
    - Building parameters, shower duration, refined model, bioavailability

Preliminary Dermal Doses

$$DAD = \left(\frac{Cw \cdot SA \cdot Kp \cdot t \cdot F \cdot (1 - TE)}{BW} \right)$$

DAD = Dermally Absorbed Dose (mg/kg-day)

TE = transfer efficiency for benzene volatilization in the shower (0.88; Lindstrom et al., 1994) (OR, take average (1, 0.88) = 0.56)

Cw = concentration in shower water (ug/L) (5 ug/L = AENV DWG for benzene)

SA = skin surface area (cm^2) (18,200 cm^2; or 1.82 m^2)

Kp = permeability coefficient (m/min) (3.5E-5 m/min or 0.21 cm/hr)

t = time of event (min) (10 minutes shower)

F = frequency of showers (events/day) (0.74 showers/day; US EPA, 1997)

BW = body weight

Exposure	Absorbed Dose	Dose Ratio	HC Ratio
	mg/kg-d	Derm/Oral	Derm/Oral
Shower - Dermal	1.72E-05	0.17	0.88
Drinking Water - Oral	**1.02E-04**	1.00	

Rationale for Differences: volatilization loss of benzene in water (using average of head/drain concentration), 10 minute actual shower time not 30 minutes used by HC (Krishnan work) to address other potential exposures

