Reconciling Personal Exposure Measurements and Biomarkers of Exposure

Richard Fenske
School of Public Health and Community Medicine
University of Washington

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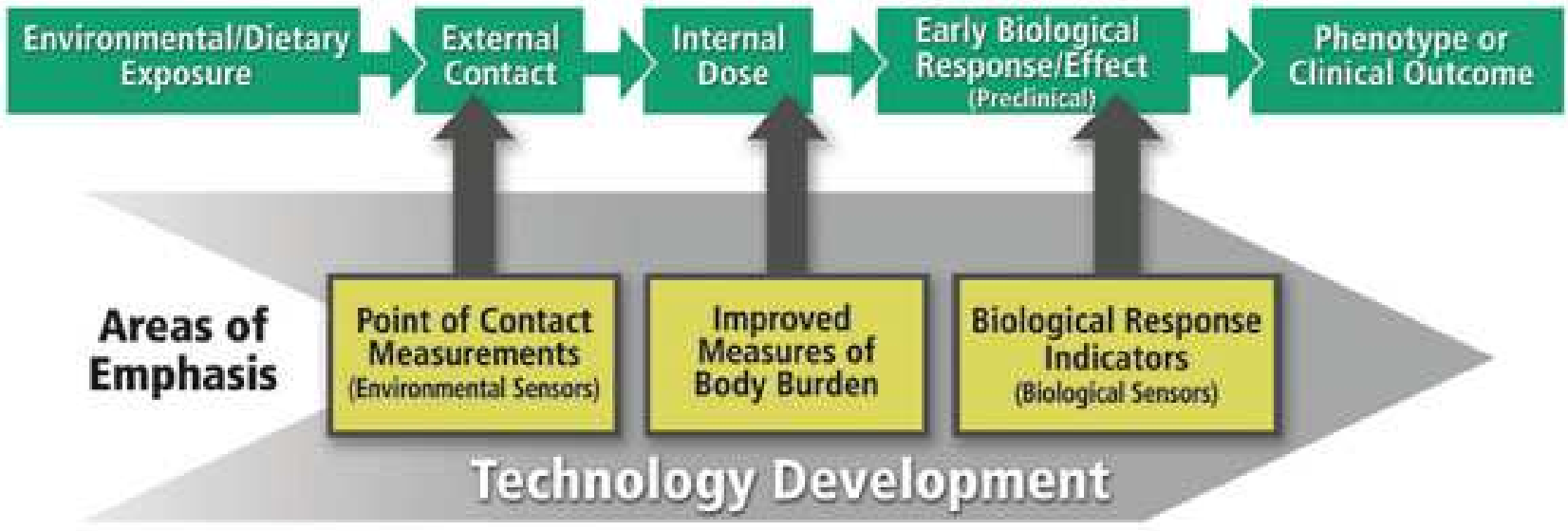
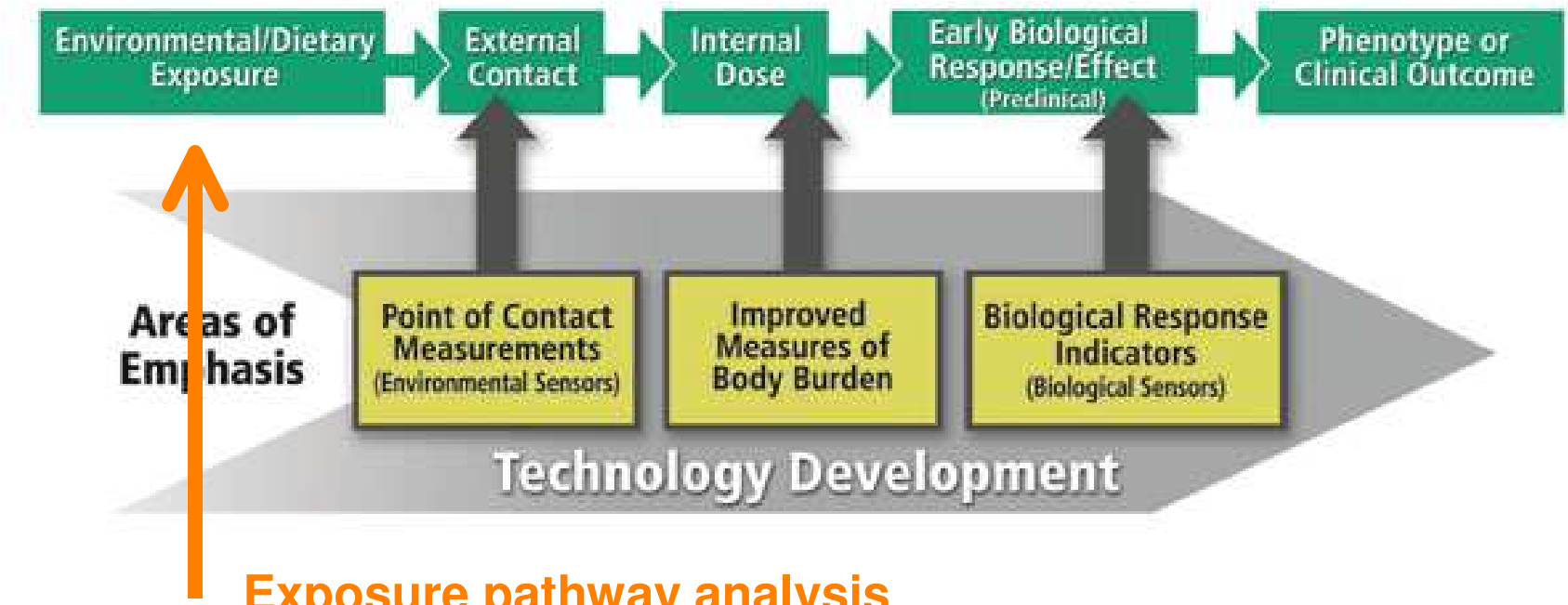
Exposure Health Sciences Framework



