



Inhalation Exposure and Disposition of PCBs

NIEHS Superfund Research Program and EPA Clu-In Webinar
PCBs in Schools: Session 1 Overview and Exposure Assessment
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Human Exposure to PCBs

Ingestion and Occupational → Inhalation



- Legacy pollution – Highly stable PCB mixtures
 - Aroclors (US and UK) Clofen (Germany)
 - Phenoclor (France) Kanechlor & Santotherm (Japan)
- Sources: transformers, capacitors, machining oils, hydraulic fluids, plasticizers in caulk
- Modern day PCB exposures: (legacy), paints, pigments - 50 PCB congeners detected in yellow paint
 - Most frequently detected in yellow azo pigments¹:
PCB 11, 8, 6, 4, 1, 12/13, 2, 3, 209, 52
 - Includes non-aroclors: PCB 11, 209

¹Hu and Hornbuckle. ES&T. 2010, 44, 2822–27.

Human Exposure to PCBs

Ingestion → Inhalation



- Increasing awareness of PCBs in schools
 - Airborne exposures are important
 - How to remediate contaminated schools?
 - How low is safe?
- PCBs in homes and apartment buildings in Denmark, Germany, U.S.
 - Caulk and sealants, paints and pigments
 - Other synthetic building materials?
- Dredging, hauling, disposal of contaminated sediments concern for community level exposures

Marek et al. (2010) ES&T, 44, 2822–2827.

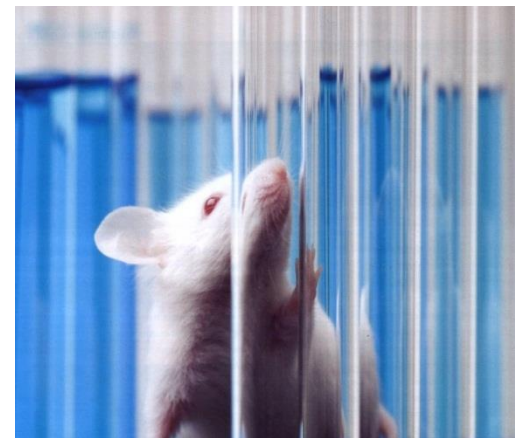
Meyer et al. (2013) Int J Hyg Environ Hlth, 216, 755-762.

Kohler et al. (2005) ES&T, 39 167-173.

Herrick et al (2004) EHP, 112, 1051-1053.

What do we know about the fate of inhaled PCBs?

- We have conducted 6 inhalation studies in rodents
 - Aroclor 1242
 - Chicago Air Mixture (CAM)
 - PCB 11
 - PCB 3
 - ^{14}C -PCB 11
 - CAM+ (CAM supplemented with PCB 11)
- Studies include acute, subacute, subchronic



Our rodent studies show rapid distribution and metabolism of inhaled PCB congeners

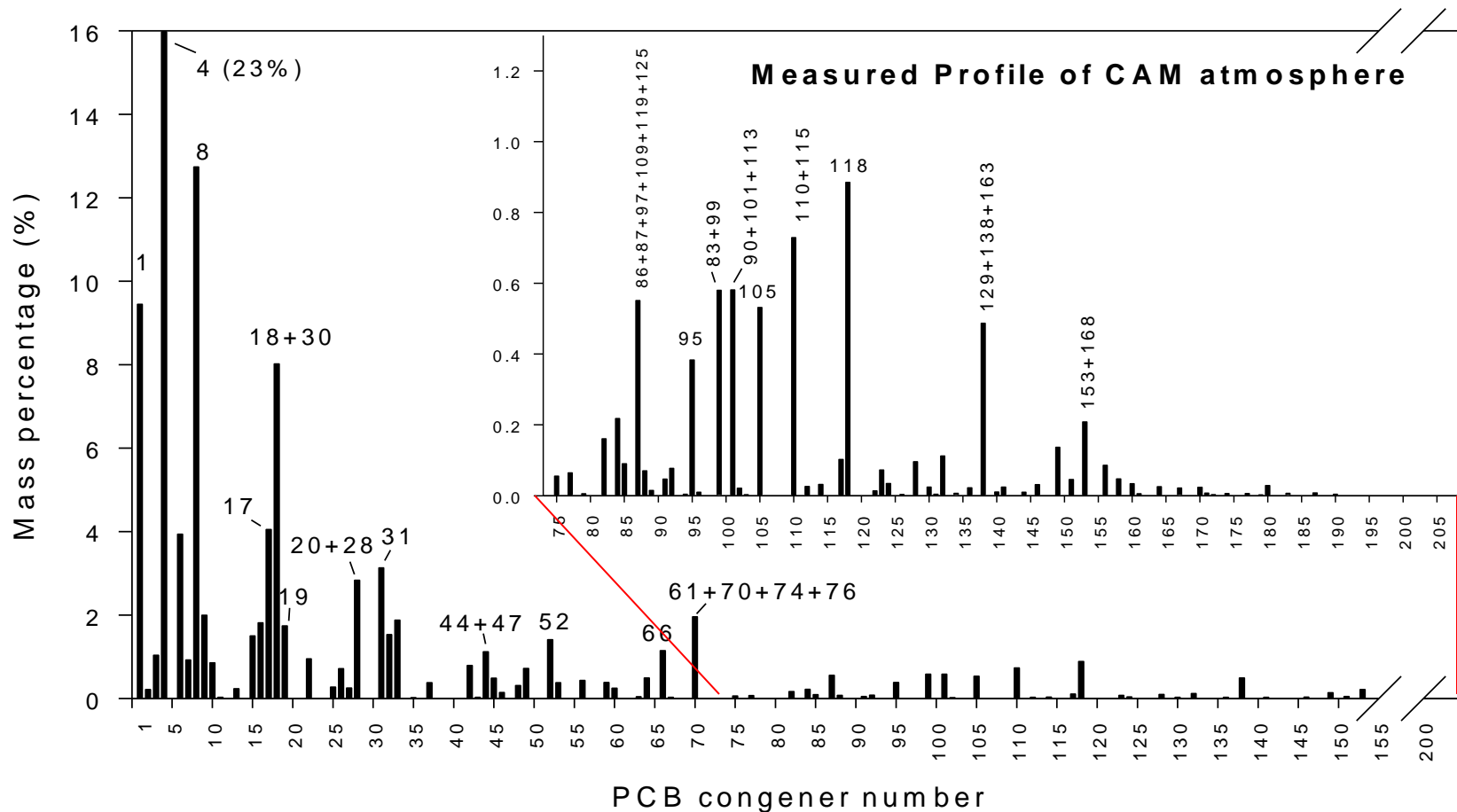
- **Aroclor 1242 study**
- Acute and subacute inhalation studies
- Rats exposed via inhalation
- $t_{1/2}$ = liver: 5.6 h; lung: 8.2 h; brain: 8.5 h; blood: 9.7 h
- Lung, liver, adipose tissue levels higher than brain or blood
- 10 d exposure \rightarrow 6.6 $\mu\text{g/g}$ lipid weight in lung & liver
- Minimal toxicity at 1400 μg (5.6 mg/kg)

- Hu X, Adamcakova-Dodd A, Lehmler HJ, Hu D, Kania-Korwel I, Hornbuckle KC, Thorne PS. Time course of congener uptake and elimination in rats after short-term inhalation exposure to an airborne polychlorinated biphenyl(PCB) mixture. *Environ Sci Technol*, 44(17):6893-6900, 2010.

Our rodent studies show rapid distribution and metabolism of inhaled PCB congeners

- **CAM Subchronic Study**
- Exposure atmospheres match the PCB profile of urban air
- 4-week nose-only inhalation studies.
- Inhalation exposure contributes to body burden of mostly tri- to hexa-chlorobiphenyls
- Distinct congener spectrum was found: similar between lung, serum, liver, brain and adipose tissue.
- Accumulation of neurotoxic PCBs in brain: PCB28, 105 and 118.
- Hu X, Adamcakova-Dodd A, Lehmler HJ, Hu D, Hornbuckle K, Thorne PS. Subchronic inhalation exposure study of an airborne polychlorinated biphenyl mixture resembling the Chicago ambient air congener profile. *Environ Sci Technol*, 14(59):9653-62, 2012. PMID: 22846166

