Interpretation of Human Biomonitoring Data Using a Forward Dosimetry Approach

Permethrin: A Case Study

EPA Research & Development
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Issues

• 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)

• 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

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

• Involved approximately 260 preschool children and their adult caregivers.

States :	North Carolina and Ohio
Counties:	Six in both states; 4 urban and 2 rural
Sampling sites:	Child daycare centers and residences
Socioeconomic status:	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*

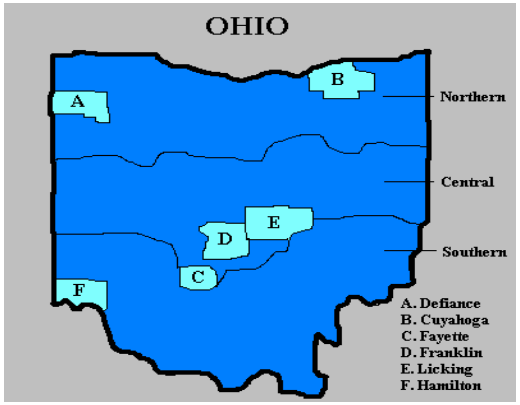
  Rural - *Fayette, Defiance*

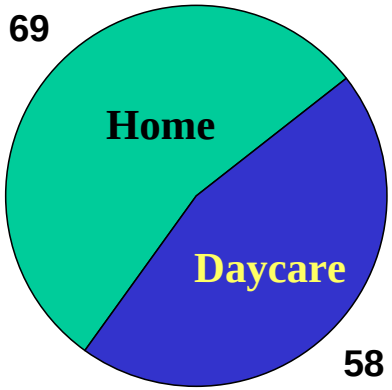
- Recruitment:

  Feb. – Nov. 2001

- Field sampling:

  Apr. – Nov. 2001





Study Procedures

Samples:

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

SOIL SAMPLE


OUTDOOR AIR SAMPLE

INDOOR AIR SAMPLE


INDOOR FLOOR DUST SAMPLE
HVS3


HAND WIPE SAMPLE

SOLID AND LIQUID FOOD SAMPLES


URINE SAMPLE

Chemical Analysis

Environmental Media → ***cis*-Permethrin**

***trans*-Permethrin**

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

Permethrin

- About 2 million lbs of permethrin are used each year mainly in agricultural and residential settings in the United States.

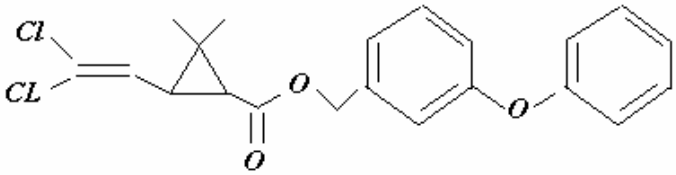
- Today, especially due to the phase-outs of residential use of the organophosphate insecticides chlorpyrifos and diazinon, the pyrethroids are frequently being used at places where children spend their time.

- 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).

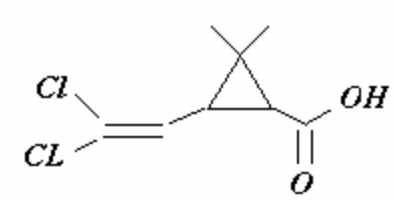
- Little information exists on the toxicokinetics of permethrin in humans in the published literature.