PBPK Modeling of Benzene

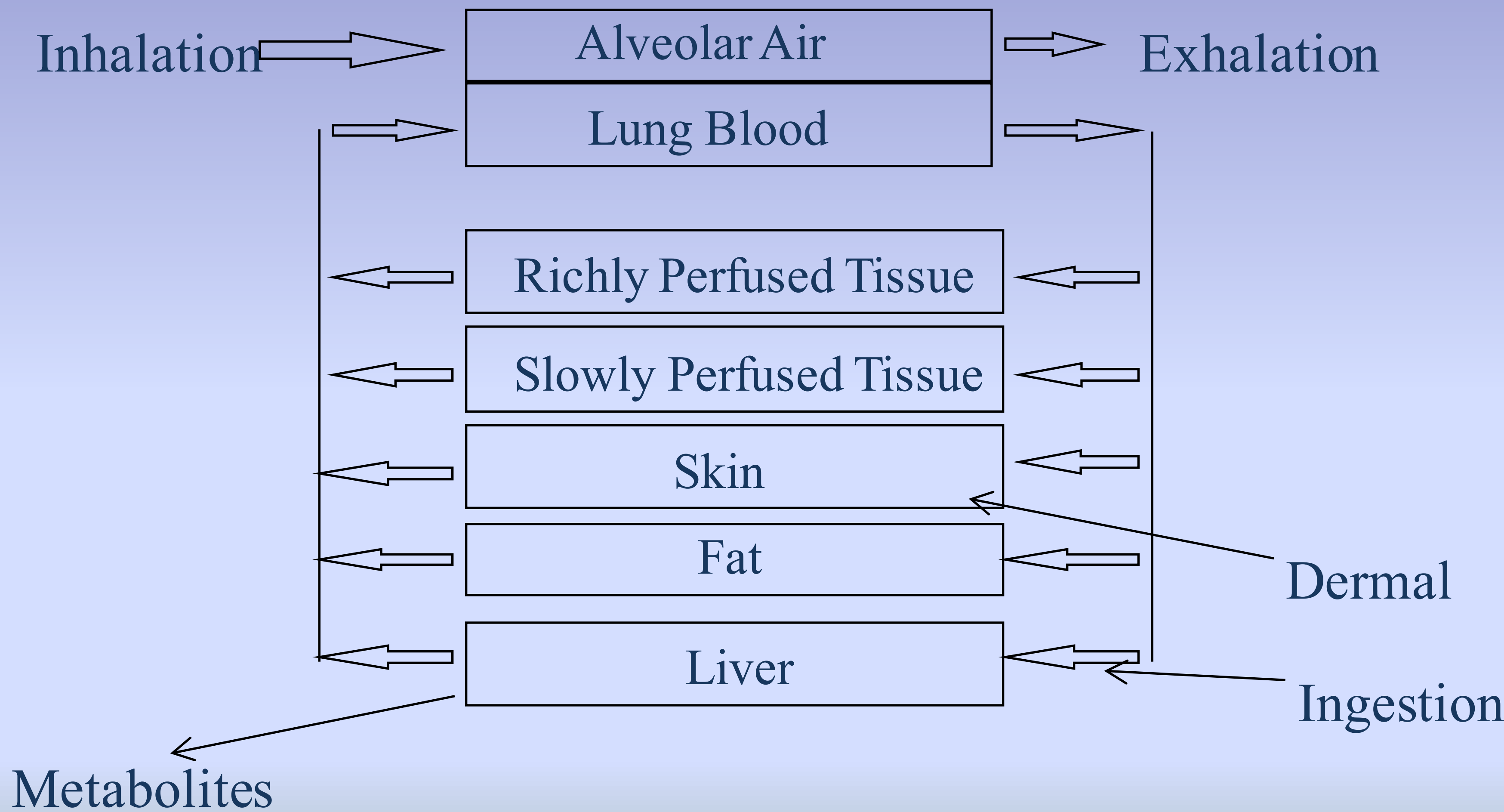
What We Know About Benzene

- Hematopoetic effects require metabolism to occur
- Hematopoetic effects are not likely dependent upon route of exposure (inhalation, oral, dermal)
- Kinetics (absorption, distribution, metabolism and excretion) of benzene in humans have been well studied
- Numerous physiologically based pharmacokinetic (PBPK) models have been developed for benzene
- Absorbed dose (or some measure of it) has been used extensively by regulatory agencies to conduct route-to-route extrapolation

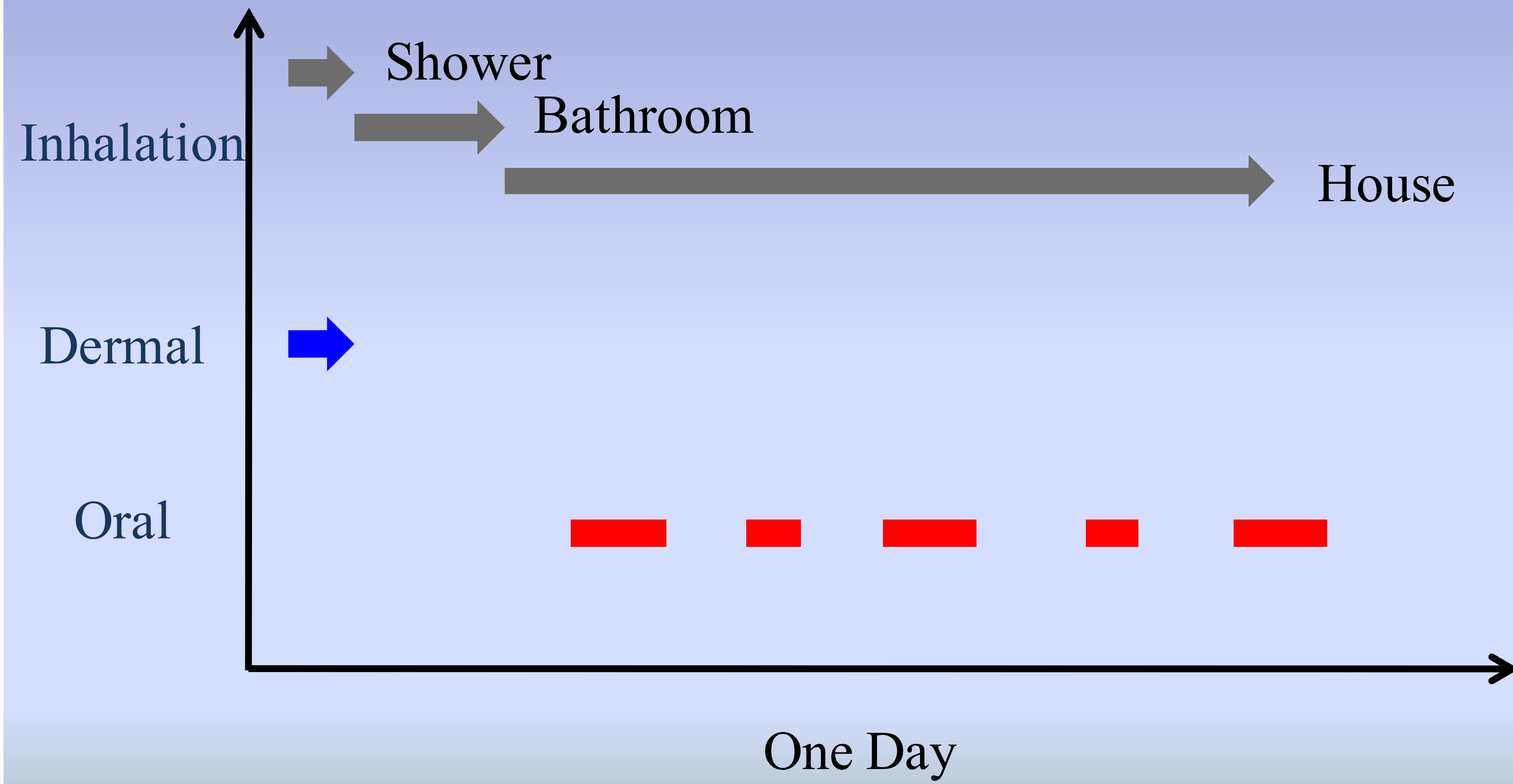
Objective

- Model the kinetics of multi-media/multi-route exposures to benzene to estimate key dose metrics (benzene in blood or amount metabolized) in humans associated with shower and in-home exposures
- Compare to inhalation guideline for benzene
- Assess the validity of Health Canada drinking water guideline

