

# Interpretation of Human Biomonitoring Data Using a Forward Dosimetry Approach

## Permethrin: A Case Study



*EPA Research & Development  
National Exposure Research Laboratory*

**Marsha Morgan, Linda Sheldon, and Miles Okino**  
**US Environmental Protection Agency, National Exposure Research Laboratory**

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# Issues

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- One of the greatest challenges today is using biomarkers of exposure to quantitatively estimate human exposures to non-persistent chemicals.
- Chemicals or their metabolites in body fluids are commonly used as biomarkers of human exposure.
- In recent years, there has been an explosion of available human biomonitoring data.
- Unfortunately, many of these studies have collected little or no environmental measurement data.



# Issues (continued)

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- Environmental measurement data are vital in understanding the important sources, pathways, and routes of human exposures to chemicals.
- Biomarker data by themselves only show that humans were exposed to a chemical at some point in time.
- The CTEPP study is an excellent example that shows the importance of simultaneously collecting both environmental measurements and biomarker data in human exposure studies.



# The Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) Study

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## Objectives:

- Measure the aggregate exposures of about 260 preschool children to persistent pesticides and other persistent organic pollutants in their everyday environments.
- Apportion the exposure pathways and identify important exposure media.



# Study Design

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- Involved approximately 260 preschool children and their adult caregivers.

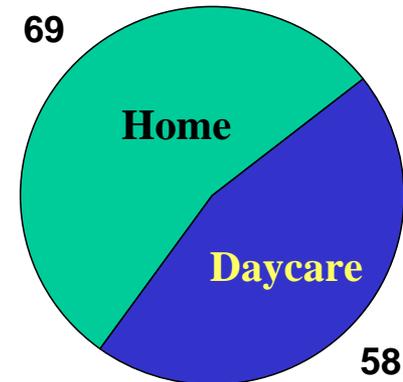
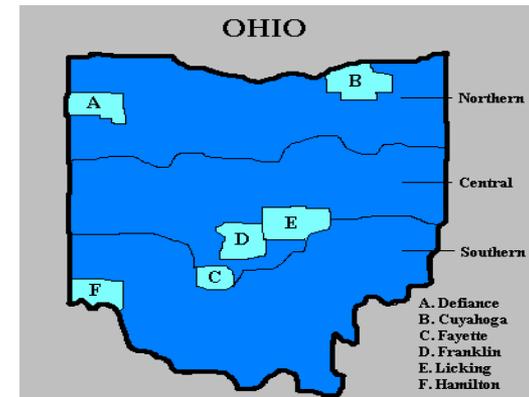
<b>States :</b>	North Carolina and Ohio
<b>Counties:</b>	Six in both states; 4 urban and 2 rural
<b>Sampling sites:</b>	Child daycare centers and residences
<b>Socioeconomic status:</b>	Low-income and middle/high-income

- Stratification
  - Child daycare vs. home
  - Urban vs. rural
  - Low-income vs. middle/high-income



# OHIO

- Six counties:
  - Urban - *Hamilton, Franklin, Licking, Cuyahoga*
  - Rural - *Fayette, Defiance*
- Recruitment:
  - Feb. – Nov. 2001
- Field sampling:
  - Apr. – Nov. 2001



# Study Procedures

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## Samples:

- **Food**
- **Drinking Water**
- **Hand Wipes**
- **Beverages**
- **Indoor Air**
- **Soil**
- **Urine**
- **Outdoor Air**
- **Dust**