Permethrin

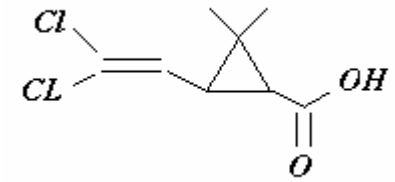


Ester Cleavage

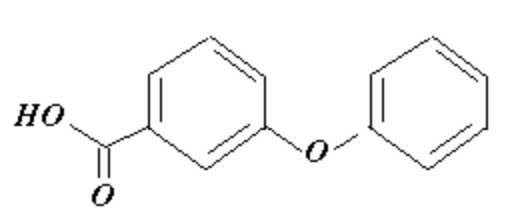
Oxidation



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



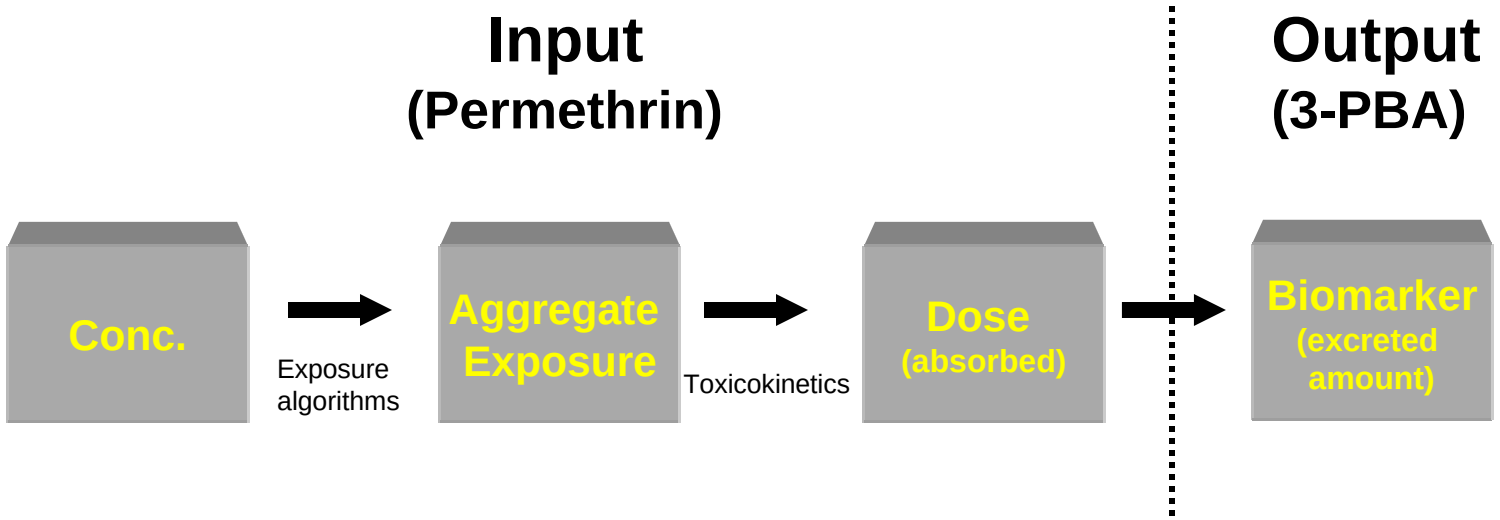
trans-3(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid)



3-Phenoxybenzoic acid (3-PBA)

Forward Dosimetry Approach

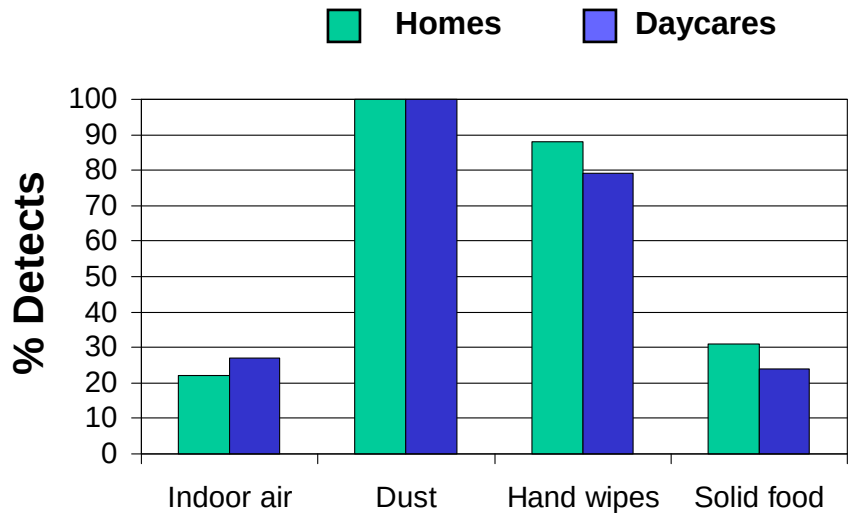
(CTEPP study)