Proposed by NIEHS

Environmental Health Perspectives 113:A650 (2005)

Exposure Health Sciences Framework



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EHP 113:A650 (2005)

Key Themes

The ‘gold standard’ concept and urinary biomonitoring

- Coping with intra-individual variability

Personal exposure and biomarker reconciliation

- A quick review of the CTEPP Study

Uptake rates for the dermal, oral, and respiratory routes

- Relevance of high dose studies

A new focus on exposure and absorption processes

Urinary Biomonitoring as a Gold Standard

A valid measure by which to judge other measures

- In medicine, a diagnostic test regarded as definitive
- In chemistry, an analytical standard for calibration

Population estimates

- CDC report of NHANES samples

Testing determinants of exposure

- Potential risk factors compared to biomonitoring data

Exposure measurement calibration

- Testing measurement accuracy and assumptions

Longitudinal Biomonitoring Study in an Agricultural Community

Koch et al. Environ Health Perspect 110:829-33 (2002)

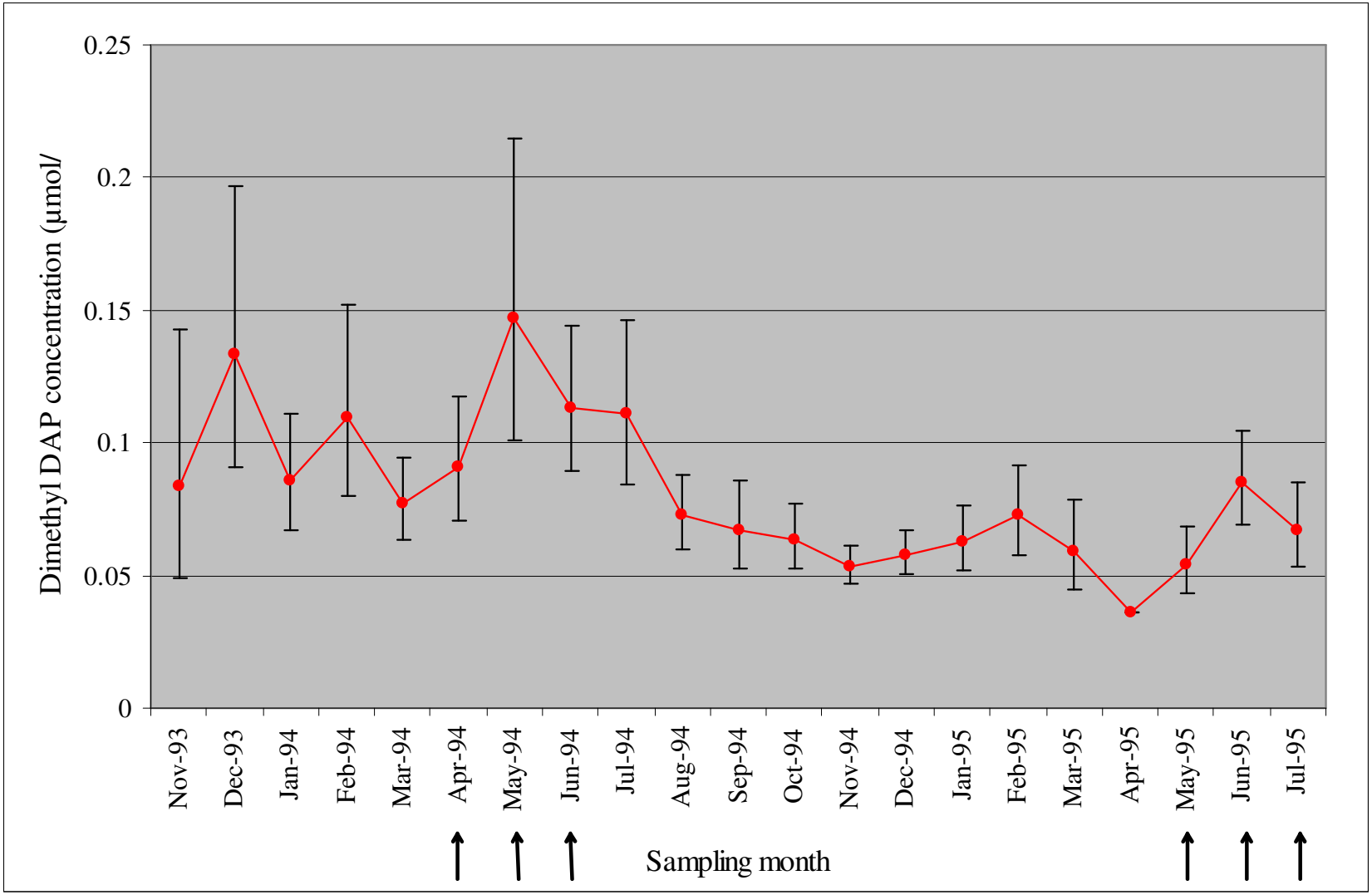
Design

- Washington State community in tree fruit region
- Spot urine samples collected on bi-weekly for one year from 44 preschool children
- Dialkylphosphate metabolites measured