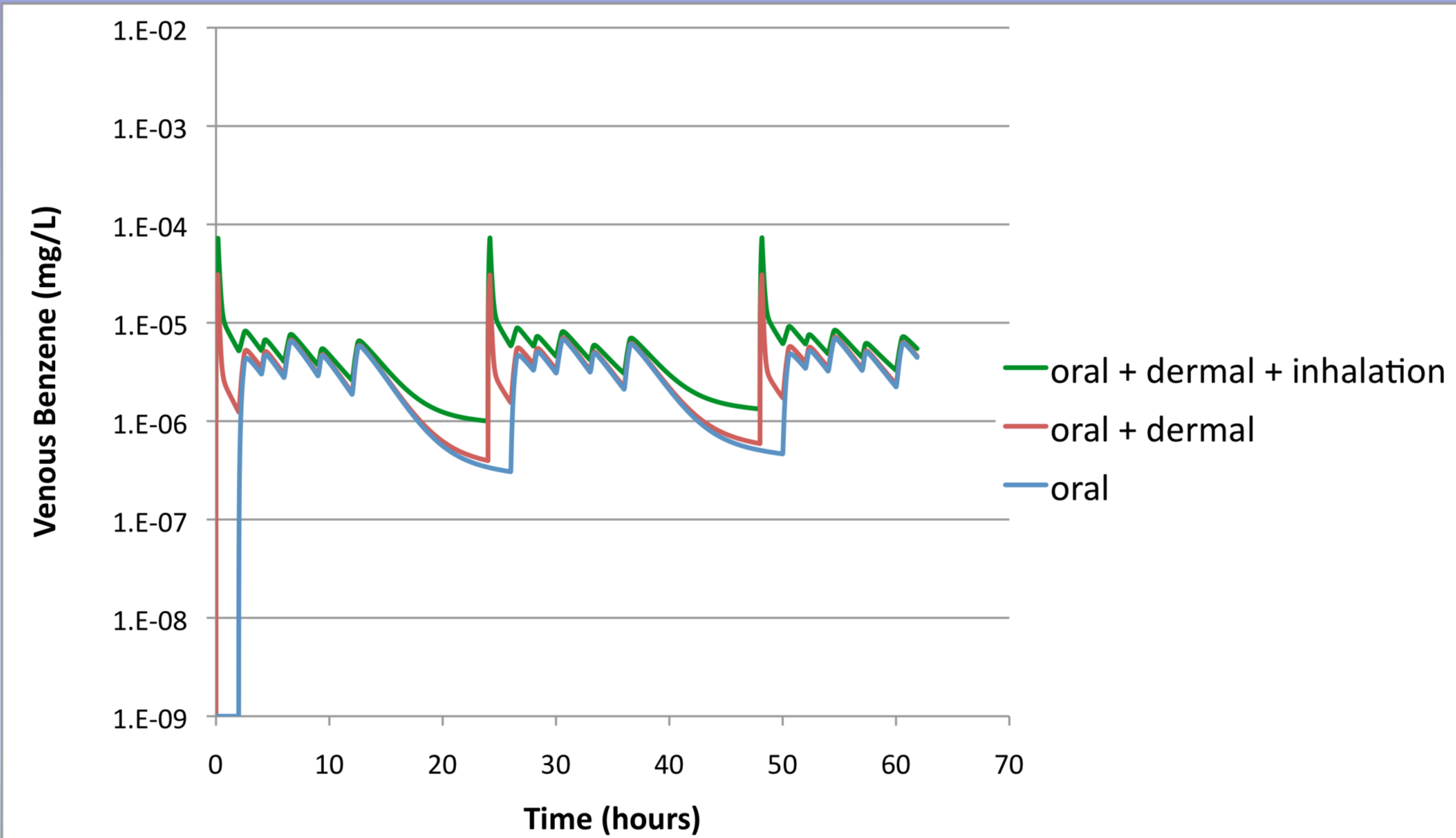
Benzene PBPK Model



Exposure Scenarios



Model Simulations



Conclusions

- Modeling benzene specific kinetics associated with home water supply exposure) was used to set a more defensible DWG

- PBPK modeling results suggest lowering of water standard is not necessary
  - DWG (0.005 mg/L) is sufficiently protective

- Toxicity data used to develop the drinking water standard may be overly conservative for assessing shower inhalation exposures

Future Directions

- Refine and adjust shower model
- Explore gender differences in benzene metabolism
- Conduct Monte Carlo simulations to address variability in exposure and kinetic parameters

- Evaluate the development of a benzene drinking water standard using PB/PK modeling and extrapolation from human inhalation epidemiological data rather than using animal bioassay results and extrapolating to humans