Children's Non-dietary Chemical Exposure: Is PLACE (Persistent Low-level Ambient Contact Exposure) the Missing Link?

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Acknowledgments

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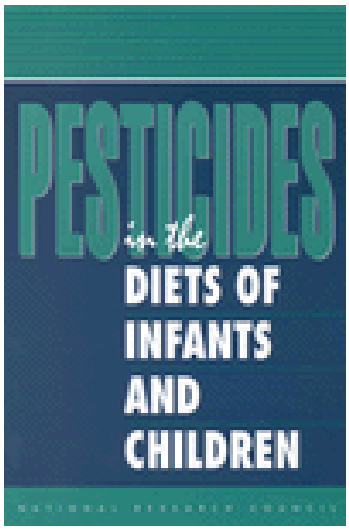
- Material presented here has not been reviewed by EPA and no Agency endorsement should be inferred.

Some impediments to understanding children's non-dietary chemical exposure:

- Epi/Tox outlook
- Misperceptions regarding diet
- Pseudo-mass balance approaches

Preamble - Does diet dominate?

NRC, 1993



NRC, 1993 (cont'd.)

[child dietary dose > adult dietary dose]

is not equivalent to

[child dietary dose > child non-dietary dose]

Dietary Interventions

- Lu et al, *EHP* 2006a OPs (TCP, MDA)
  - Seattle: reduction at the median c. 80%, 100%
- Lu et al., *EHP* 2006b (3-PBA, trans DCCA)
  - Seattle: reduction at the median c. 30%
- Bradman et al., ISES 2008 (DAPs)
  - Oakland: reduction at the median 26%
  - Salinas: reduction at the median 44%

A Pilot Study of Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP)

M.K. Morgan, L.S. Sheldon, and C.W. Croghan.
U.S. Environmental Protection Agency
Research Triangle Park, NC

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M. Brinkman, N. Morse, Y.L. Chou,
C. Hamilton, J.K. Finegold, K. Hand,
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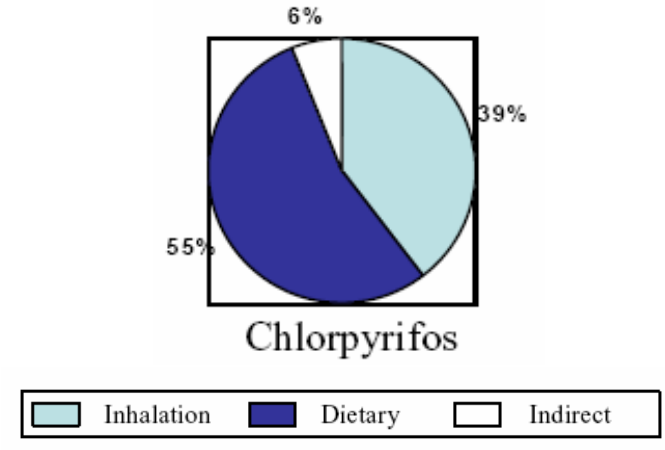
CTEPP Overview

- > 250 preschool-age children in NC and OH
- home only and home + daycare
- environmental, behavioral, biomarker data
- > 50 analytes

CTEPP Final Report, 2004



Morgan et al., *JEAEE* 2005

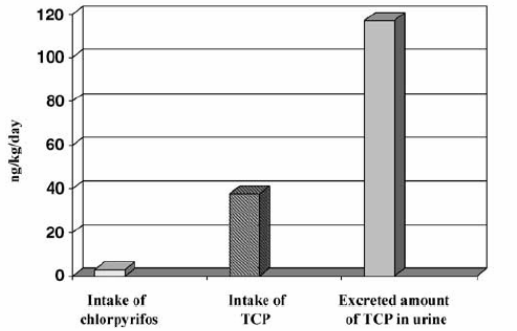


Figure 1. The median potential aggregate absorbed doses of chlorpyrifos and TCP compared with the excreted median amounts of TCP in the preschool children's urine.

Basis for assumption that diet is dominant source of children's exposure to pesticides:

- misinterpretation of 1993 NRC report
- selective reading of intervention studies
- misinterpretation of CTEPP results
- attribution of metabolite excretion to parent compound exposure

Q. If diet cannot be proven to dominate children's exposure to pesticides used on food crops, why should we assume it is dominant for chemicals not used on food, but present in homes in bulk quantities (e.g., phthalates, flame retardants)?