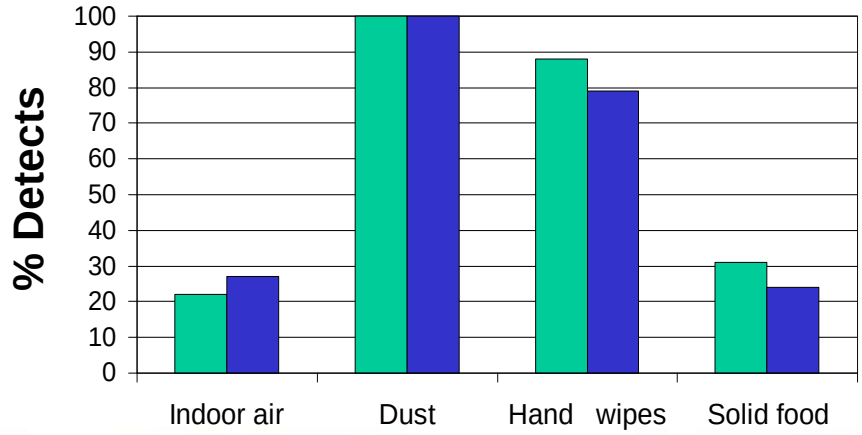
Results

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

[a]Sample level
[b]Limit of detection (indoor air=0.4 ng/m^3; solid food=0.08 ng/g; hand wipe=0.003 ng/cm^2; dust=2.3 ng/g)