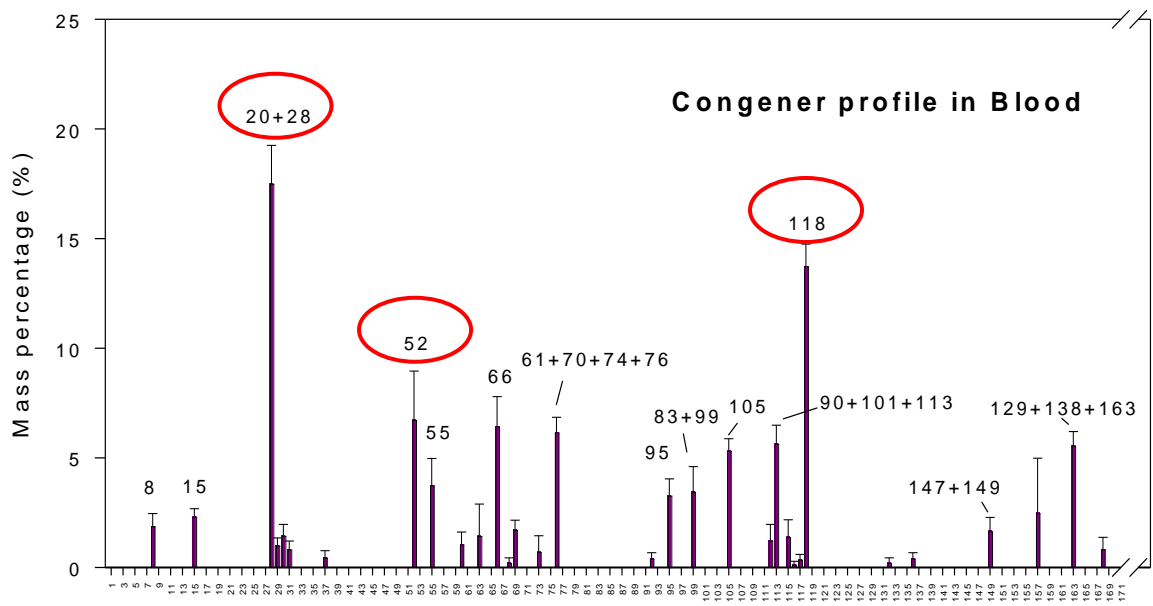
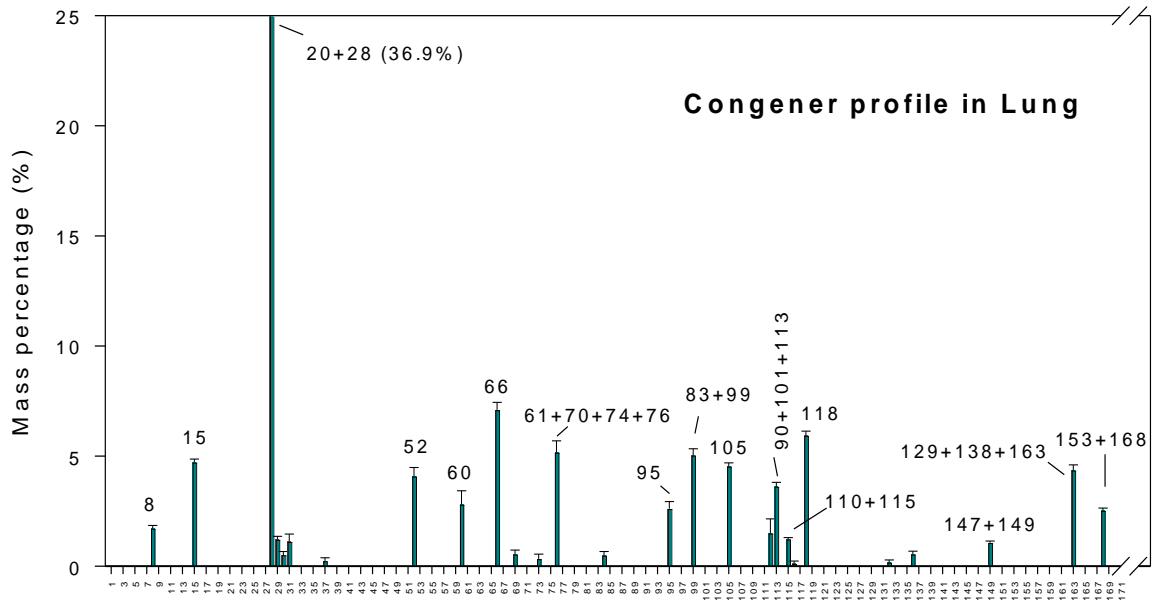
- Generation: 520 $\mu\text{g}/\text{m}^3$



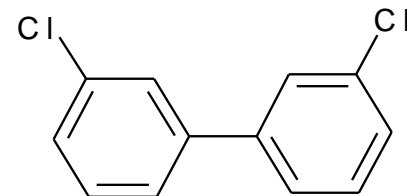
- A distinct profile of ~25 accumulated congeners in tissue

Tissue	Blood	Lung
4 wk PCB Exposed	12.88 ± 1.38*	67.19 ± 4.14**
Sham Exposed	2.30 ± 1.29	7.46 ± 0.98
Sentinels	2.65	6.85

ΣPCB in tissue after exposure (ng/g tissue weight)
 *p < 0.001, **p < 0.0001



Our rodent studies show complete uptake from the lung and rapid metabolism of inhaled PCB 11

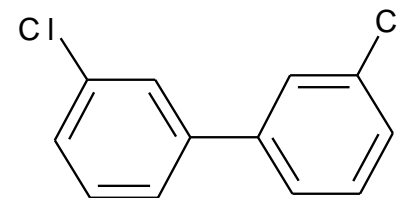


3,3'-Dichlorobiphenyl

- **¹⁴C-PCB 11 ADME study**
- Time course studies of absorption, distribution metabolism and excretion of ¹⁴C PCB11 and its metabolites were conducted and achieved a mass balance.
- Hu X, Adamcakova-Dodd A, Thorne, PS. The fate of inhaled ¹⁴C-labelled PCB11 and its metabolites *in vivo*. *Environ. Internat.*, 63:92-100, 2014.

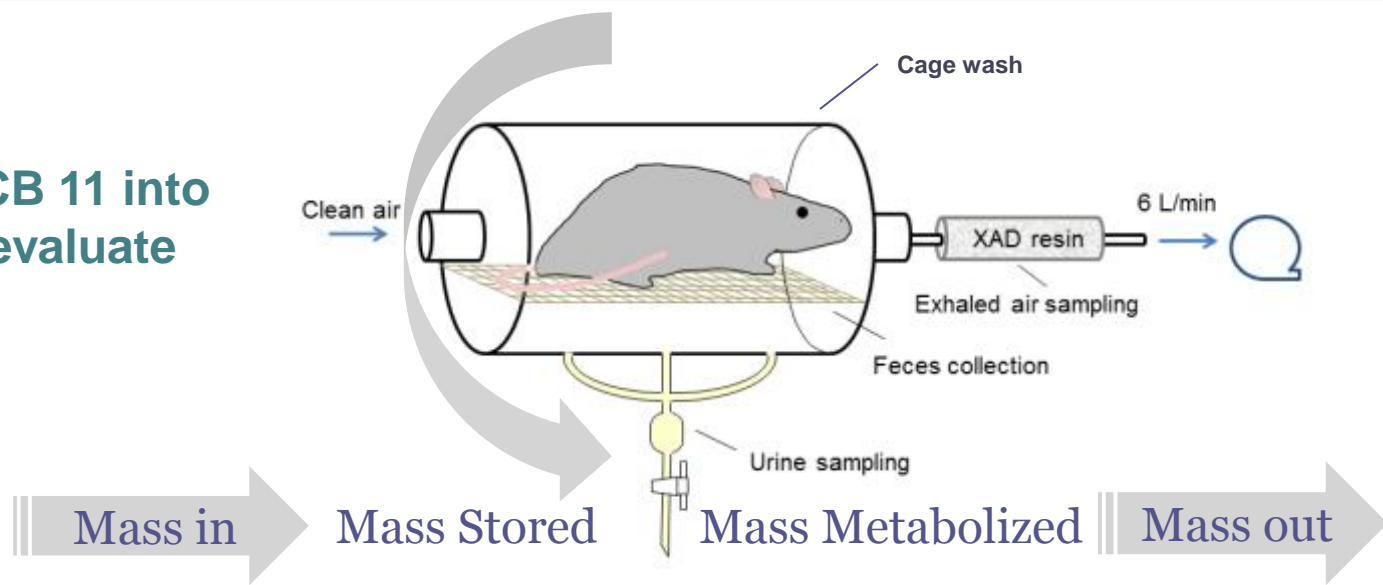
[¹⁴C]-PCB11 Study

3,3'-Dichlorobiphenyl



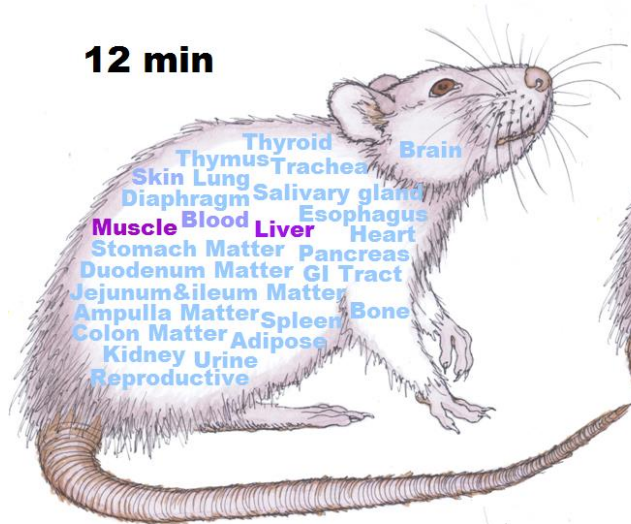
- Even though we find PCB 11 in the indoor air of every home and school, virtually nothing is known about its fate and toxicity
- Objective: To determine the fate of PCB 11 in rats
- Approach: build a mass balance model for PCB 11 and its metabolites