We need to understand other pathways:

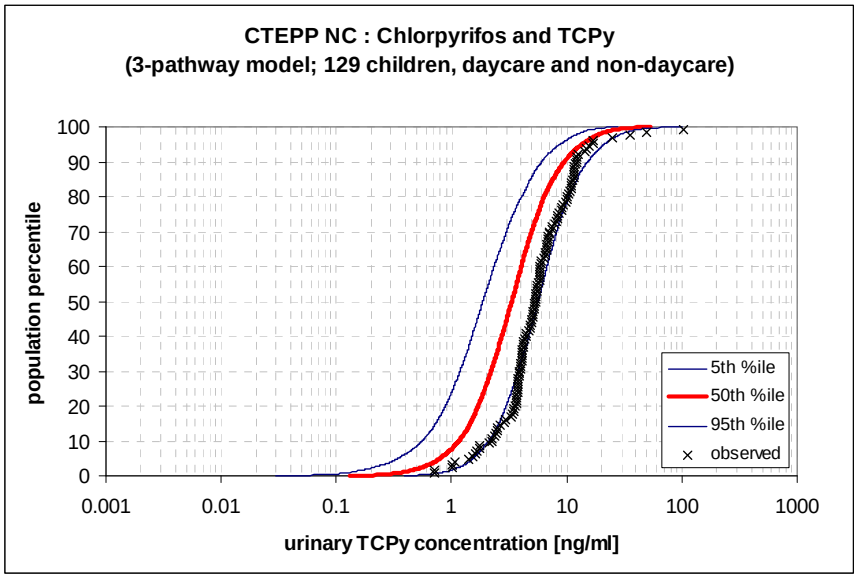
- Dust ingestion
- Hand-to-mouth
- Object-to-mouth
- Direct dermal

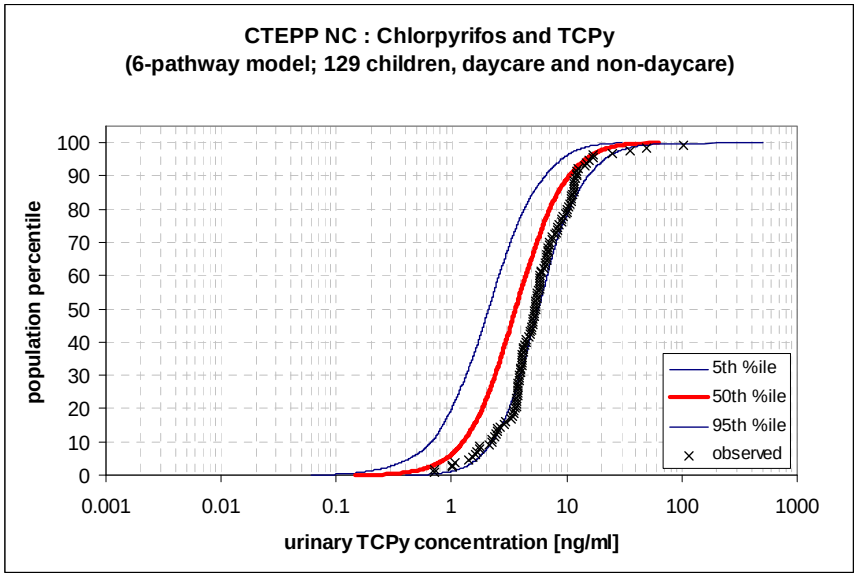
Q. Where can we find data adequate to support mass balance studies?