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

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

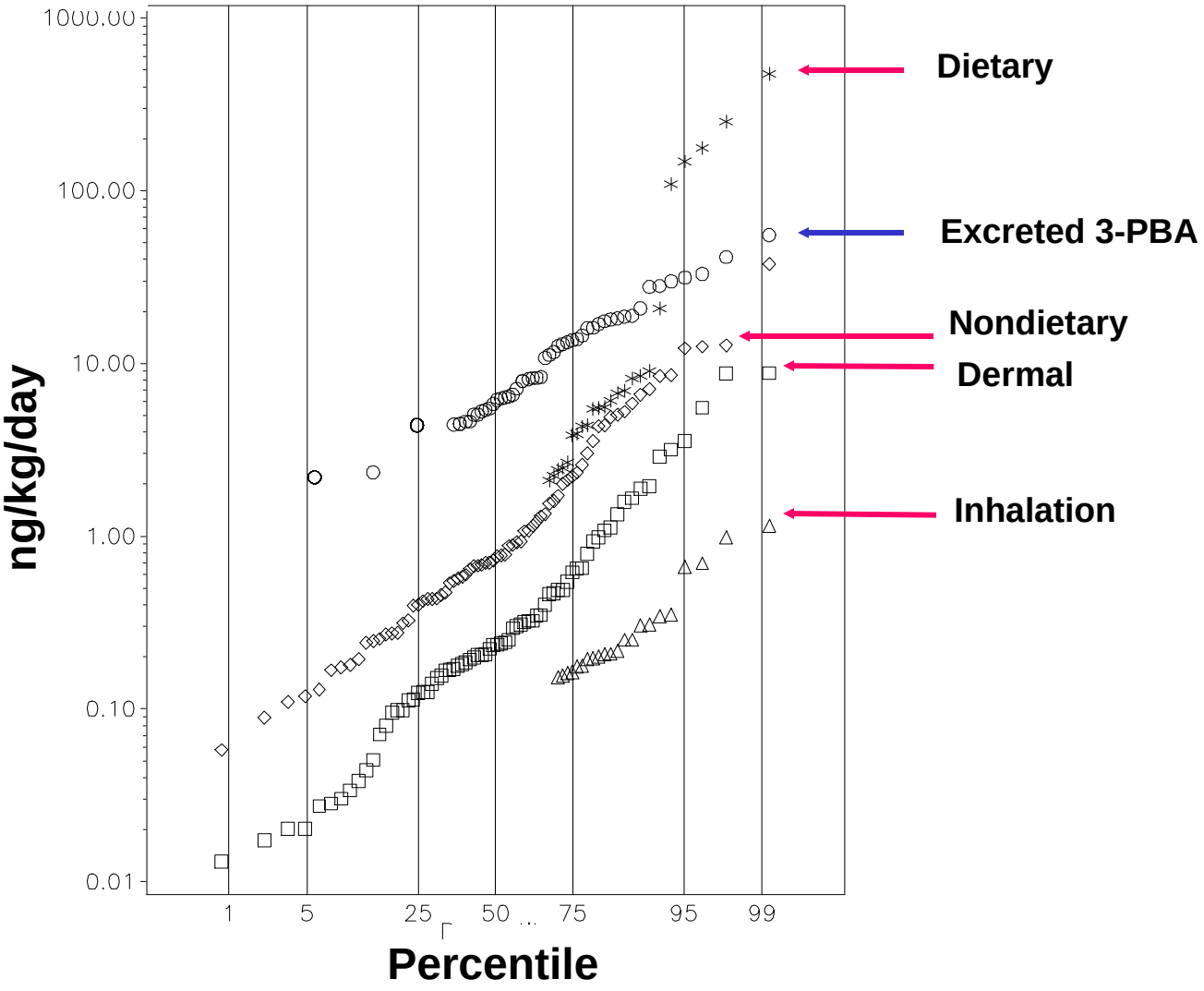
[a]Sample level

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

Urinary 3-PBA concentrations for OH preschool children

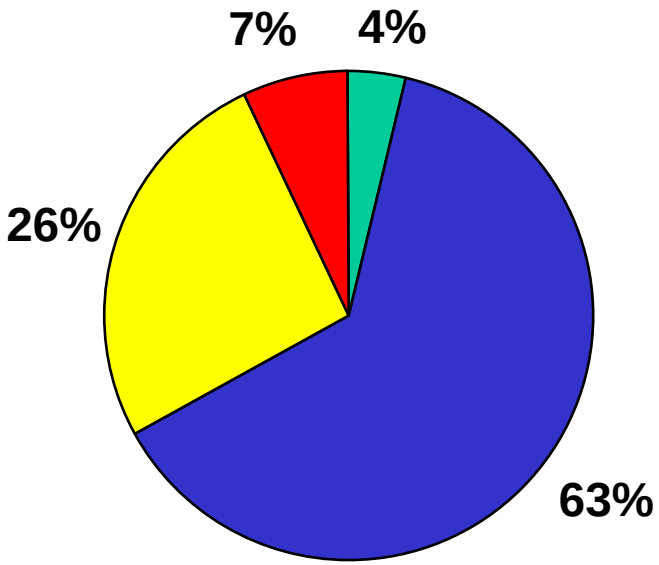
Medium (ng/mL)	N	Min	50th	75th	95th	Max
Overall	126	<	0.3	0.6	1.8	27.8
Home Group	69	<	0.2	0.6	1.9	2.3
Daycare Group	57	<	0.3	0.4	1.8	27.8