Intra-individual variability

- Average of 16 samples per child in off-season
- Coefficient of variation range = 40 - 340%
- Median CV = 107%

Geometric means (µmol/L) and 95% C.I. for dimethyl metabolite concentrations by sampling month



(Arrows indicate months of OP pesticides spraying)

NJ Crack-and-Crevice Application Study

Hore et al. Environ Health Perspect 113:211-219 (2005)

Goals

- Look at the distribution of chlorpyrifos in the home environment
- Determine amount of chlorpyrifos absorbed by children

Design

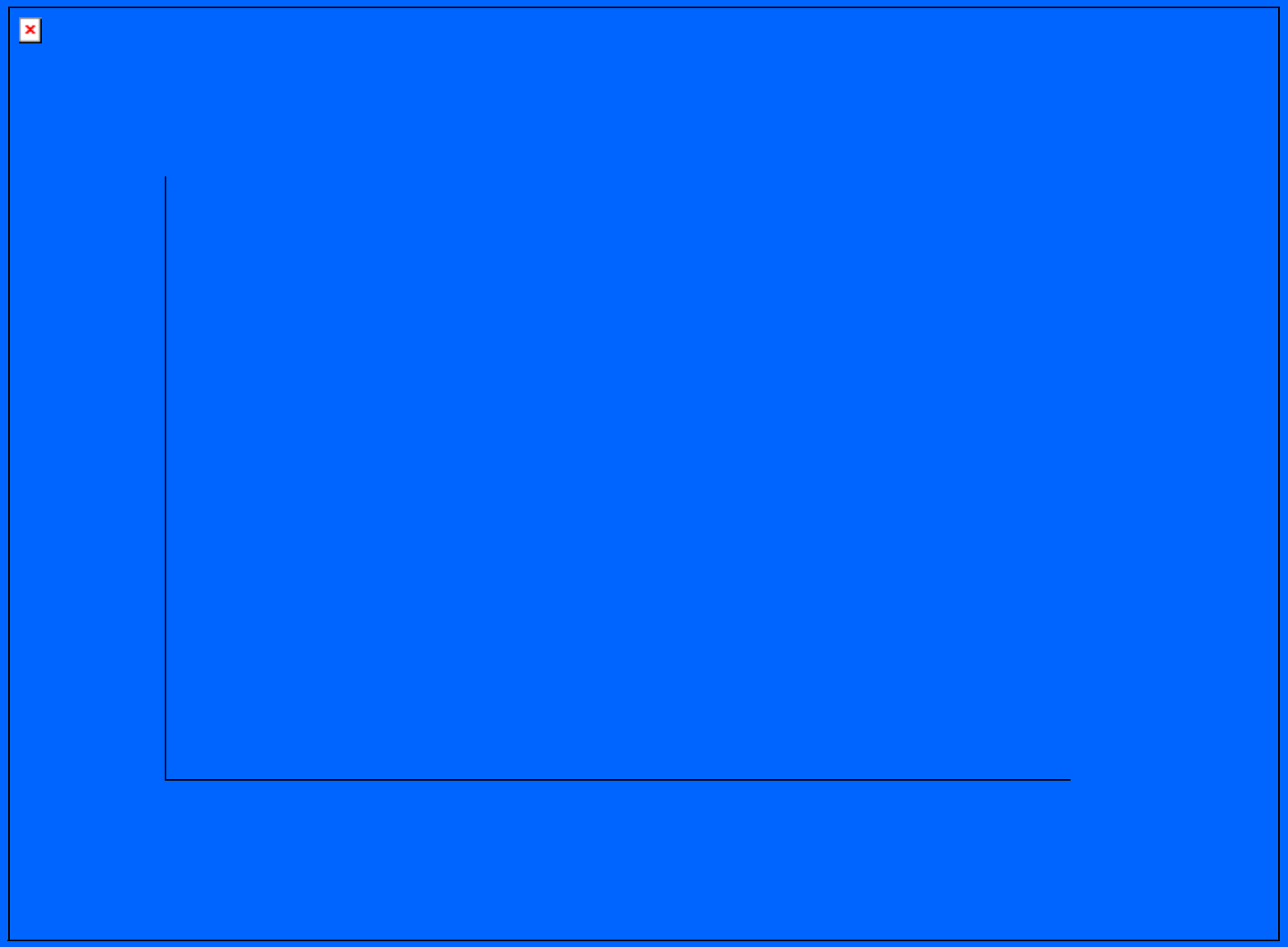
- 10 homes and preschool children
- One morning void sample prior to treatment
- Morning void samples collected 7 days post-treatment
- Chlorpyrifos metabolite, TCPy, measured

Conclusion

- A significant increase was not observed in the amount of chlorpyrifos absorbed by the children after treatment

NJ Crack-and-Crevice Study

Child #4: Baseline TCPy concentration < LOD



Dietary Intervention Study

Lu et al. Environ Health Perspect 114:260-263 (2005)

Goal

- Determine if substitution of conventional produce with organic produce reduces OP pesticide metabolites in children's urine