A. CTEPP: CPS/TCP; 2,4-D; PCP

Approach

- 3-pathway model (diet, inhalation, soil ingestion) and quantify the daily dose shortfall
- 6-pathway model (3 prior + dust ingestion, h-t-m & o-t-m) and estimate TC necessary to explain remaining shortfall
- 7-pathway model (6 prior + direct dermal) and examine fit


CTEPP NC : Chlorpyrifos and TCPy
(3-pathway model; 129 children, daycare and non-daycare)
population percentile
100
90
80
70
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
urinary TCPy concentration [ng/ml]
5th %ile
50th %ile
95th %ile
observed


CTEPP NC : Chlorpyrifos and TCPy
(6-pathway model; 129 children, daycare and non-daycare)
population percentile
100
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0.001
0.01
0.1
1
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urinary TCPy concentration [ng/ml]
5th %ile
50th %ile
95th %ile
observed

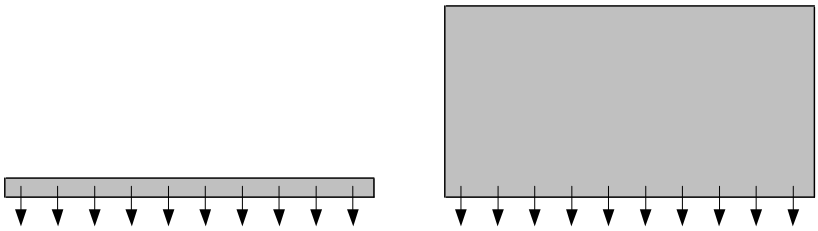
Rethinking Dermal Exposure

mass transferred to skin	x	fraction absorbed	=	dermal dose
mass recovered from skin	x	fraction absorbed in high load trials	=	??

Rethinking Dermal Exposure

- inverse relationship between mass loading and fraction absorbed
- The few ng/cm^2 absorption studies in the literature show relatively high uptake efficiency
- low recovery in washing/transfer tests - recovery declines as time increases or initial load decreases
- underprediction of observed biomarker output in occupational studies (Geer et al., 2004)
- organic film on indoor surfaces
- air-to-skin transport (Weschler and Nazaroff, 2008)

Loading Effect



Loading Effect

$$J_{thin} = J_{thick}$$

$$SL_{thin} < SL_{thick}$$

$$\left(\frac{J}{SL}\right)_{thin} > \left(\frac{J}{SL}\right)_{thick}$$

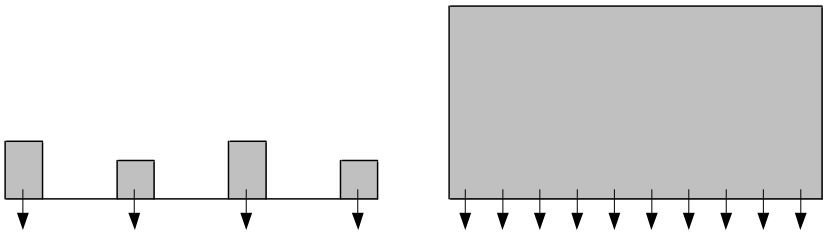
Inversely Linear Proportionality

- Meuling et al., *Int Arch Occ Environ Health* 2005
  - CPS, human, in vivo
  - 3X load, 3.5X lower fractional efficiency
- Hughes et al., *Food Chem Toxicol* 2001
  - DBDPO, mouse in vitro
  - 10X load, 11X lower fractional efficiency

Loading effect

- Buist et al., *Reg Tox & Pharm* 2009
- Thongsinthusak et al. 1999 (CA EPA DPR, HS-1801)
- Zendzian, *AIHAJ* 2000 (US EPA)
- For SVOCs, fractional absorption goes up as loading goes down (generally not inversely linear) - opposite effect for VOCs