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

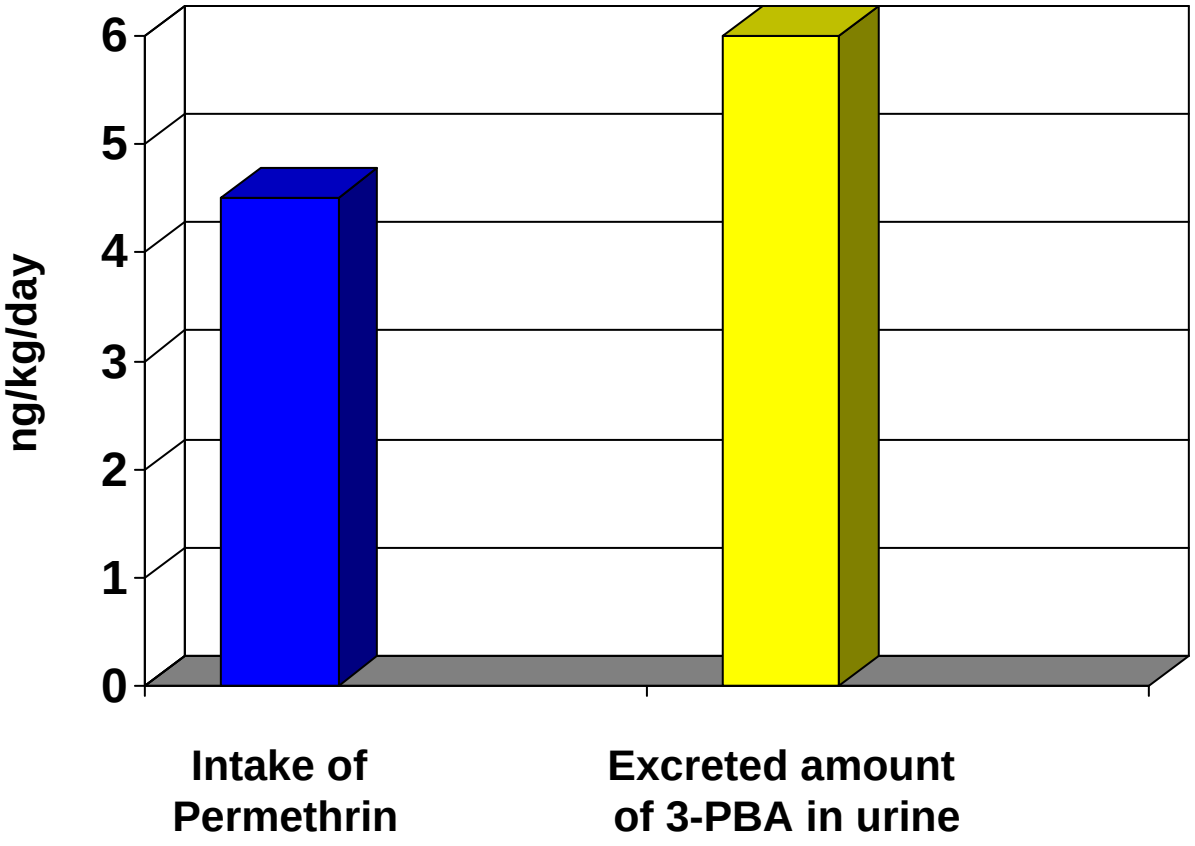


Exposure Routes

Permethrin



Intake vs. Output



3-PBA Issues

- 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

• These preschool children were exposed to *cis*- and *trans*-permethrin from several sources and through several pathways and routes in their daily environments.

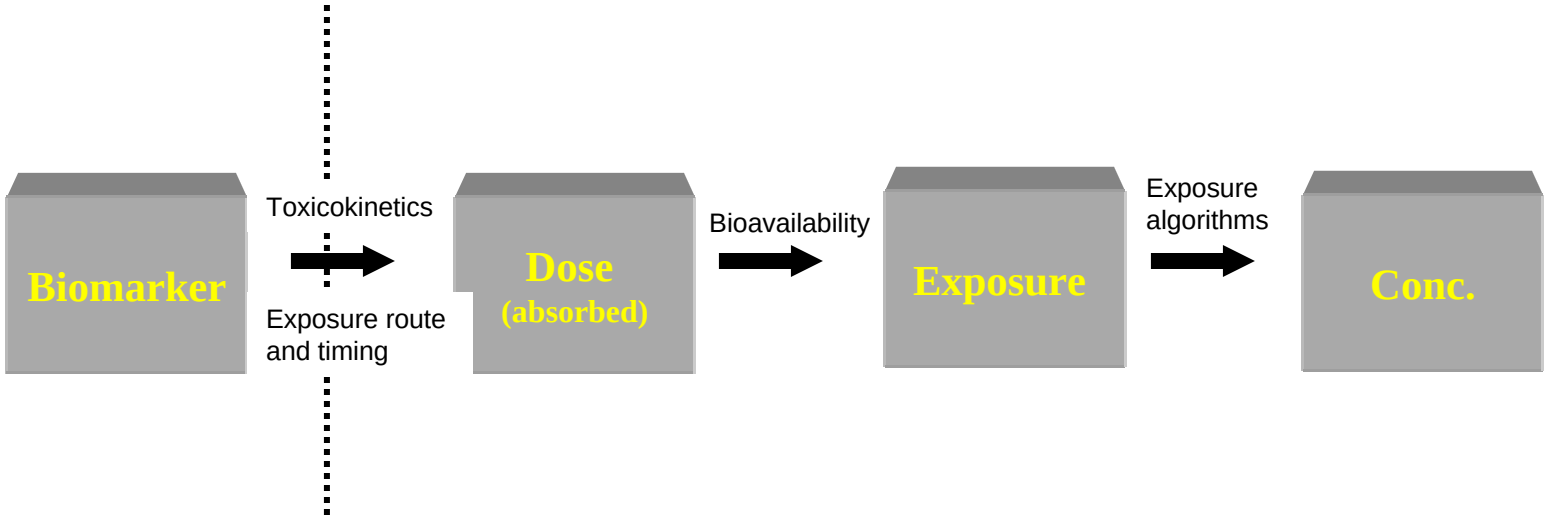
• The primary route of the OH children's exposure to permethrin was through ingestion (dietary and nondietary).

• 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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Parents, children, and child daycare centers

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