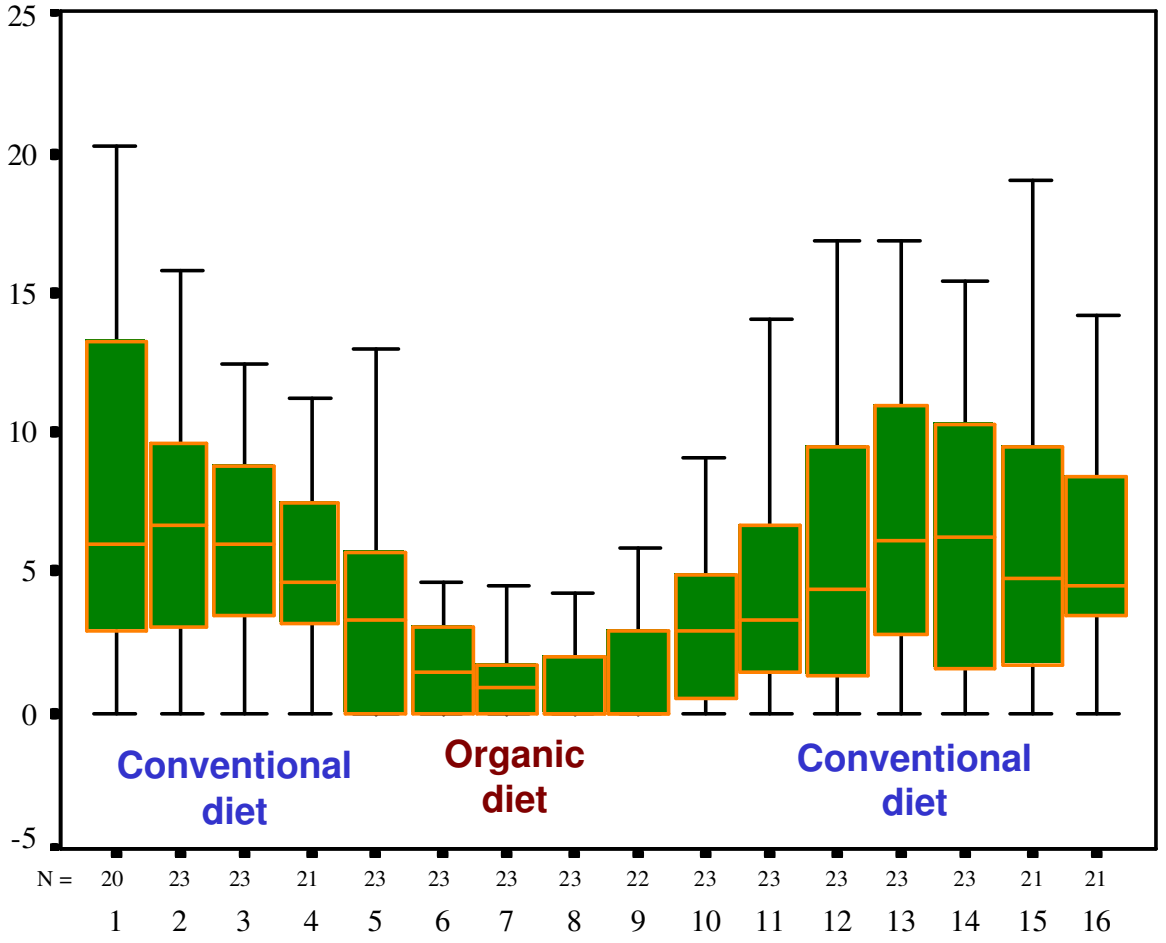
Design

- 22 suburban children
- Bedtime and morning voids samples combined for daily exposure
- 3 day pre-intervention, 5 day intervention, 7 day post-intervention

Conclusion

- Significant decrease in metabolite levels due to dietary intervention

TCPY Concentrations in the Urine of 22 Children Before, During, and After an Organic Diet Intervention



CTEPP Study

Morgan et al. 2005. JEAEE 15:297-309

Children's Total Exposure to Persistent Pesticides and Persistent Pollutants

- 252 preschool-age children in Ohio and North Carolina
- Chlorpyrifos and TCPy measured in air, on surfaces, and in food
- Detailed behavioral analysis of children
- TCPy measured in urine samples: 3 samples per day per child

Key Finding

- Deterministic model of exposure and uptake of both chlorpyrifos and TCPy under-predicted TCPy urinary concentrations

CTEPP Exposure-Biomarker Reconciliation

Smith, Kissel and Shirai. ISEE/ISEA, Paris, 2006

Analytic Approach

- 2nd order Monte Carlo exposure modeling
- 3-pathway model: inhalation, diet, soil ingestion