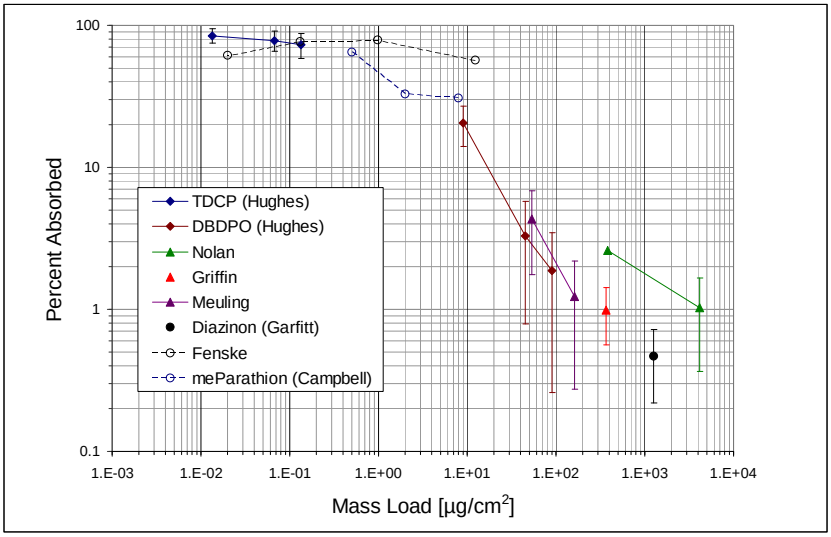
Uneven Distribution



Transfer Studies

- Fenske & Lu, *AIHAJ* 1994
  - transfer to hand and recovery, CPS
  - fraction recovery lower with decreasing loading and increasing time to wash
- Campbell et al., *AIHAJ* 2000
  - 4 pesticides applied to pig skin, wipe with each of 4 solvents at 90 minutes
  - significantly lower fractional recovery at lowest initial load in 14 of 16 cases

DAF vs Loading



7-Pathway Model: Delivery to skin?

- Borrow TC approach from agricultural practice

Transfer Coefficient (TC)

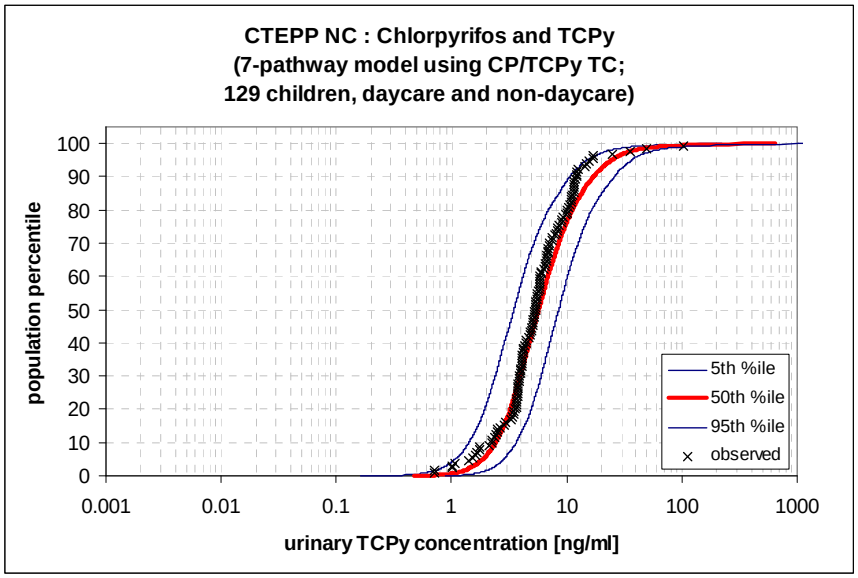
$$TC\left[\frac{cm^2}{hr}\right] = \frac{\text{mass transferred in given period}\left[\frac{\mu g}{hr}\right]}{\text{transferable residue}\left[\frac{\mu g}{cm^2}\right]\cdot}$$

Estimating Dermal TC

- Assuming dermal uptake is nearly complete, how much surface area cleaning is needed?

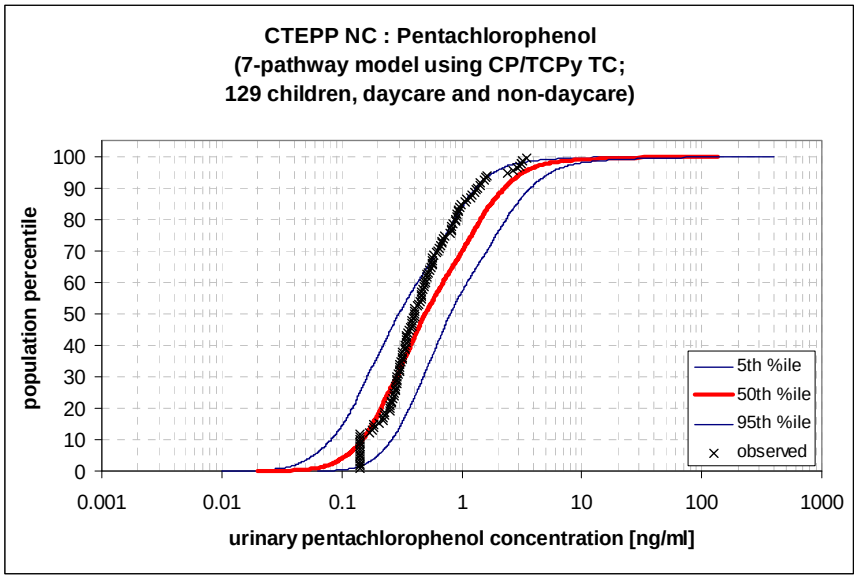
$(Dose_{6P}/Q_{ur}) + (C_{surf} * TC * t / Q_{ur})$