# SOIL SAMPLE



**RESEARCH & DEVELOPMENT**

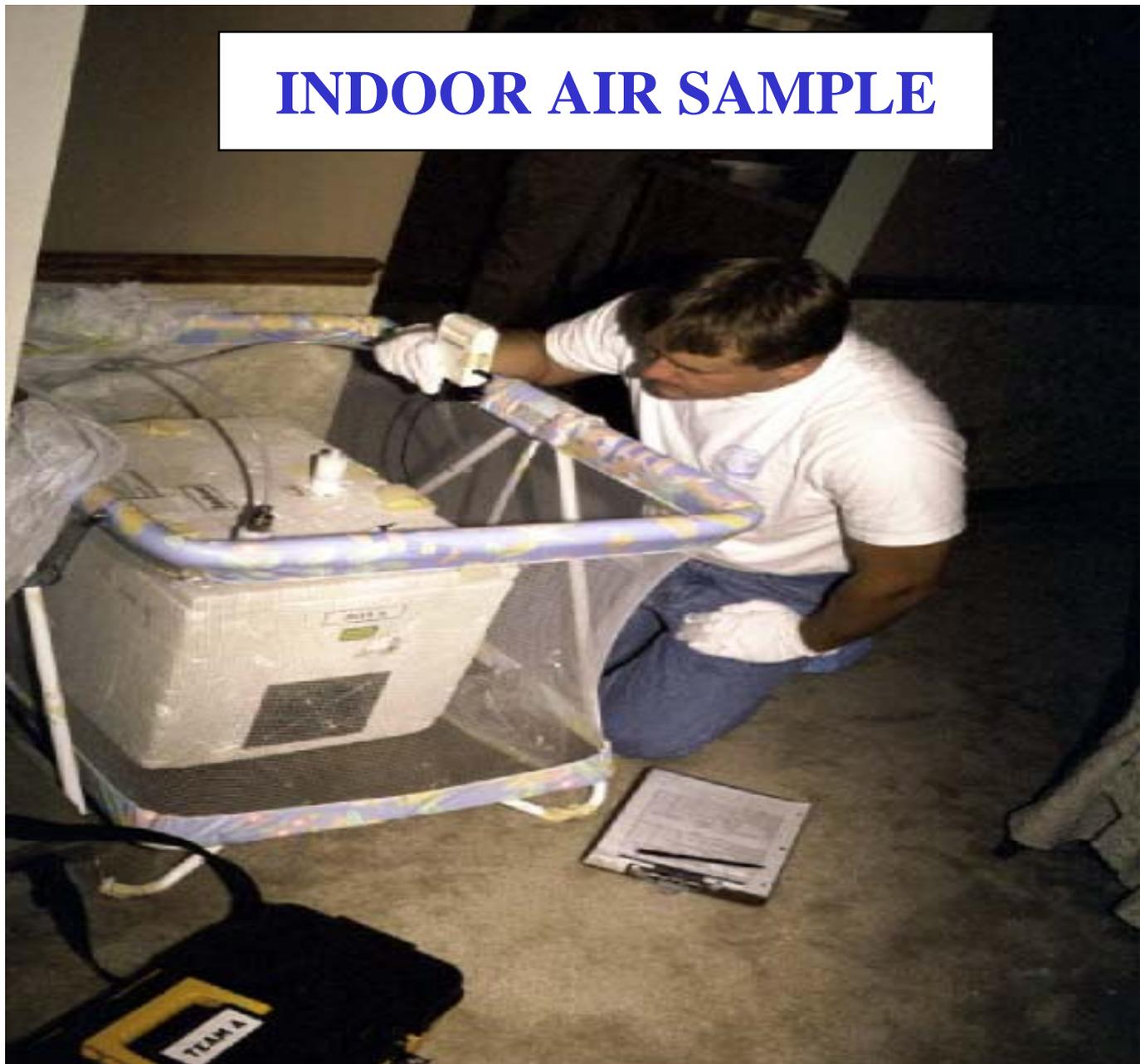
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# OUTDOOR AIR SAMPLE



# INDOOR AIR SAMPLE



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# INDOOR FLOOR DUST SAMPLE

HVS3

A blue HVS3 vacuum cleaner is positioned on a grey carpeted floor. A red square is drawn on the carpet, indicating the area for an indoor floor dust sample. The vacuum cleaner has a blue frame, a black motor unit, and a red dust bag. The background shows a wooden cabinet and a white storage unit.