Key Finding

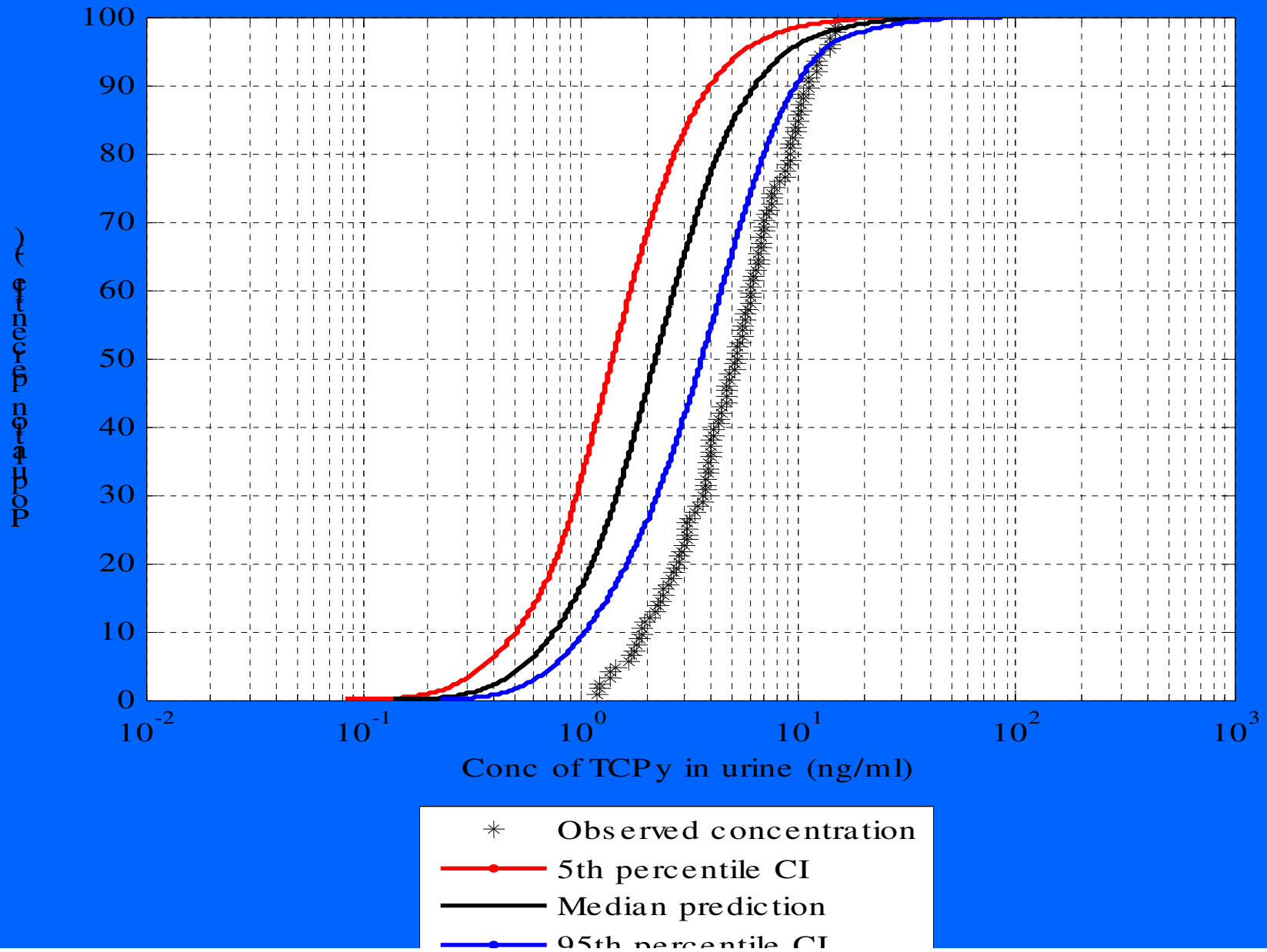
- Under-prediction reported by Morgan confirmed
- Model accounted for about 50% of urinary TCPy

Additional Pathway Analysis

- Markov Chain Monte Carlo analysis
- Additional pathways: hand-to-mouth, object-to-mouth, dust ingestion, dermal absorption

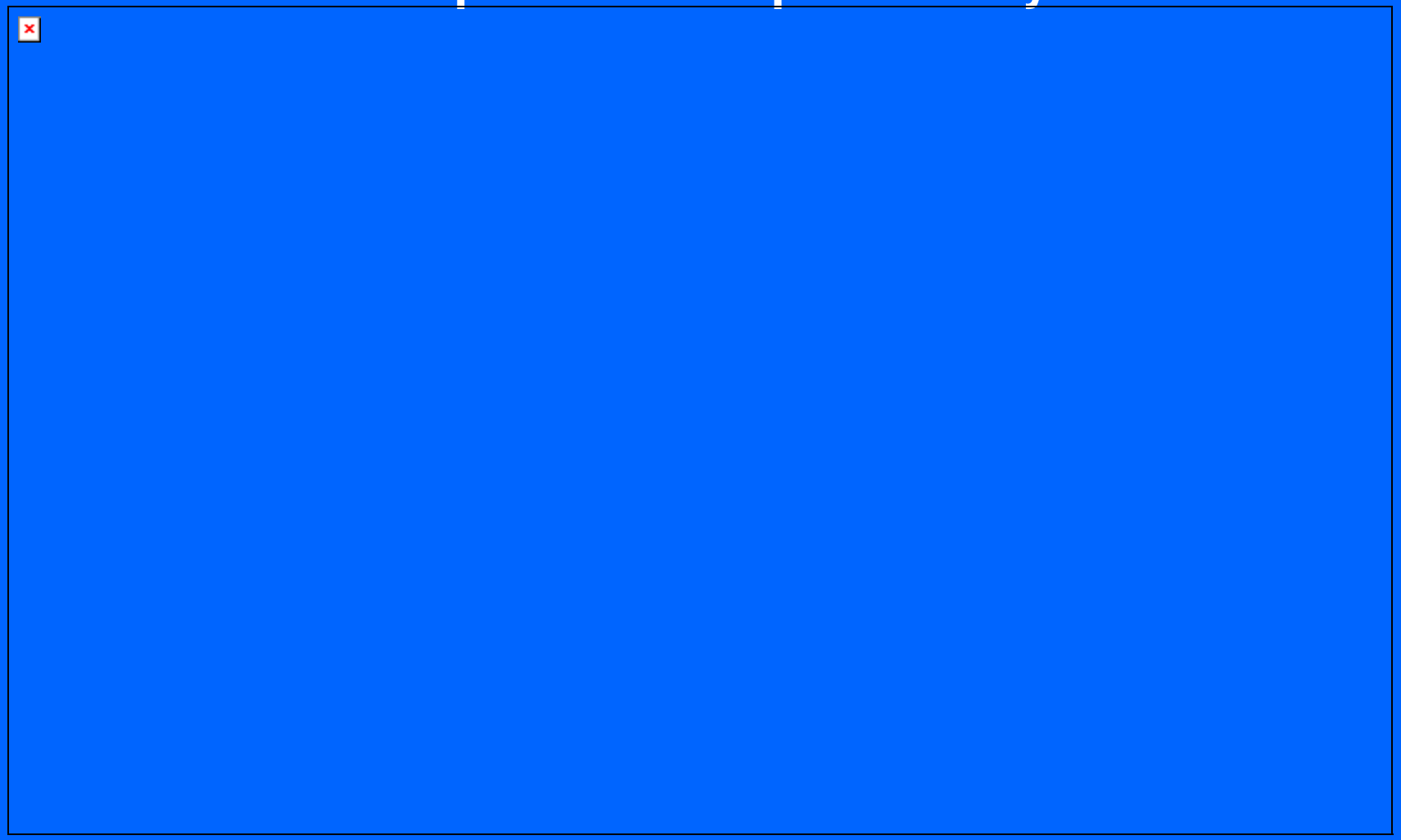
Observed and Modeled Concentrations (NC)