Instill [¹⁴C]-PCB 11 into the lung and evaluate the ADME

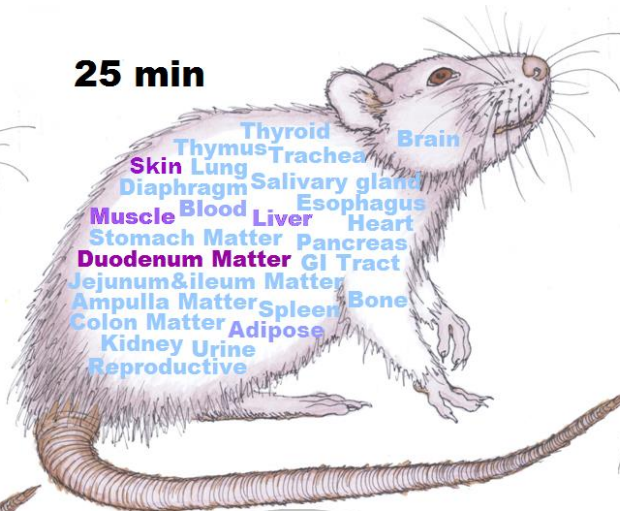


Heat Map of Radioactive PCB 11

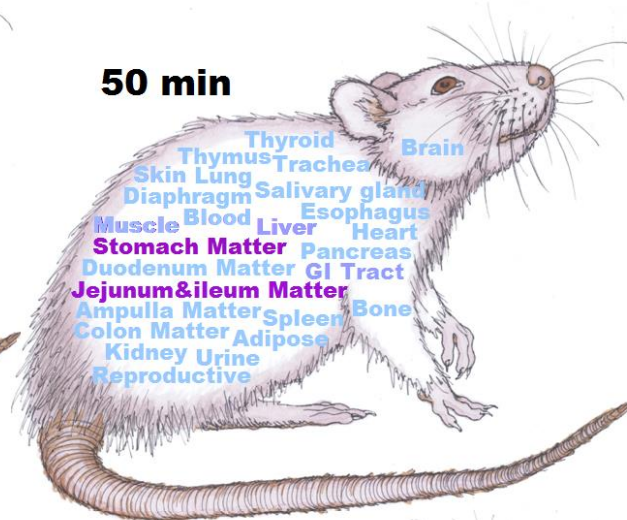
12 min



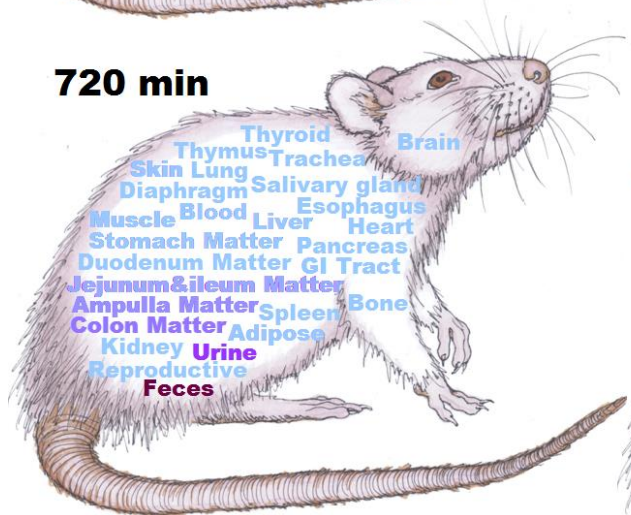
25 min



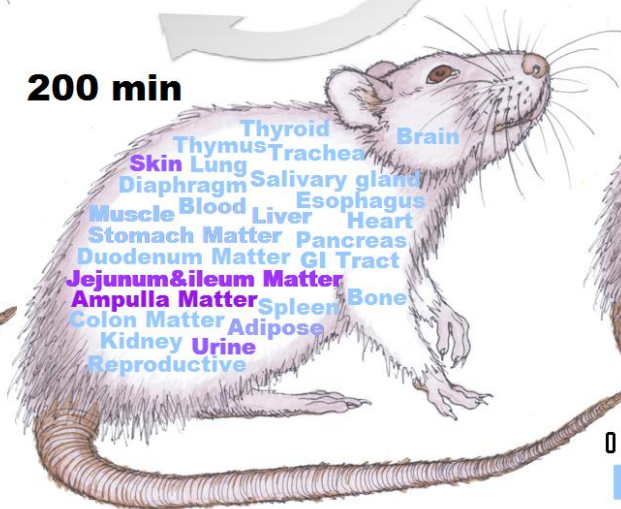
50 min



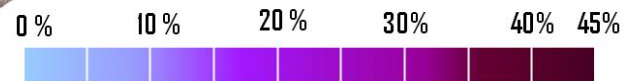
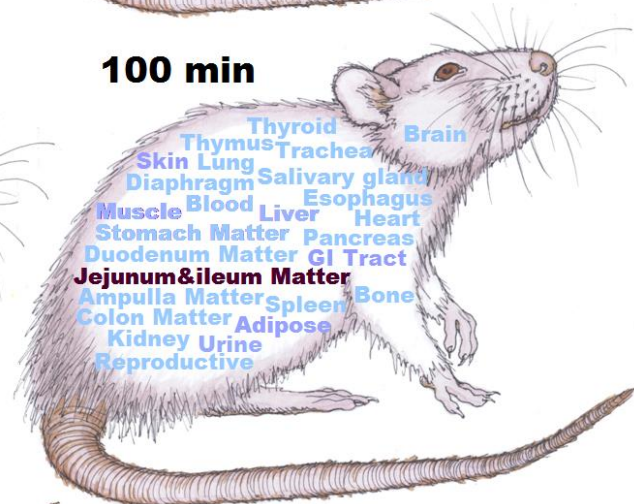
720 min



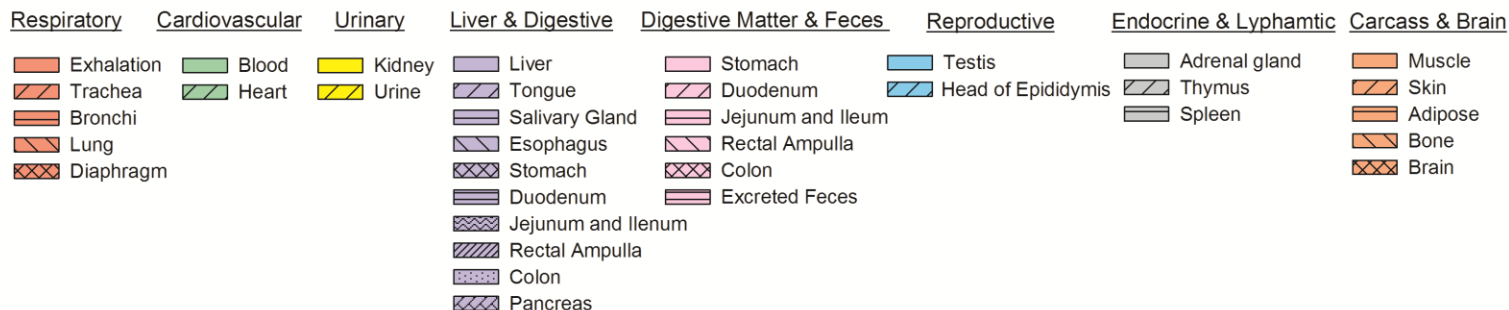
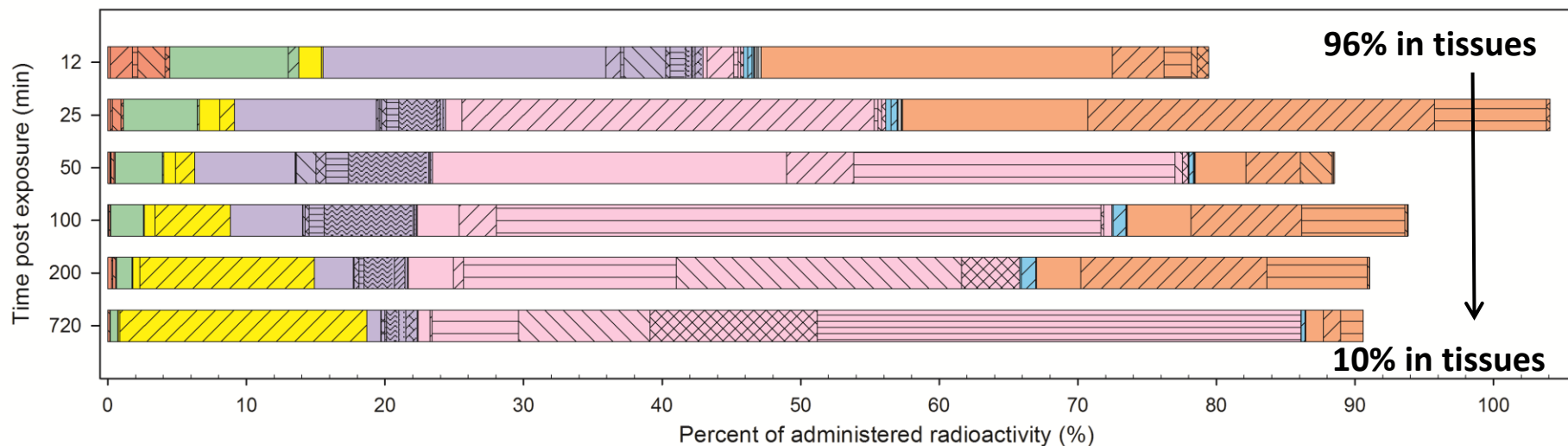
200 min