# HAND WIPE SAMPLE



## SOLID AND LIQUID FOOD SAMPLES



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# URINE SAMPLE





# Chemical Analysis

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Environmental  
Media



*cis*-Permethrin

*trans*-Permethrin

Urine



3-Phenoxybenzoic acid  
(3-PBA)



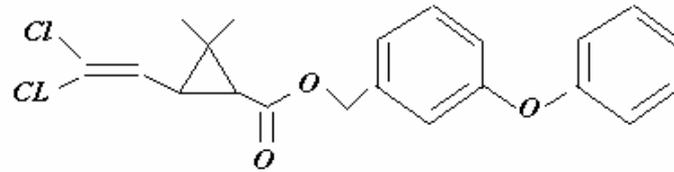
# Permethrin

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- About 2 million lbs of permethrin are used each year mainly in agricultural and residential settings in the United States.
- Today, especially due to the phase-outs of residential use of the organophosphate insecticides chlorpyrifos and diazinon, the pyrethroids are frequently being used at places where children spend their time.
- Little research has investigated the potential exposures of children to permethrin in these environments.
- A few studies have reported low levels of *cis*- and *trans*-permethrin in carpet dust, floor wipe, and air samples at homes in several states (Clayton et al., 2003; Colt et al., 2004; Quandt et al., 2004; Whyatt et al., 2002).
- Little information exists on the toxicokinetics of permethrin in humans in the published literature.

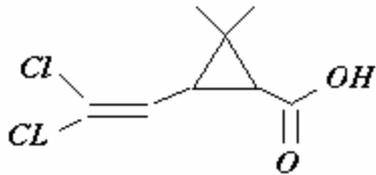


# Permethrin

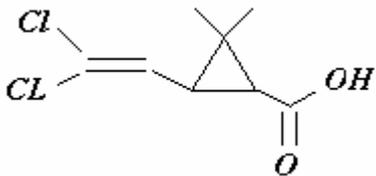


Ester Cleavage

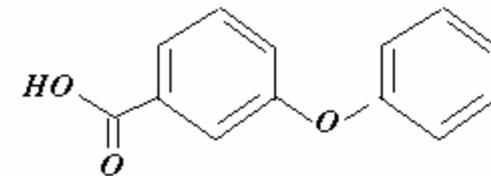
Oxidation



*cis*-3(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid)



*trans*-3(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid)