Smith, Kissel and Shirai. ISEE/ISEA, Paris, 2006



Dermal Uptake

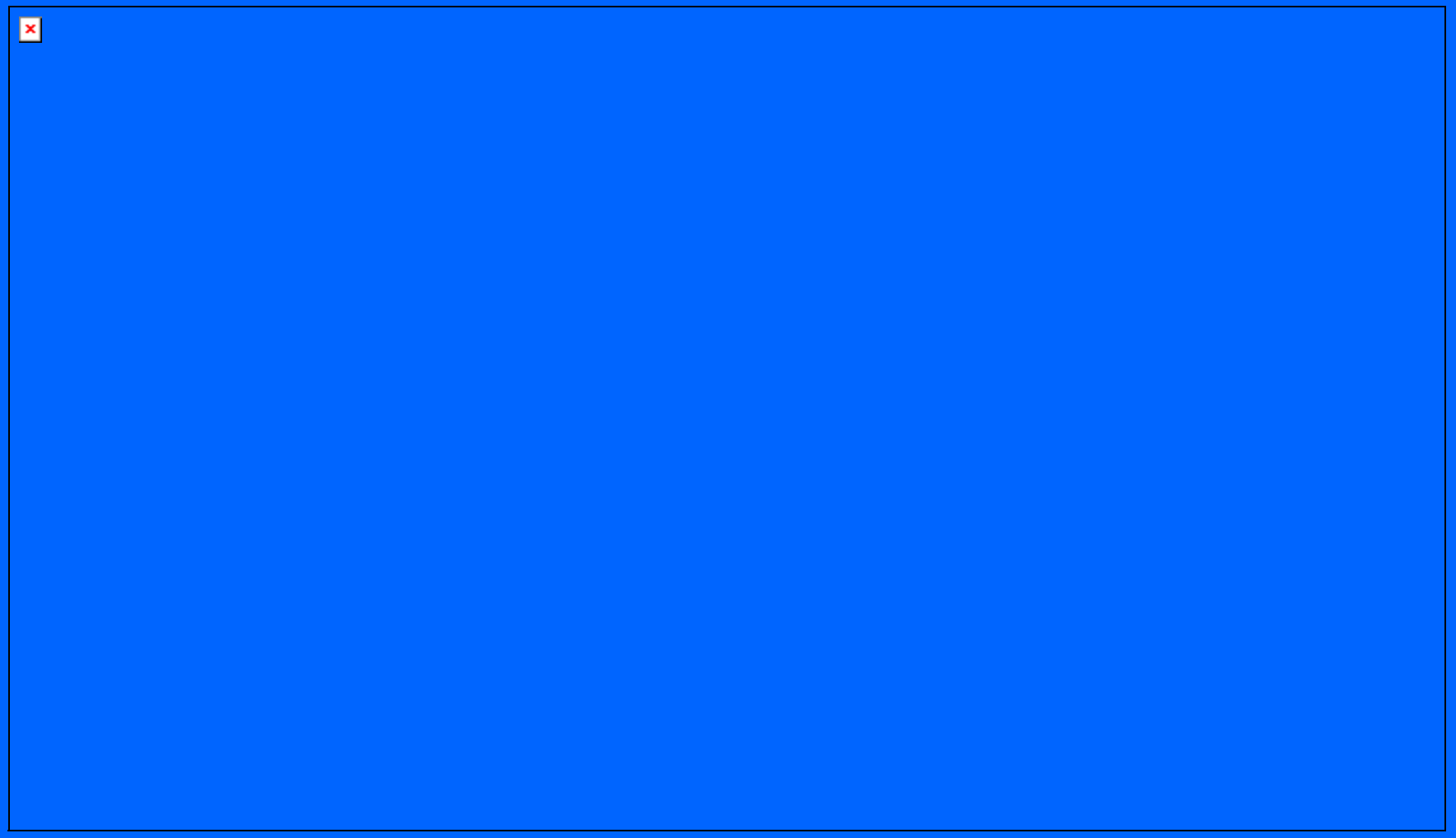
Dermal Absorption of Azinphosmethyl in Rats