100 min

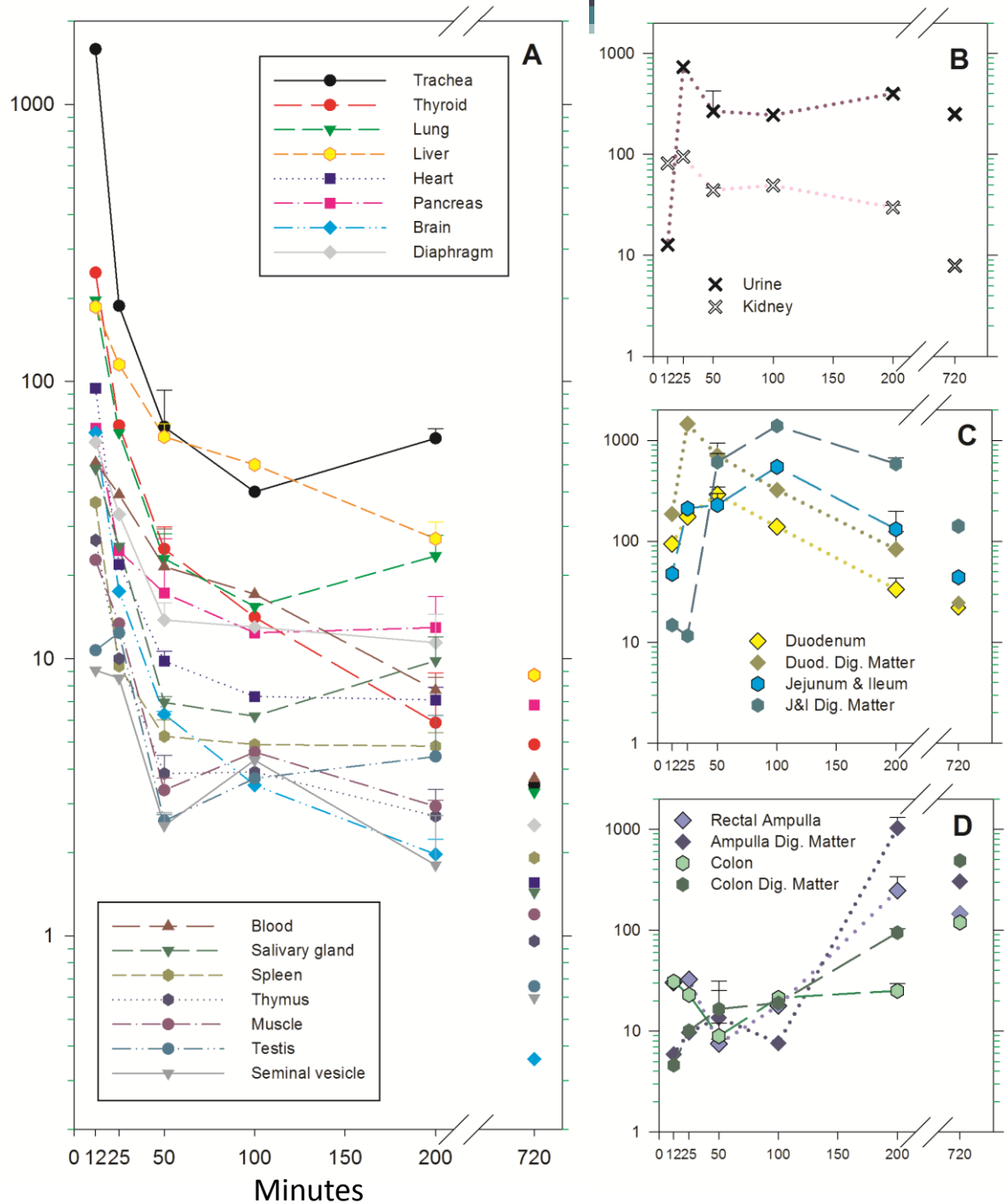


The majority of dose is excreted in hours



- Fecal elimination is the major pathway of excretion.
- Exhaled PCB 11 accounts for <0.2% of administered dose.
- Absorption of PCB in lung is complete.

[¹⁴C] concentration (dpm/mg wet weight)



Rapid elimination from most tissues

Phase	$t_{1/2-1}$	$t_{1/2-2}$
Trachea	9 min	2.6 hr
Thyroid	14 min	5.3 hr
Lung	13 min	3.7 hr
Liver	24 min	3.7 hr
Heart	12 min	3.9 hr
Pancreas	21 min	7.7 hr
Brain	12 min	2.7 hr
Diaphragm	18 min	3.9 hr
Blood	33 min	4.1 hr
Salivary gland	14min	4.3 hr
Spleen	15 min	6.3 hr
Thymus	14 min	4.7 hr
Muscle	14 min	6.4 hr
Testis	17 min	3.9 hr
Seminal vesicles	19 min	4.1 hr

Summary from PCB 11 animal studies

- Complete and fast uptake of inhaled PCB
 - PCB11 is 99.8% absorbed after lung exposure.
- Rapid distribution of PCB11
 - High tissue concentration of PCB11 at 12 min after exposure
 - Delayed uptake in adipose tissue and other fatty tissues (skin, epididymis)
- Extremely fast elimination of PCB11 and metabolites
 - 50% of dose excreted by 12 h
 - 37% of dose in intestinal digestive matter that was about to be excreted
 - The initial elimination phase is very short ($t_{1/2} = 10-30$ min)
 - **Biomarkers may demonstrate same-day exposures**
- Phase II metabolites dominate in systemic circulation
 - PCB11 and OH-PCB11s decay most rapidly to minimal levels within 25 min
 - **Phase II metabolites serve as better biomarkers of PCB11 exposure**



The AESOP Study

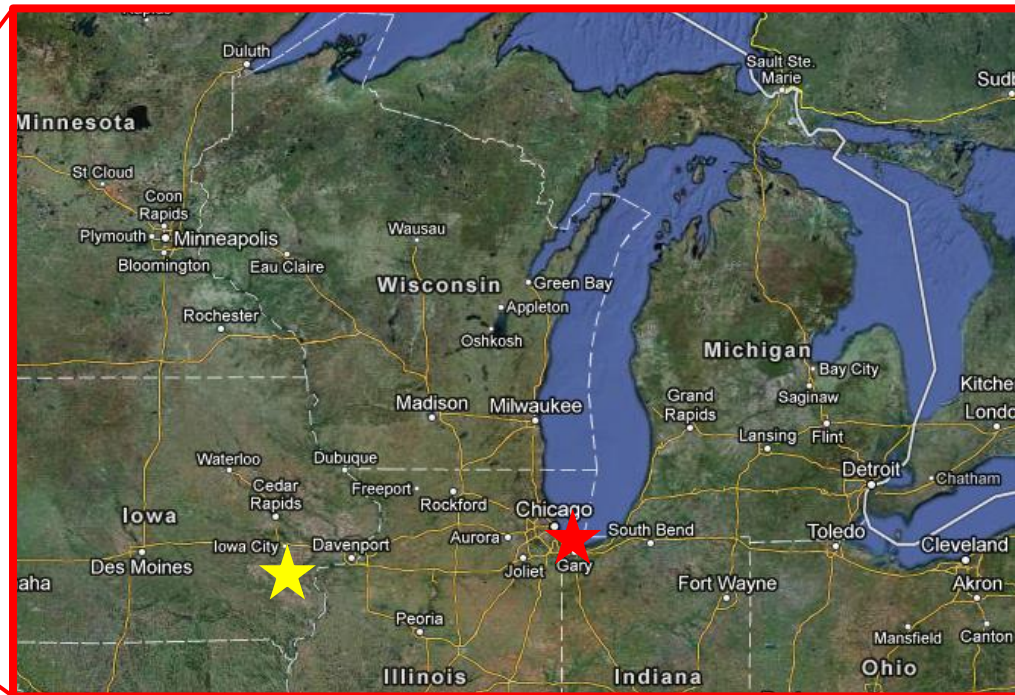
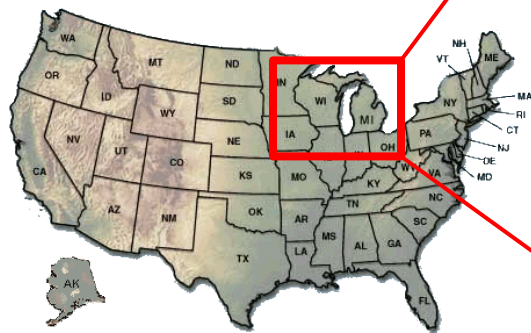
(Airborne Exposures to Semi-volatile Organic Pollutants)



- Community-based, two-cohort study of PCB exposures among adolescent children and their mothers

The AESOP Study

- Prospective cohort study of PCB exposures in school children and their mothers
- Focus on air exposures and lower chlorinated congeners
- Two communities:
 - **Columbus Junction**
 - **East Chicago**