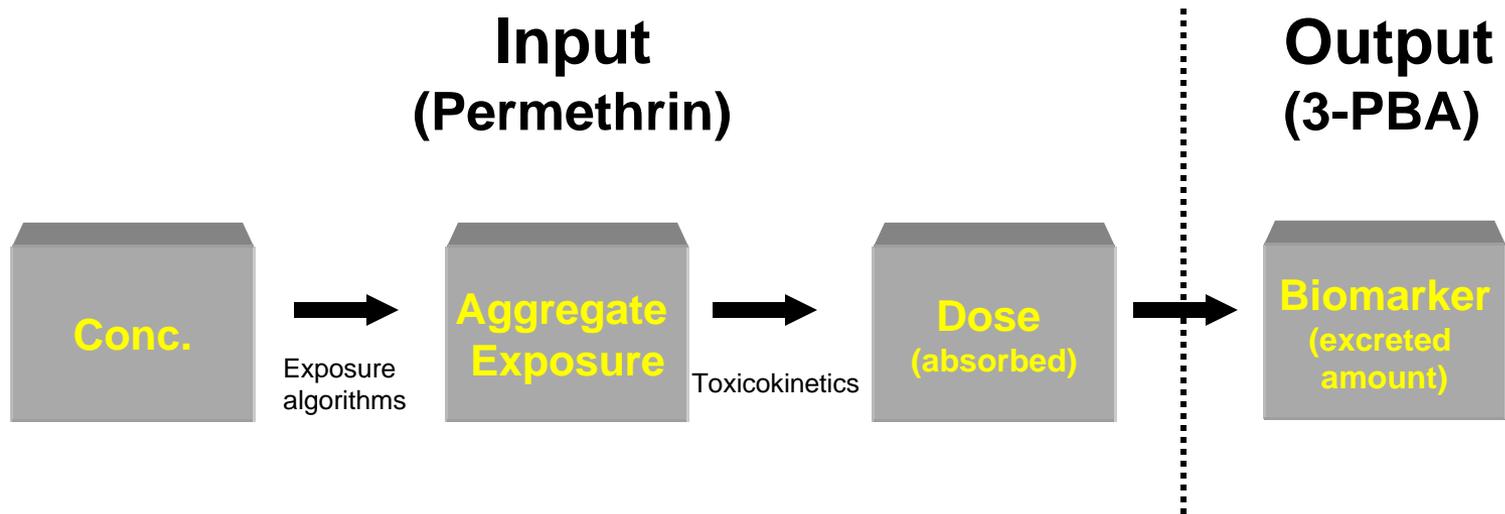


**3-Phenoxybenzoic acid  
(3-PBA)**



# Forward Dosimetry Approach

(CTEPP study)

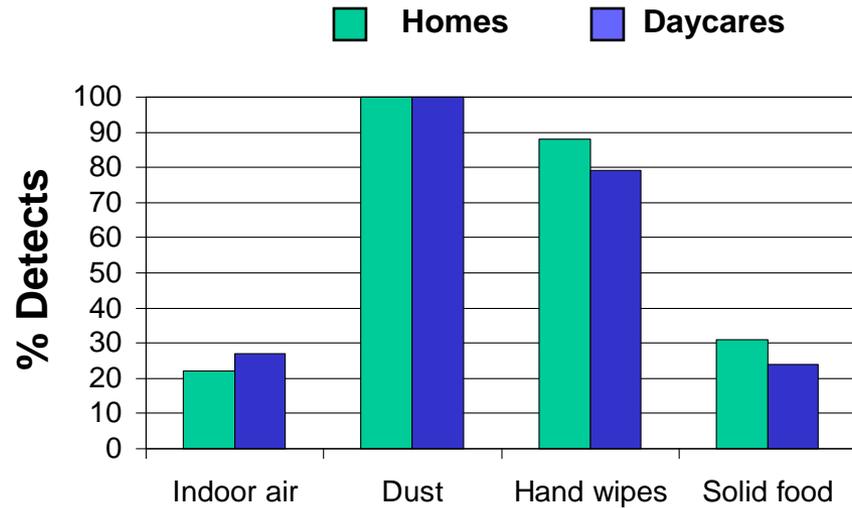


# Results

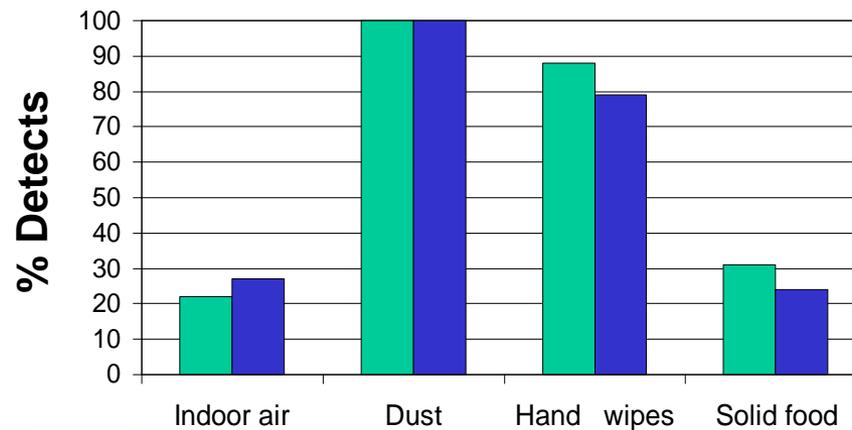
**Morgan** et al. An observational study of 127 preschool children at their homes and daycare centers in Ohio: Environmental pathways to *cis*- and *trans*-permethrin exposure. Environmental Research. 2007; 104: 266-274.