Zendzian, 2000

Dermal Absorption of a Brominated Diphenyl

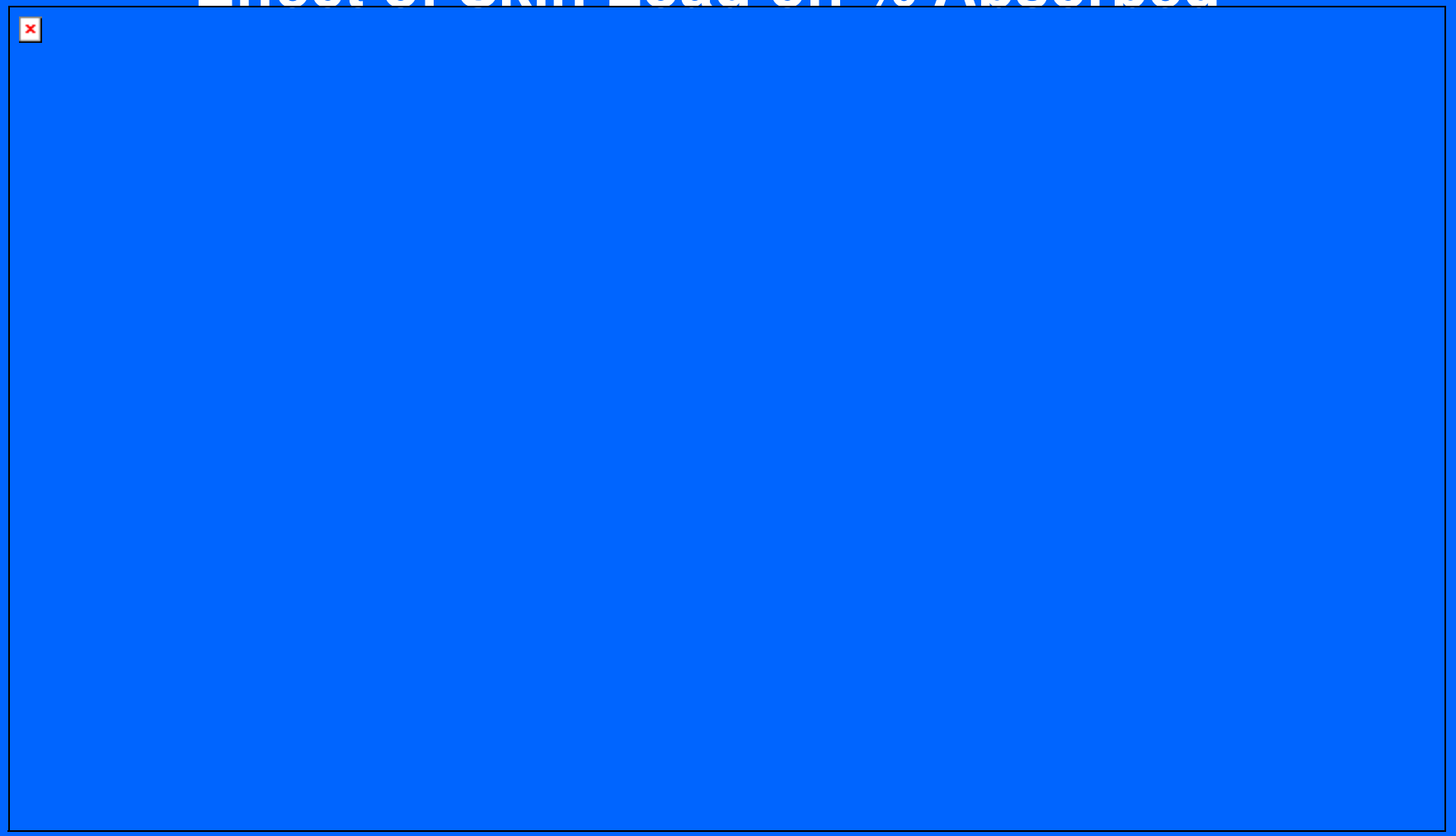
Effect of Skin Load on % Absorbed



Hughes et al. 2001. Food Chem Toxicol 39:1263-1270

Dermal Absorption of a Chlorinated Phosphate

Effect of Skin Load on % Absorbed



Hughes et al. 2001. Food Chem Toxicol 39:1263-1270

Chlorpyrifos Dermal Absorption Studies

Study	Loading (ug/cm2)	Duration (hrs)	Percent Absorbed	Percent Excreted
Nolan 84	**41,000**	**12-20**	**1.3**	**1.2**
Griffin 99	**370**	**8**	**47**	**1.0**
Meuling 05	**150**	**4**	**33**	**1.2**
	50	**4**	**58**	**4.3**
Griffin 00 (in vitro)	**730**	**24**	**35**	**20**