East Chicago and Indiana Harbor and Ship Canal

IHSC dredging began Nov 2012 - IHSC is a source of PCBs

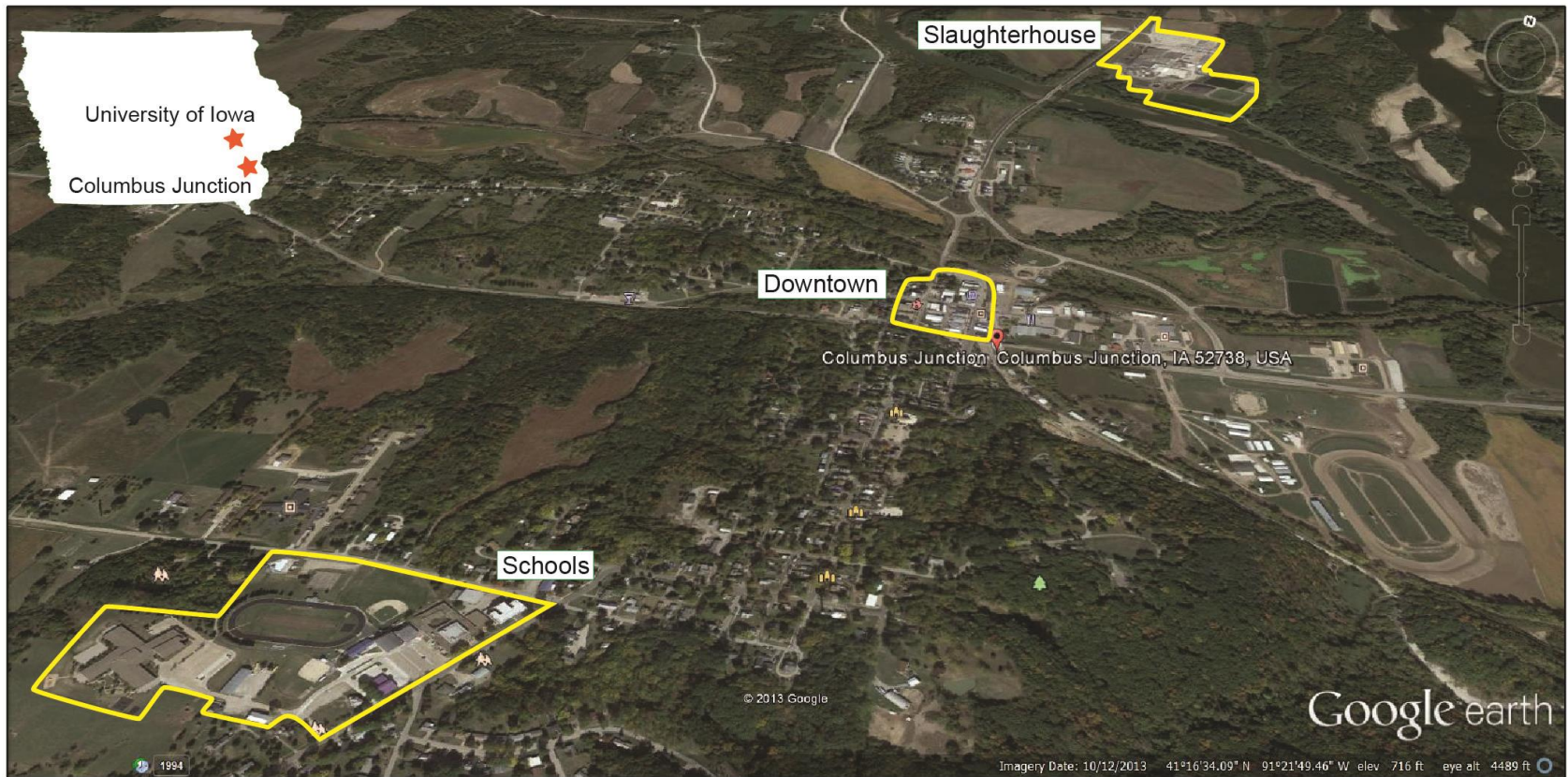


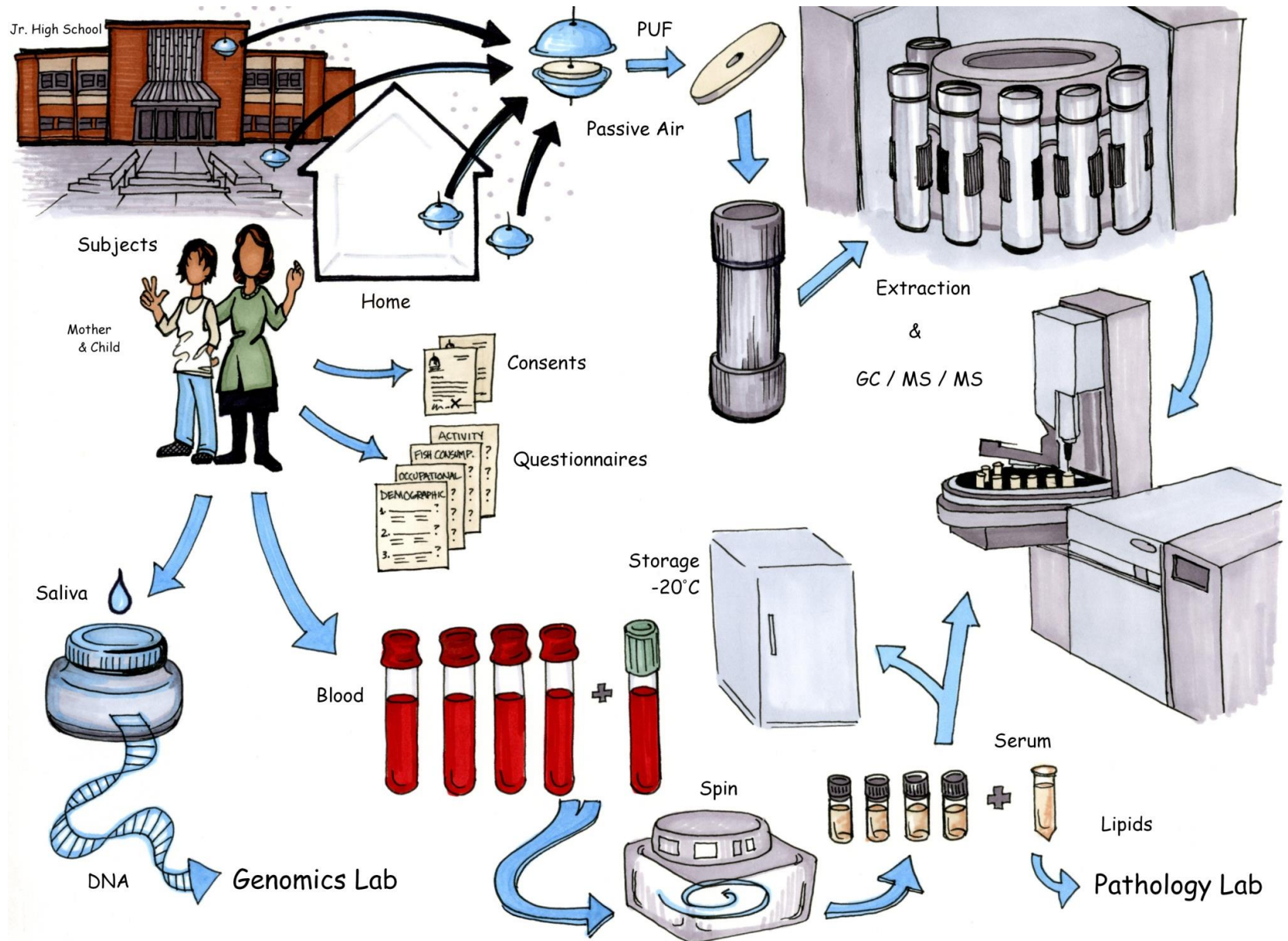
Columbus Community School District



Columbus Community Schools

Serving small rural towns and farm families





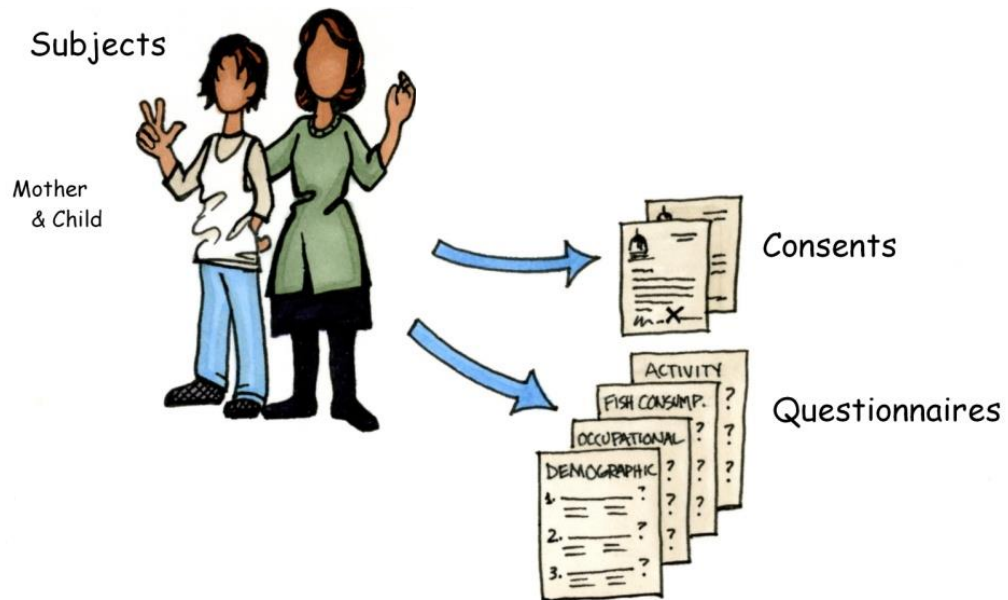
The AESOP Study Aims & Enrollment

1. Measure exposures of atmospheric PCBs at homes & schools in both cohorts.
2. Analyze blood and urine for PCBs and PCB metabolites.
3. Gather demographic, residential, occupational, activity and dietary information from subjects by questionnaire.
4. Utilize exposure and questionnaire data to develop an exposure model for the atmospheric PCB congeners.

Cohort	Location	Total	Households*	Children	Mothers
Urban	East Chicago	129	63	66 (35 girls)	63
Rural	Columbus Junction	135	61	74 (40 girls)	61
Total enrollment		264	124	140	124

*Household = home with enrolled child(ren) and his/her mother

AESOP Cohort Demographics



Demographics of the AESOP Study schools and communities.

School Data

Community Data

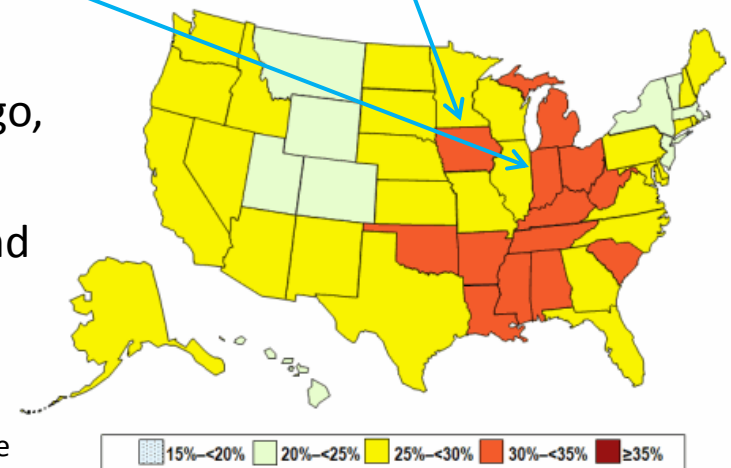
School and Community-level Data	East Chicago		Columbus Junction
	West Side Middle School	Block Middle School	Columbus Community Middle School
Grades	6-8	7-8	6-8
Year Built*	1976	1968	1918
Enrollment	497	493	237
Free/Discounted Lunch	82%	81%	63%
Hispanic	52.1%	42.0%	61.6%
White (non-Hispanic)	3.6%	0.4%	37.6%
African American	43.5%	56.0%	0.8%
Multirace/other	0.8%	1.6%	0%
Population	East Chicago (29,698)		Louisa Co. (11,278)
Median household income	\$27,700		\$47,900
Income below poverty line	35.0%		18.9%
Residents foreign born	14.7%, 91% Latino		20.9%, 97% Latino†
Education < high school	27.4%		34.2%
High school	36.0%		28.2%
Some college	23.8%		23.0%
College degree or higher	12.8%		14.6%

† Non-citizens are grossly under-represented in this figure.