# Detection frequencies by medium



*cis*-Permethrin



*trans*-Permethrin



# Concentrations of *cis*- and *trans*-permethrin in media at homes in OH

Medium	Unit	N <sup>a</sup>	Min	Median	75 <sup>th</sup>	95 <sup>th</sup>	Max
<b><i>cis</i>-permethrin</b>							
Indoor air	ng/m <sup>3</sup>	125	< <sup>b</sup>	<	<	1.6	5.4
Solid food	ng/g	125	<	<	0.2	8.8	560
Hand wipe	ng/cm <sup>2</sup>	97	<	0.03	0.1	0.8	2.1
Dust	ng/g	120	16.6	470	1,550	7,630	79,600
<b><i>trans</i>-permethrin</b>							
Indoor air	ng/m <sup>3</sup>	125	<	<	<	1.0	6.8
Solid food	ng/g	125	<	<	0.2	8.0	448
Hand wipe	ng/cm <sup>2</sup>	97	<	0.03	0.1	0.8	2.1
Dust	ng/g	118	16.5	344	1,270	9,210	78,800

<sup>a</sup>Sample level

<sup>b</sup>Limit of detection (indoor air=0.4 ng/m<sup>3</sup>; solid food=0.08 ng/g; hand wipe=0.003 ng/cm<sup>2</sup>; dust=2.3 ng/g)



# Concentrations of *cis*- and *trans*-permethrin in media at daycare centers in OH

Medium	Unit	N <sup>a</sup>	Min	Median	75 <sup>th</sup>	95 <sup>th</sup>	Max
<b><i>cis</i>-permethrin</b>							
Indoor air	ng/m <sup>3</sup>	22	< <sup>b</sup>	<	0.3	0.9	6.5
Solid food	ng/g	29	<	<	<	2.2	31.0
Hand wipe	ng/cm <sup>2</sup>	29	<	0.04	0.1	0.6	1.4
Dust	ng/g	23	127	1,010	1,850	3,830	4,630
<b><i>trans</i>-permethrin</b>							
Indoor air	ng/m <sup>3</sup>	22	<	<	<	0.7	6.8
Solid food	ng/g	29	<	<	<	1.4	26.7
Hand wipe	ng/cm <sup>2</sup>	29	<	0.03	0.1	0.8	1.5
Dust	ng/g	22	126	544	1,860	3,420	3,950

<sup>a</sup>Sample level

<sup>b</sup>Limit of detection (indoor air=0.4 ng/m<sup>3</sup>; solid food=0.08 ng/g; hand wipe=0.003 ng/cm<sup>2</sup>; dust=2.3 ng/g)