Occupational Pesticide Exposures

Airblast applicators in FL citrus

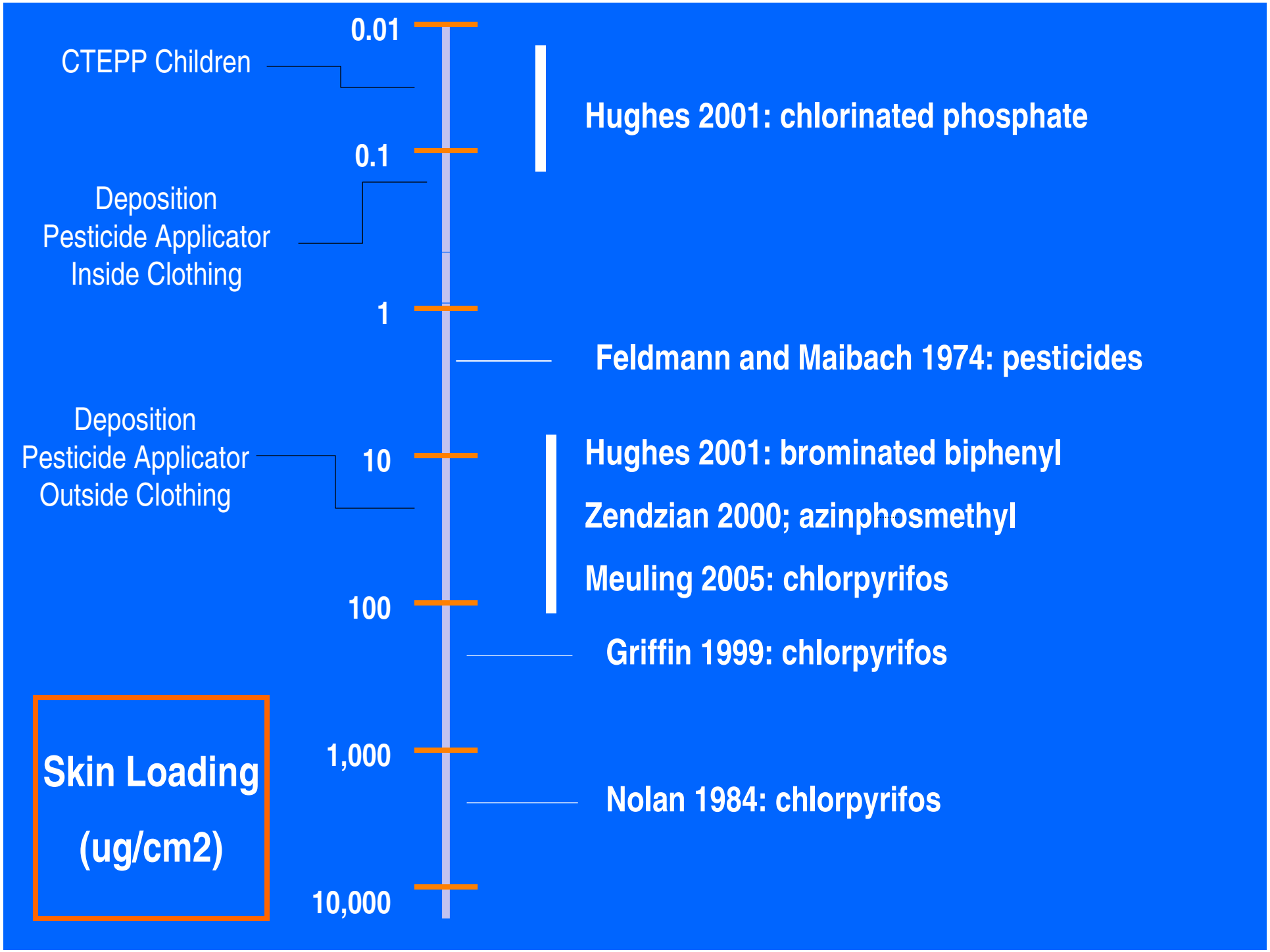
- Dermal exposure of 24 workers
- High end of applicator exposures
- OP pesticide: ethion

Deposition outside clothing

- 2.5 ug/cm^2/hr
- 20 ug/cm^2/8 hr workday

Deposition beneath clothing

- 16 ng/cm^2/hr
- 128 ng/cm^2/8 hr workday


0.01
CTEPP Children
0.1
Deposition
Pesticide Applicator
Inside Clothing
1
Deposition
Pesticide Applicator
Outside Clothing
10
100
1,000
10,000
Skin Loading
(ug/cm2)
Hughes 2001: chlorinated phosphate
Feldmann and Maibach 1974: pesticides
Hughes 2001: brominated biphenyl
Zendzian 2000; azinphosmethyl
Meuling 2005: chlorpyrifos
Griffin 1999: chlorpyrifos
Nolan 1984: chlorpyrifos

Oral and Respiratory Uptake

CTEPP assumption of 50% retention of inhaled chlorpyrifos

- Based on controlled laboratory studies designed to simulate occupational exposures
- Exposures 3-4 orders of magnitude higher than those of CTEPP children

Common assumption of 70% excretion of TCPy following oral chlorpryifos exposure

- Based on oral dose of 40 mg chlorpyrifos
- Dietary exposures typically **???**

No standard "exposure factors" for uptake

Next Steps for Exposure Science

Focus on human studies to understand linkage between personal exposures and biomarkers

- Develop standard factors for absorption processes
- Develop a science of “dermalomics”?

Improve the quality of biomonitoring studies

- Design studies to account for inter- and intra-individual variability

Adapt new technologies to measure personal exposures

- GPS for time-location activities
- Data loggers for self-reported behaviors

Devote sufficient attention to the source-receptor component of the continuum

- Knowledge critical for disease prevention