Health status data for AESOP Study subjects (mean ± stddev or %)

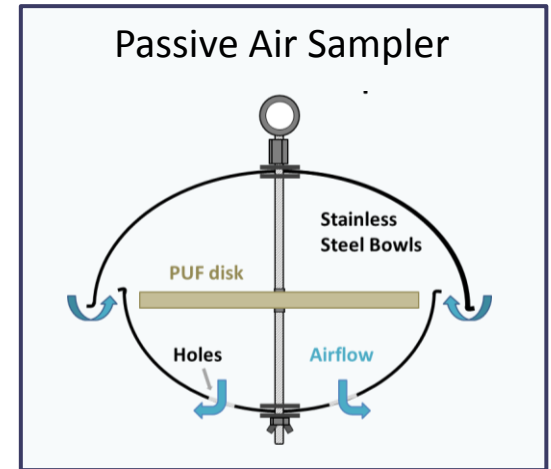
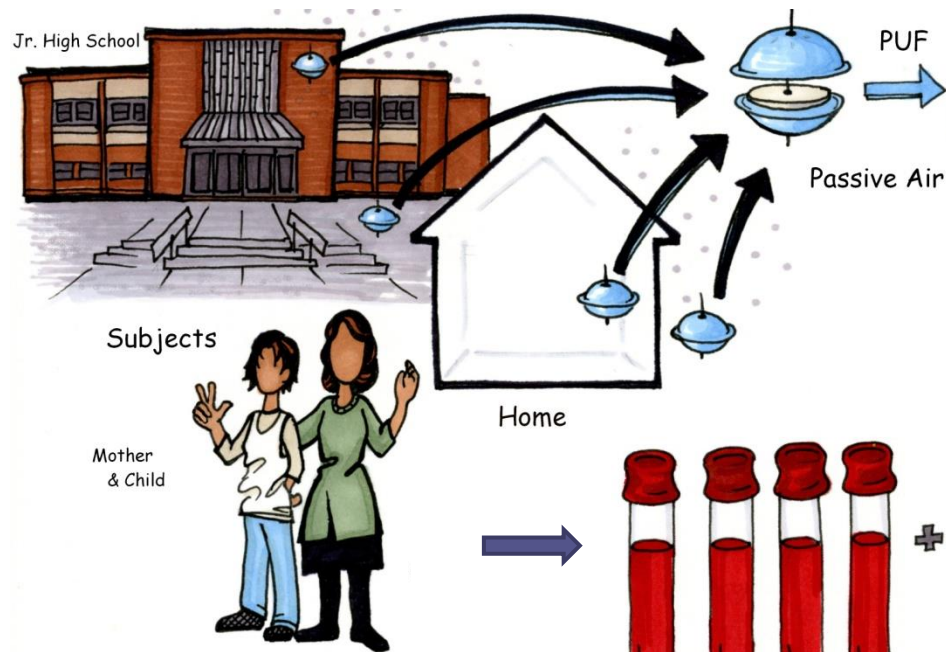
	East Chicago		Columbus Junction	
	Children	Mothers	Children	Mothers
Age at enrollment, yrs	13 ± 1	41 ± 6	13 ± 1	46 ± 4
Body Mass Index, kg/m ²	24.0 ± 6.6	33.7 ± 8.2	23.8 ± 5.3	30.4 ± 7.4
% Breastfed	33 %	--	68 %	--
Cholesterol, mg/dL	149 ± 26	179 ± 37	145 ± 25	170 ± 30
% Overweight (Obese)	33 (15)	90 (61)	36 (14)	70 (41)

- Rates of breastfeeding were low in East Chicago, especially among Black women
- The community is concerned about obesity and type II diabetes



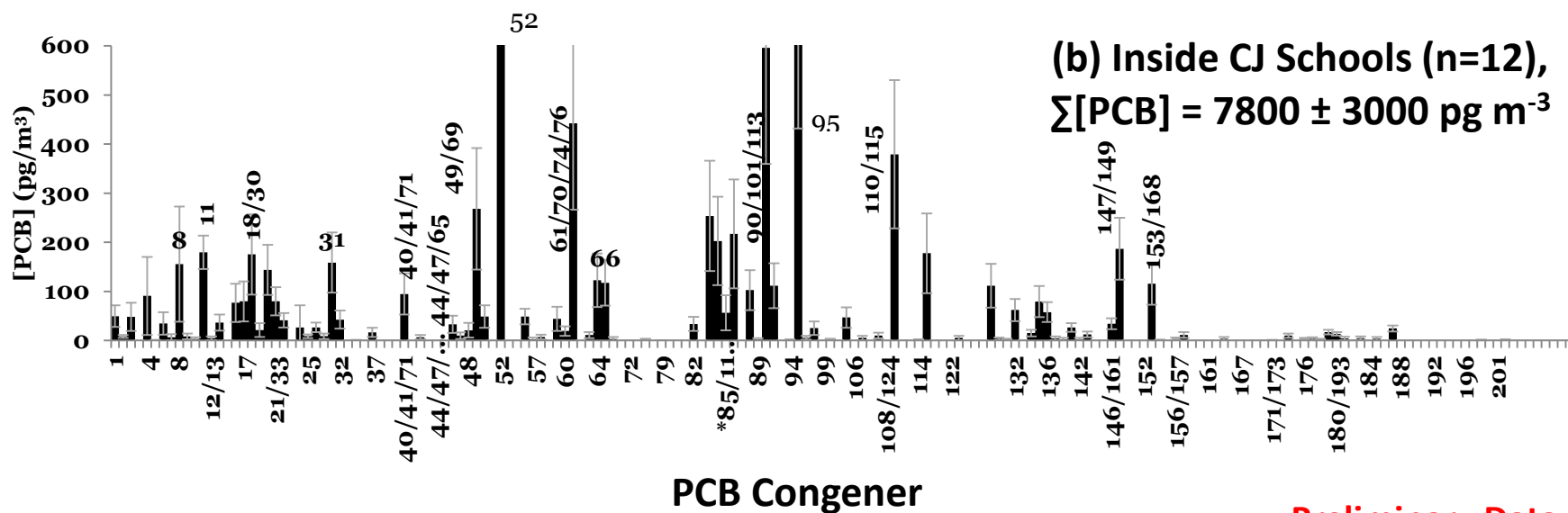
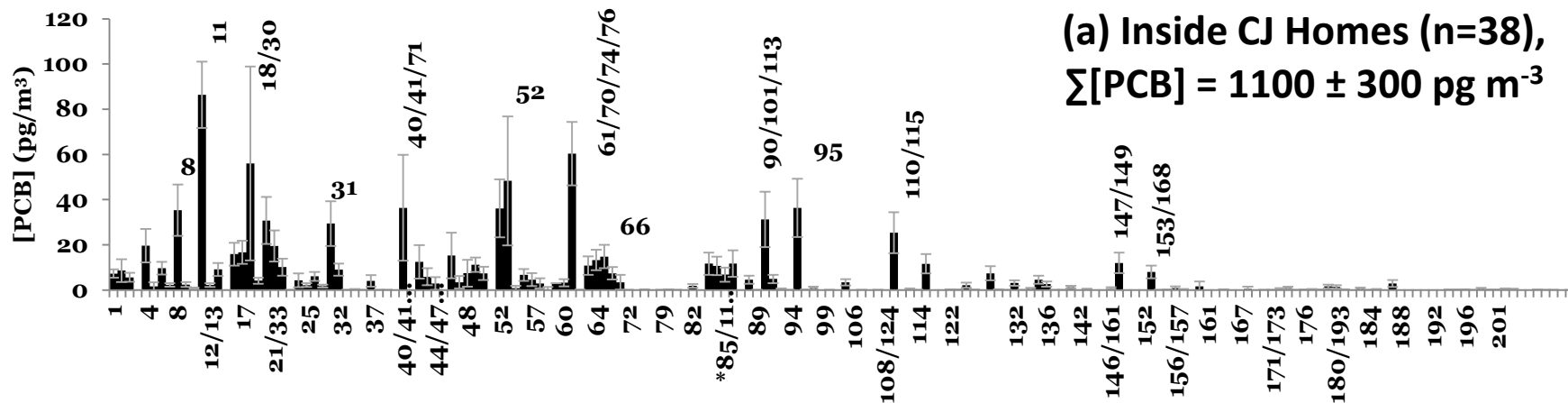
AESOP Exposure Measurements

Paired indoor and outdoor samples quarterly at homes and schools (N=3200)

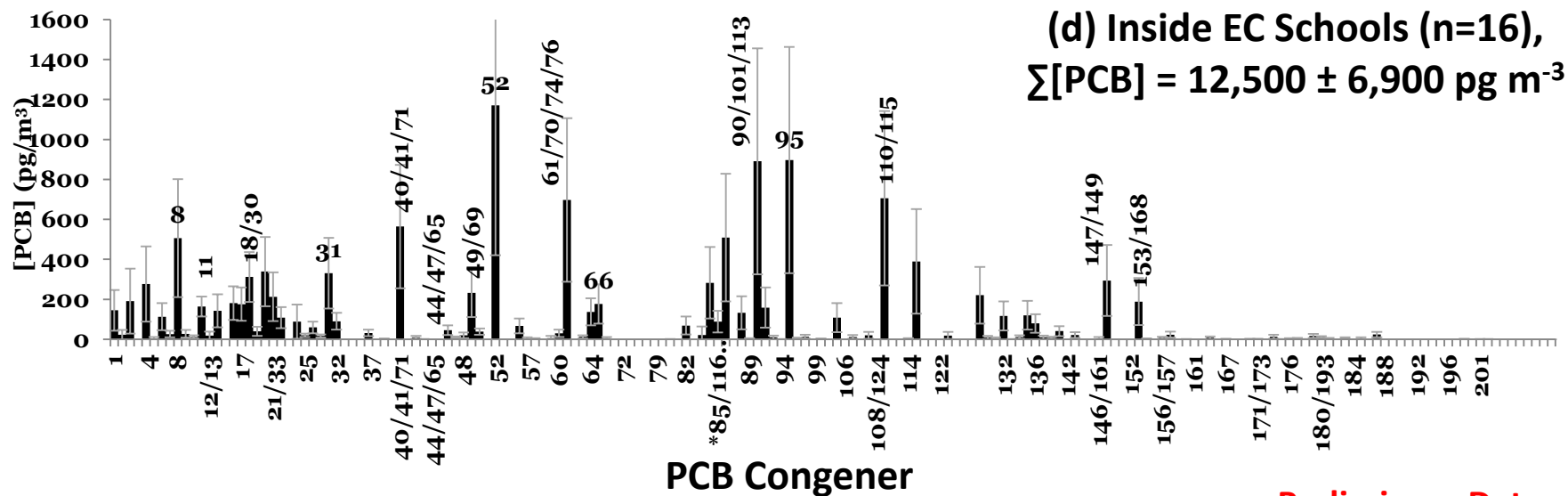
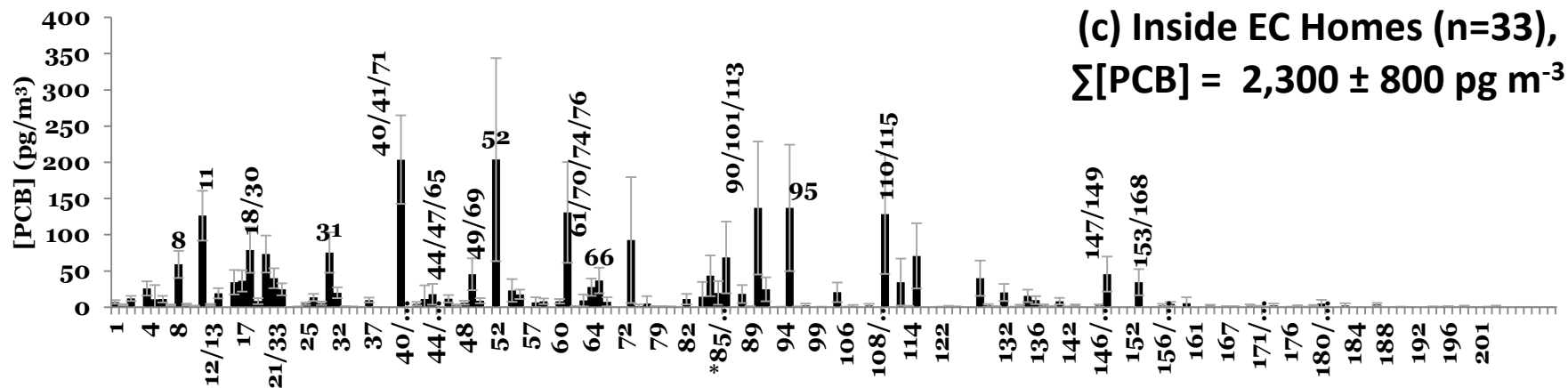