$= Obs\ C_{TCPy,\ ur}$



7-Pathway Results for 2,4-D and PCP

- Using TC backfit from CP/TCP simulations


CTEPP NC : Pentachlorophenol
(7-pathway model using CP/TCPy TC;
129 children, daycare and non-daycare)
population percentile
100
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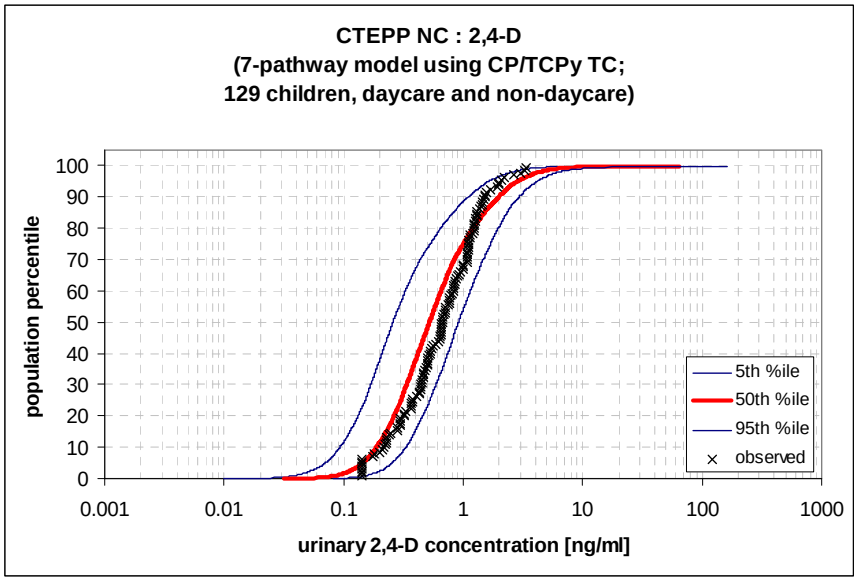
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urinary 2,4-D concentration [ng/ml]
5th %ile
50th %ile
95th %ile
observed

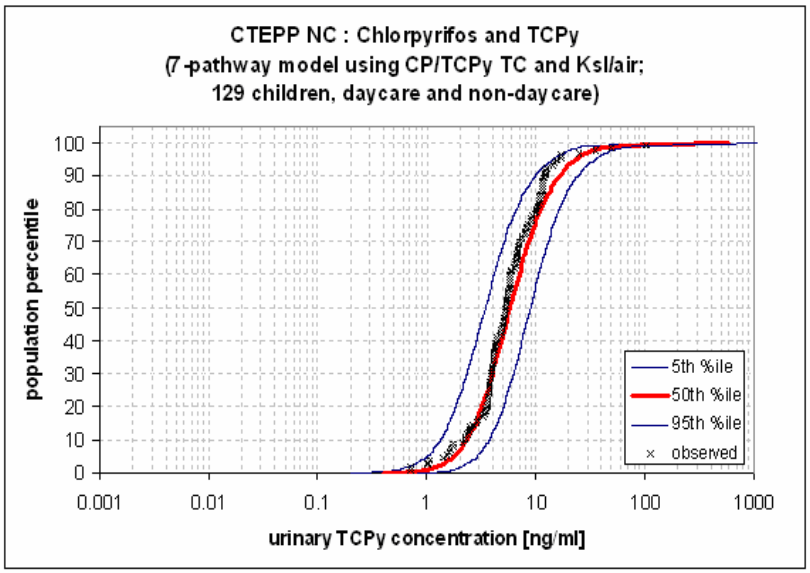
Issues

- permutations
- chlorpyrifos-methyl and hexachlorobenzene
- sparse surface data in CTEPP (14/129 in NC)
- 1.5 ml propanol/wipe
- particle-bound vs. unbound in wipe and air samples