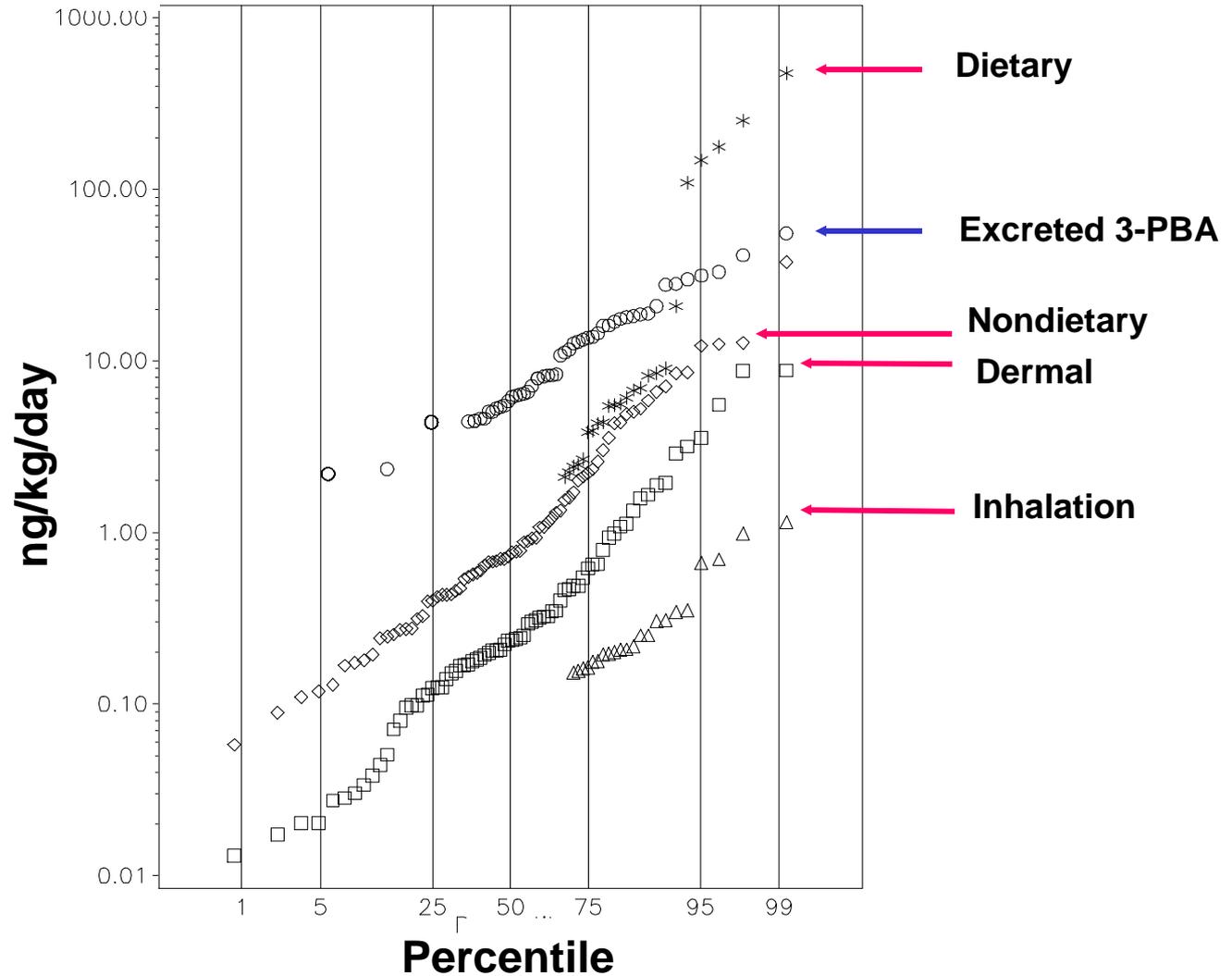


# Urinary 3-PBA concentrations for OH preschool children

Medium (ng/mL)	N	Min	50 <sup>th</sup>	75 <sup>th</sup>	95 <sup>th</sup>	Max
Overall	126	<	0.3	0.6	1.8	27.8
Home Group	69	<	0.2	0.6	1.9	2.3
Daycare Group	57	<	0.3	0.4	1.8	27.8