Blood collected annually in the home from mother and child (N=940)

Columbus Junction Schools have 7 times the Σ [PCB] of Homes



East Chicago Schools have 5 times the Σ [PCB] of Homes



Modeling Approach

$$Exp_{PCB_j} = \sum_{i=1}^3 T_i * Q * [PCB_j] [=] (\mu g yr^{-1})$$

Where Exp_{PCB_j} is PCB exposure for the j th congener,

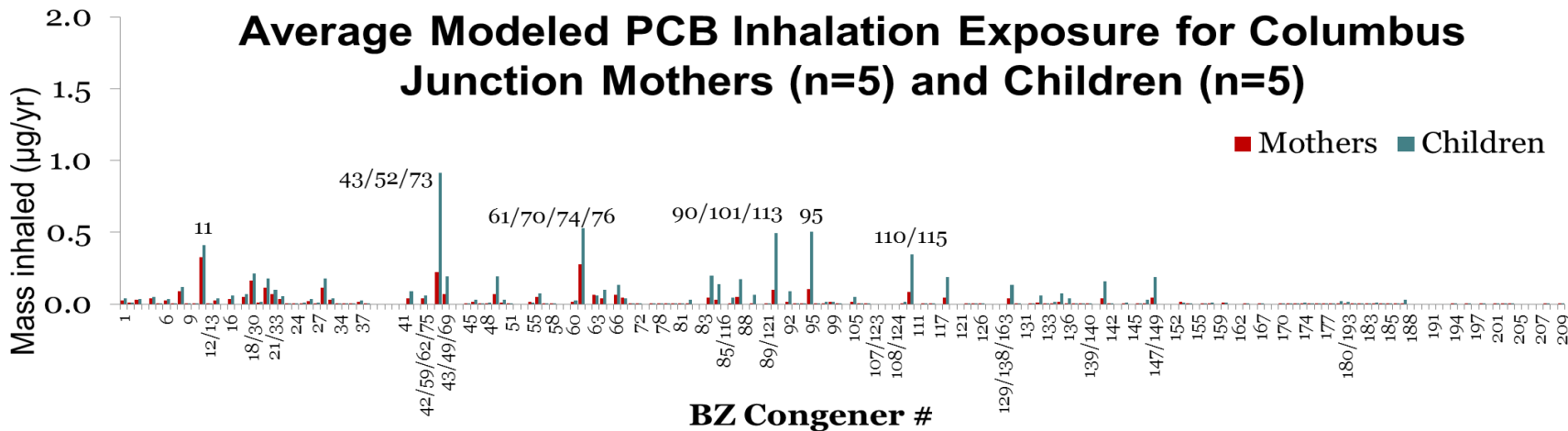
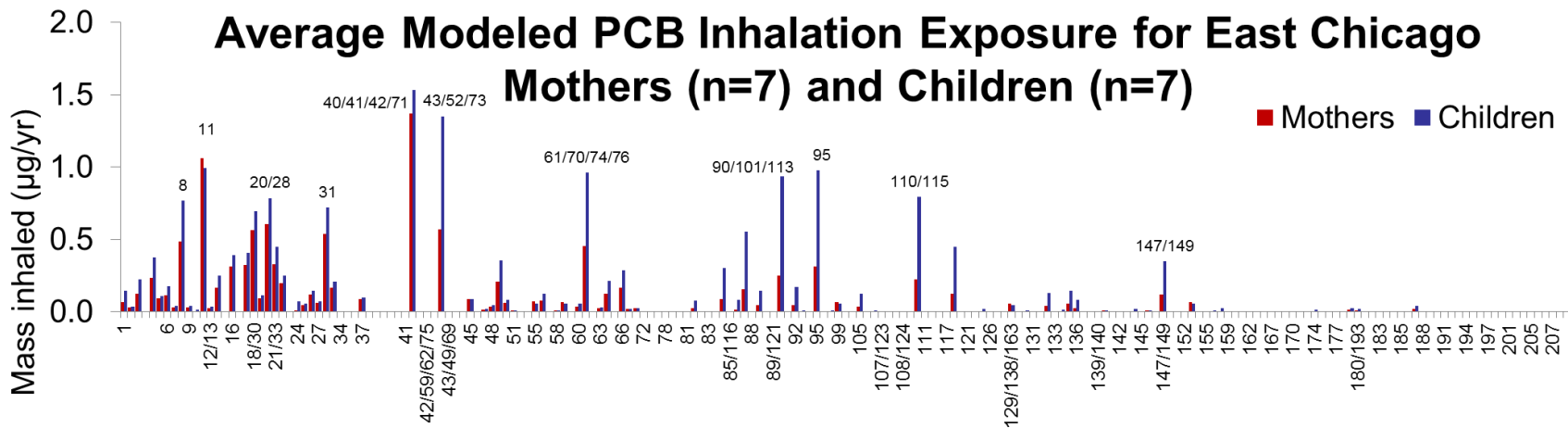
T_i is the time spent in location i in hours per year;

Q is the inhalation rate in $m^3 d^{-1}$; and

$[PCB]_j$ ($ng m^{-3}$) is the measured airborne concentration of PCB_j .

T_i values have been obtained for three locations (home, schools, and outside) using time-activity questionnaires completed each year.

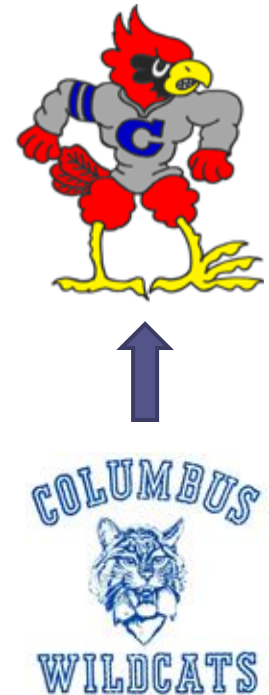
Q will be calculated based on age, sex, height, and race/ethnicity.



Average modeled PCB inhalation exposure for EC children and mothers average 20.1 µg/yr and 13.2 µg/yr. CJ children and mothers average 7.4 µg/yr and 3.0 µg/yr. Inhalation exposure for CJ subjects is less than half that of modeled exposure for EC subjects.

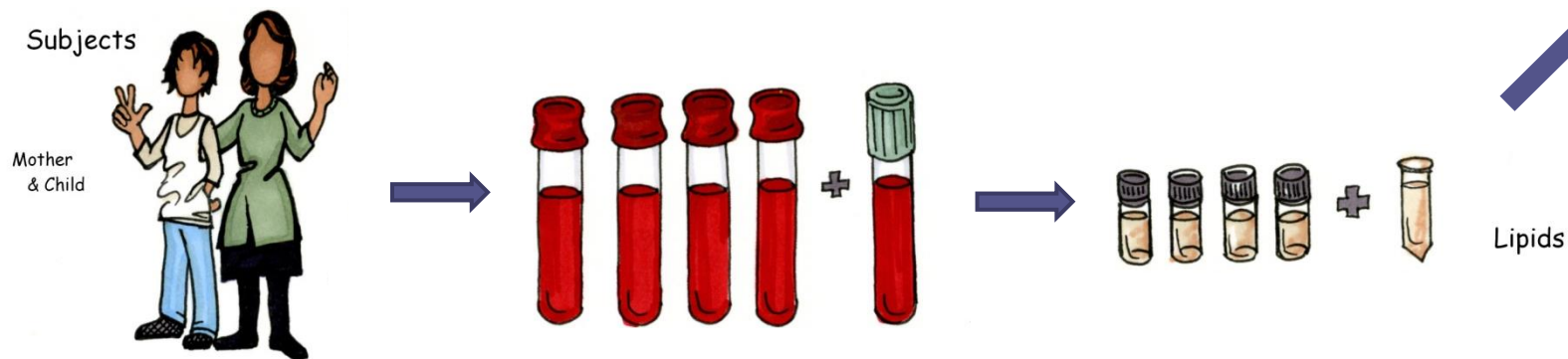
Indoor Air PCB Concentrations in Homes

- Median \sum PCB indoor air concentrations for EC homes (3.37 ng m^{-3}) were significantly higher ($p=0.05$) than for CJ homes (1.05 ng m^{-3})
- One outlier home in EC had \sum PCB concentrations of 164 ng m^{-3}
- Two outlier homes in CJ had \sum PCB concentrations of 16 ng m^{-3} and 23 ng m^{-3}
- PCB inhalation exposure for individuals in these homes were 20 to 50 times greater than the median PCB inhalation exposures in EC, and CJ, respectively.