Second Approach

$$C_{air}[\frac{ng}{m^3}] \cdot \left(TC[\frac{cm^2}{hr}] \cdot K_{SL/air} \left[\frac{\frac{ng}{cm^2}}{\frac{ng}{m^3}} \right] \right)$$

instead of $$SL\,[\frac{\mu g}{cm^2}] \cdot TC\,[\frac{cm^2}{hr}]$$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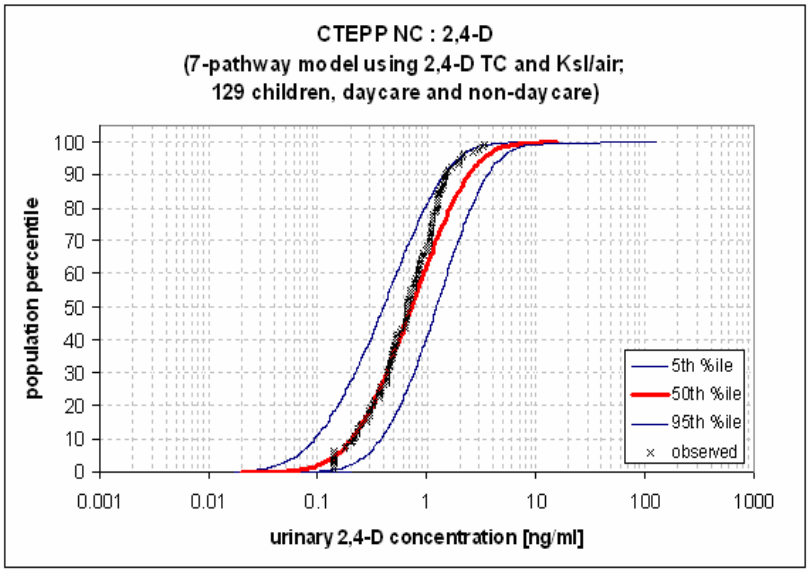
CTEPP NC : 2,4-D
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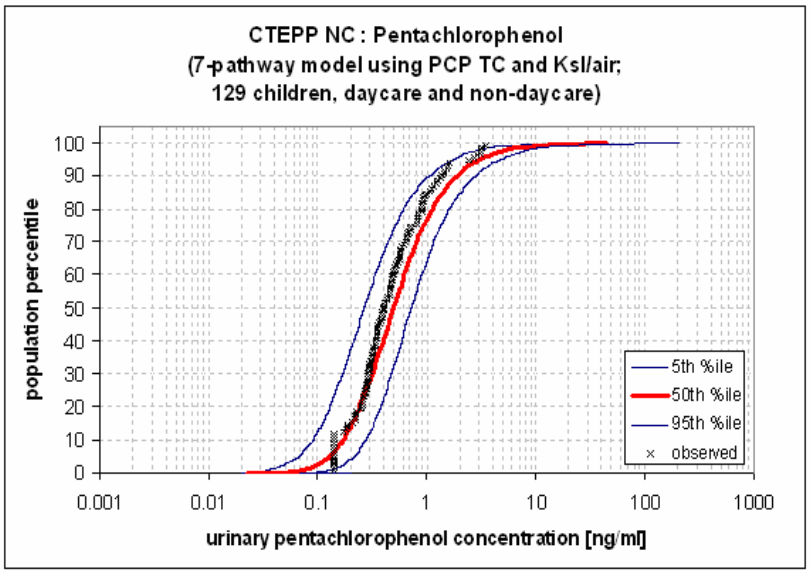

Primary Finding

Delivery to the skin via active mechanical harvesting and passive deposition from air followed by dermal absorption can plausibly explain the apparent shortfall between predicted exposure and observed biomarker excretion of three of three pesticides in CTEPP for which mass balance can be attempted.

Why PLACE?

- The dose makes the poison (Paracelsus 1493-1541)
- "The place [proximity] makes the poison" (K. Smith, *JEAEE* 2002)

Why PLACE?

- If the place is contaminated, Persistent Low-level Ambient Contact Exposure (PLACE) happens