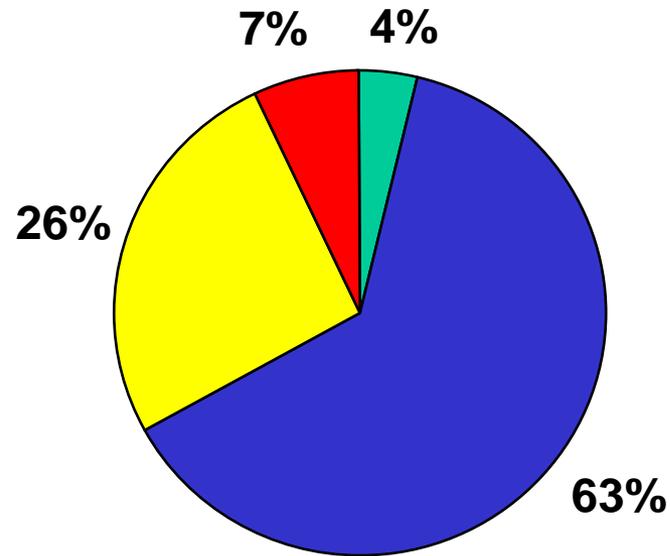


# Estimated absorbed doses of OH children to the combined isomers by each exposure route compared to their excreted amounts of 3-PBA in urine