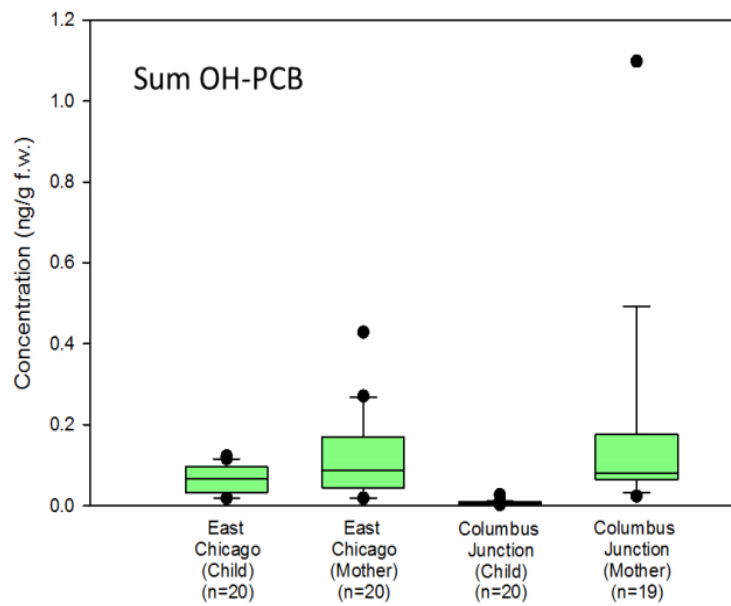
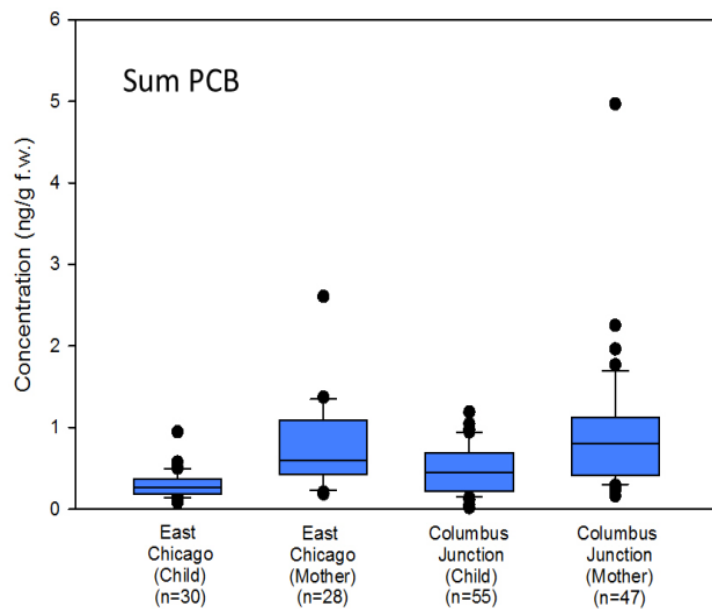


Evaluation of Lipids, PCBs, OH-PCBs

- 30 mL blood collected **annually** from each subject
- Cholesterol, triglycerides, HDL
- 209 PCB congeners
- 64 OH-PCBs
- Urine collection next year → PCB sulfates

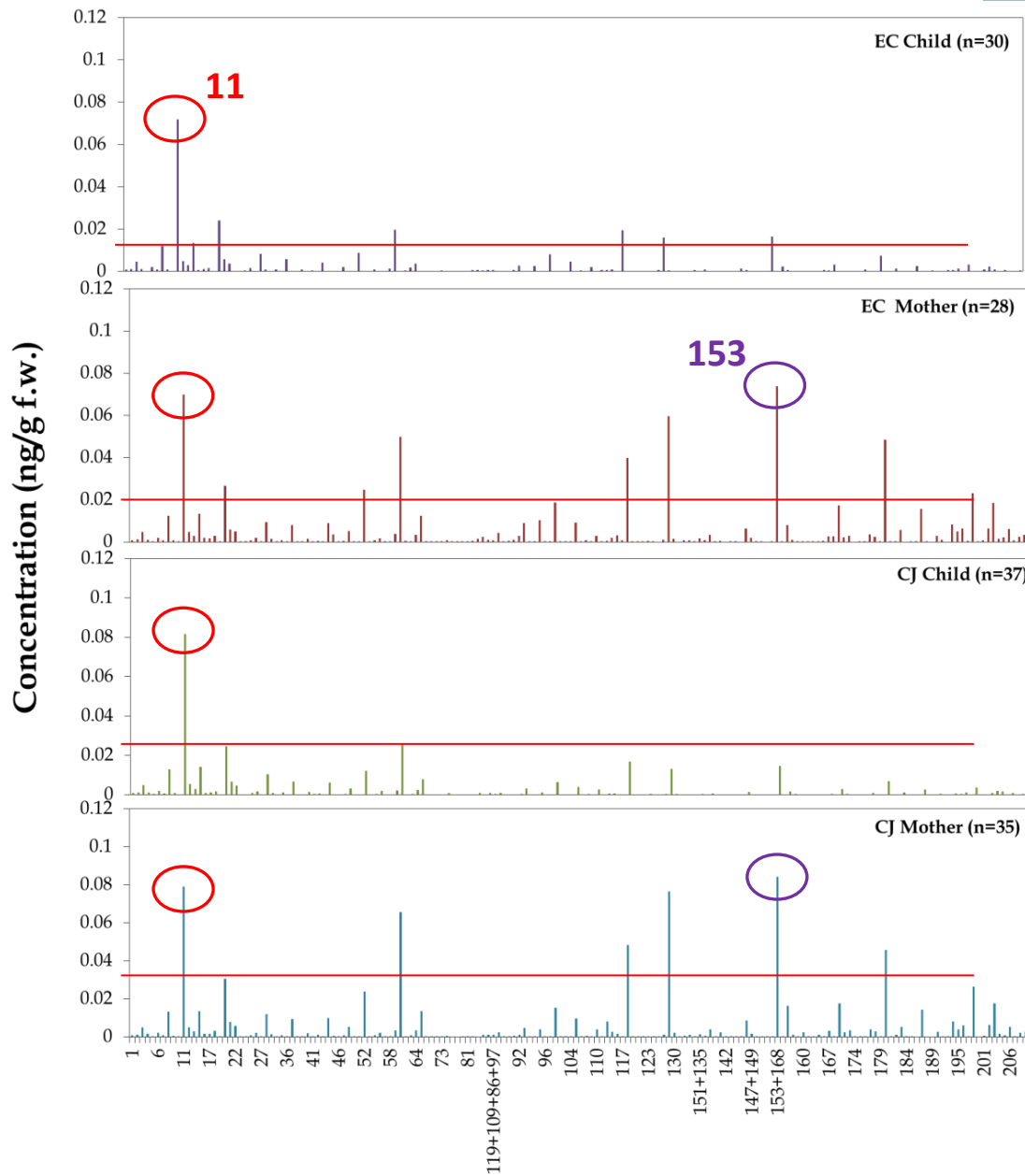


Concentrations of the sum of all detected PCBs (left) and OH-PCBs (right). Mothers > Children. Several individuals have values well above the 95% percentile (circles)



Most frequently detected congeners (red=100% detection)

	East Chicago		Columbus Junction	
	Children	Mothers	Children	Mothers
	153+168	153+168	153+168	153+168
	138+163+129	138+163+129	138+163+129	193+180
	193+180	193+180	193+180	203
Children are Enriched with Lower chlorinated PCBs	11	203	15	170
	15	187	3	146
	8	202	2	137
	3	137	11	138+163+129
	2	167	14	198+199
	28+20	118	146	156+157



PCB Congeners in Serum

A total of 174 PCB congeners were detected in the samples

Conclusions from the AESOP Study

- PAS facilitate exposure assessment for mono- to hexa-chlorinated PCBs
- Children & adults have significant inhalation exposures
- Older schools represent a 10-fold higher source of semi-volatile PCBs than most homes
- Children's sera are enriched with lower chlorinated PCBs compared to their mothers
- PCB 11, a non-Aroclor, is among the highest serum PCBs and reflects current exposure
- PCB 153 is high in adults but low in children and reflects legacy exposure



The AESOP Study

- It takes a village:

AESOP Study Team:

Jeanne DeWall, Study Coordinator

Barb Mendenhall, Nancy Morales, Bilingual Field Staff

Keri C. Hornbuckle, Analytical Core Director & Co-Investigator

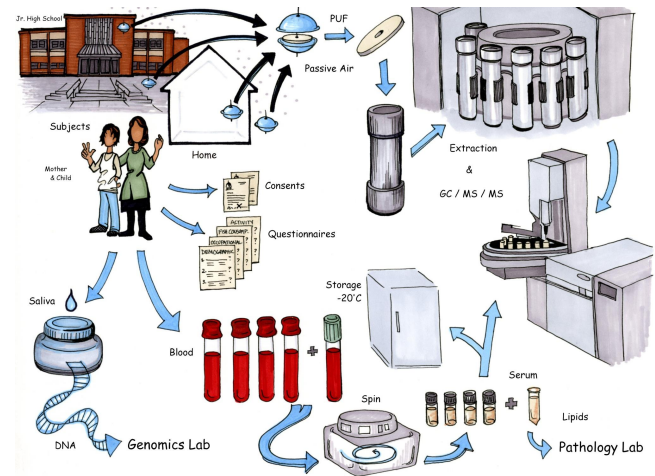
Rachel Marek, Wen Xin Koh, Blood Analyses

Matt Ampleman, Air & Questionnaire Data Analysis

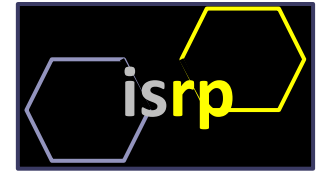
Andres Martinez, Dingfei Hu, Air Analyses

Kai Wang, Mike Jones, Biostatistics

Craig Just, David Osterberg, Comm. Outreach



Acknowledgements



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