# Exposure Routes

## Permethrin



Inhalation



Dietary



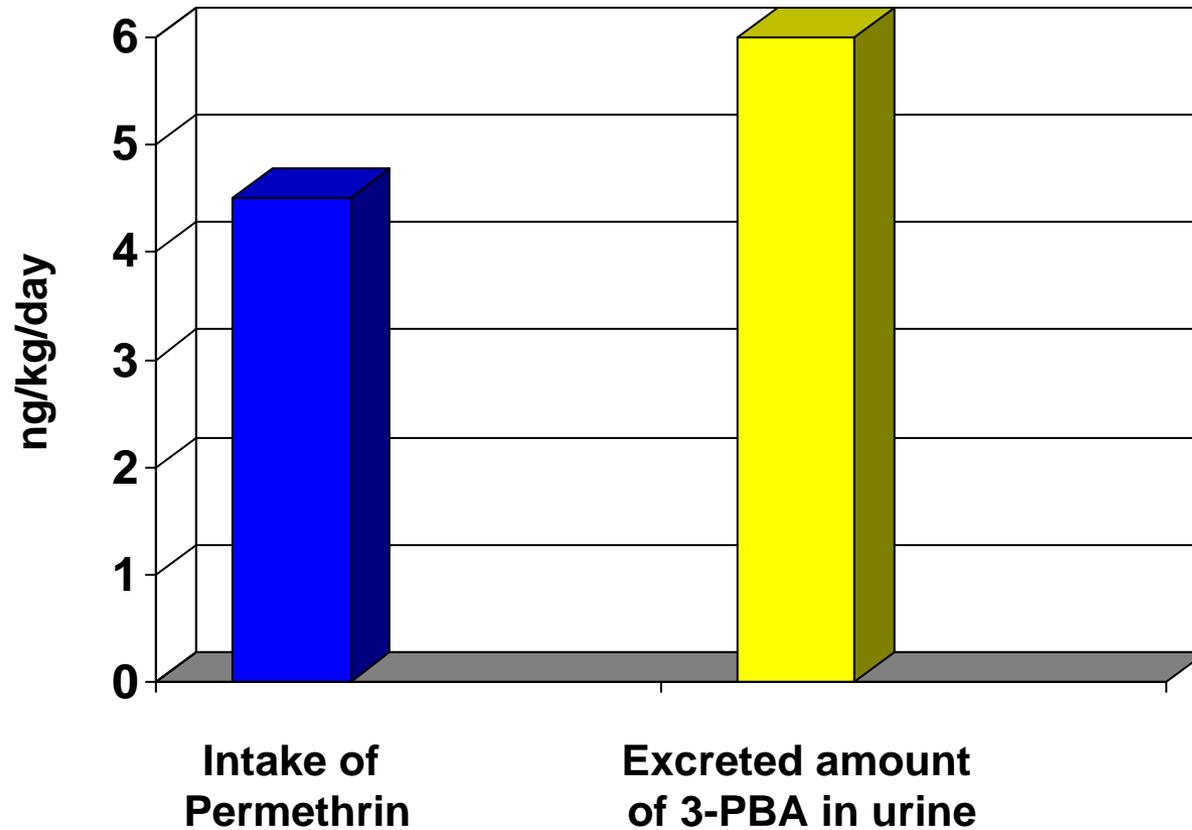
Nondietary



Dermal



# Intake vs. Output



# 3-PBA Issues

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- Wilson et al. 2004 showed that 3-PBA was measurable in several media (air, dust, and hand wipes) at residences.
- 3-PBA is a non-specific urinary biomarker of exposure for several pyrethroids.
- 3-PBA may not be a reliable urinary biomarker of exposure for children exposed to low levels of permethrin in their everyday environments.
- Inputs for ADME unknown.



# Conclusions

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- These preschool children were exposed to *cis*- and *trans*-permethrin from several sources and through several pathways and routes in their daily environments.
- The primary route of the OH children's exposure to permethrin was through ingestion (dietary and nondietary).
- These participants were exposed to and absorbed one or more of the pyrethroids, likely including permethrin.



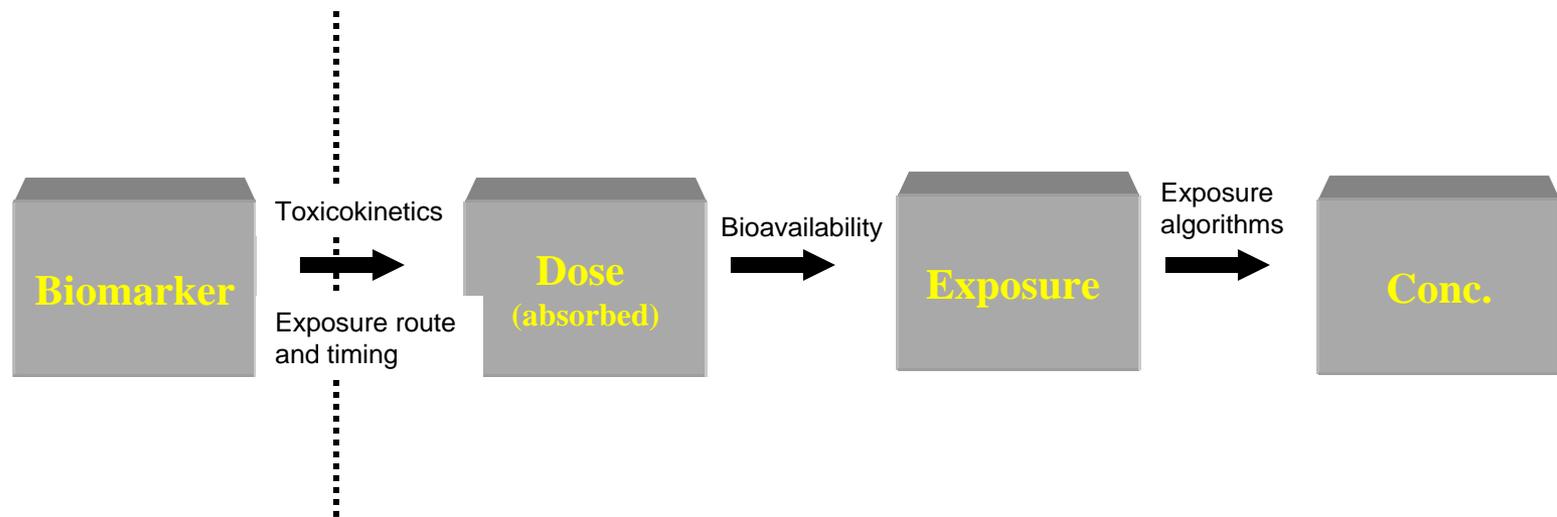
# Future Analysis



# Reverse Dosimetry Approach

(CTEPP Study)

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*Disclaimer: Although this work was reviewed by EPA and approved for publication, it may not reflect official Agency policy.*

