

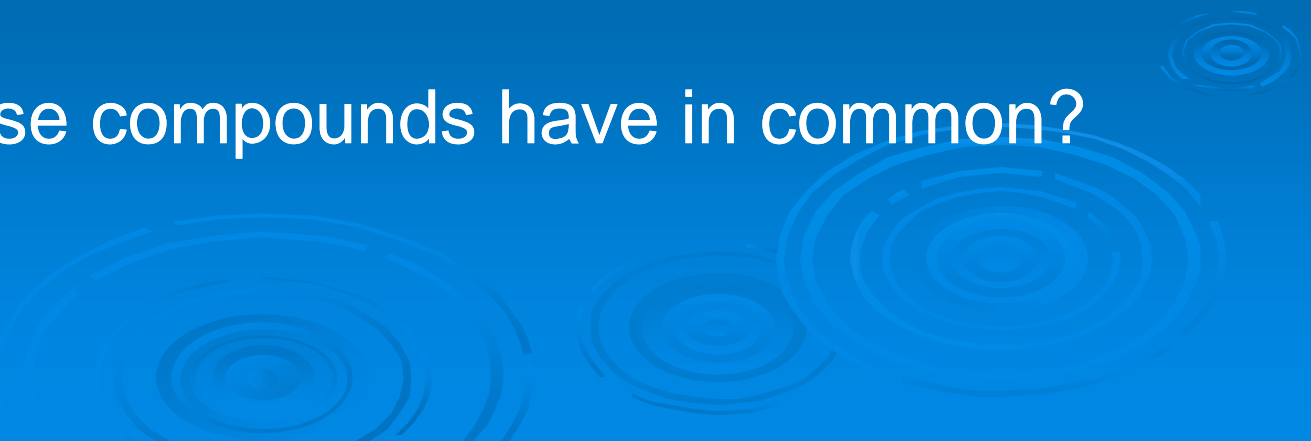
Assessing Human Exposure to Halogenated Compounds

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Assistant Professor

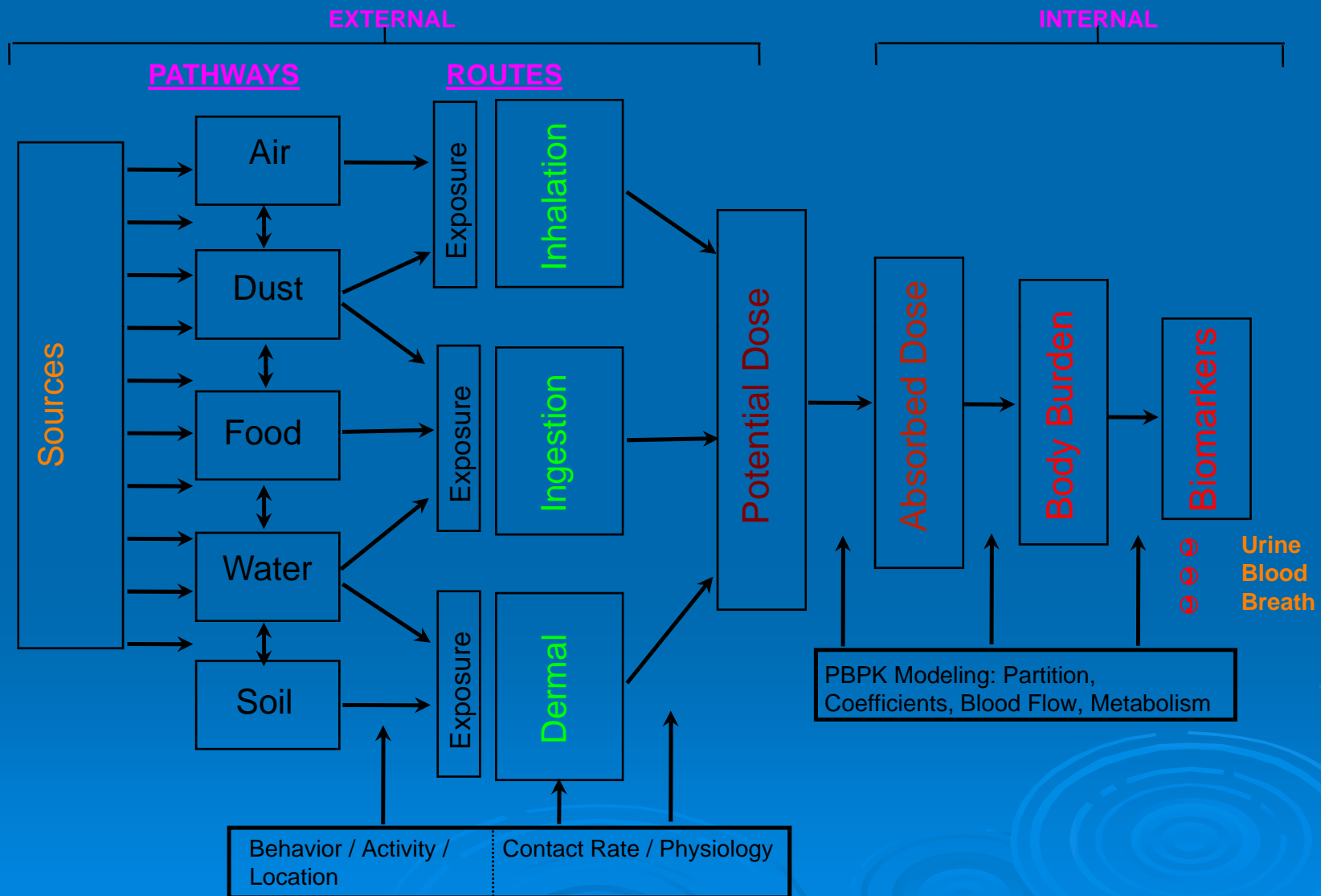
Dept. Environmental and Occupational Health
The State University of New York
Downstate Medical Center

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Green Science Policy Symposium
The Fire Retardant Dilemma: Part VII
UC Berkeley

Presentation Outline

- Issues in assessment of human exposure
 - Triclosan/triclocarban
 - Background/usage
 - Environmental occurrence
 - Exposure and epidemiologic data
 - Toxicology
 - Ongoing SUNY Exposure Study
 - PBDEs
 - What do these compounds have in common?
- 

Exposure Assessment is Multi-Dimensional



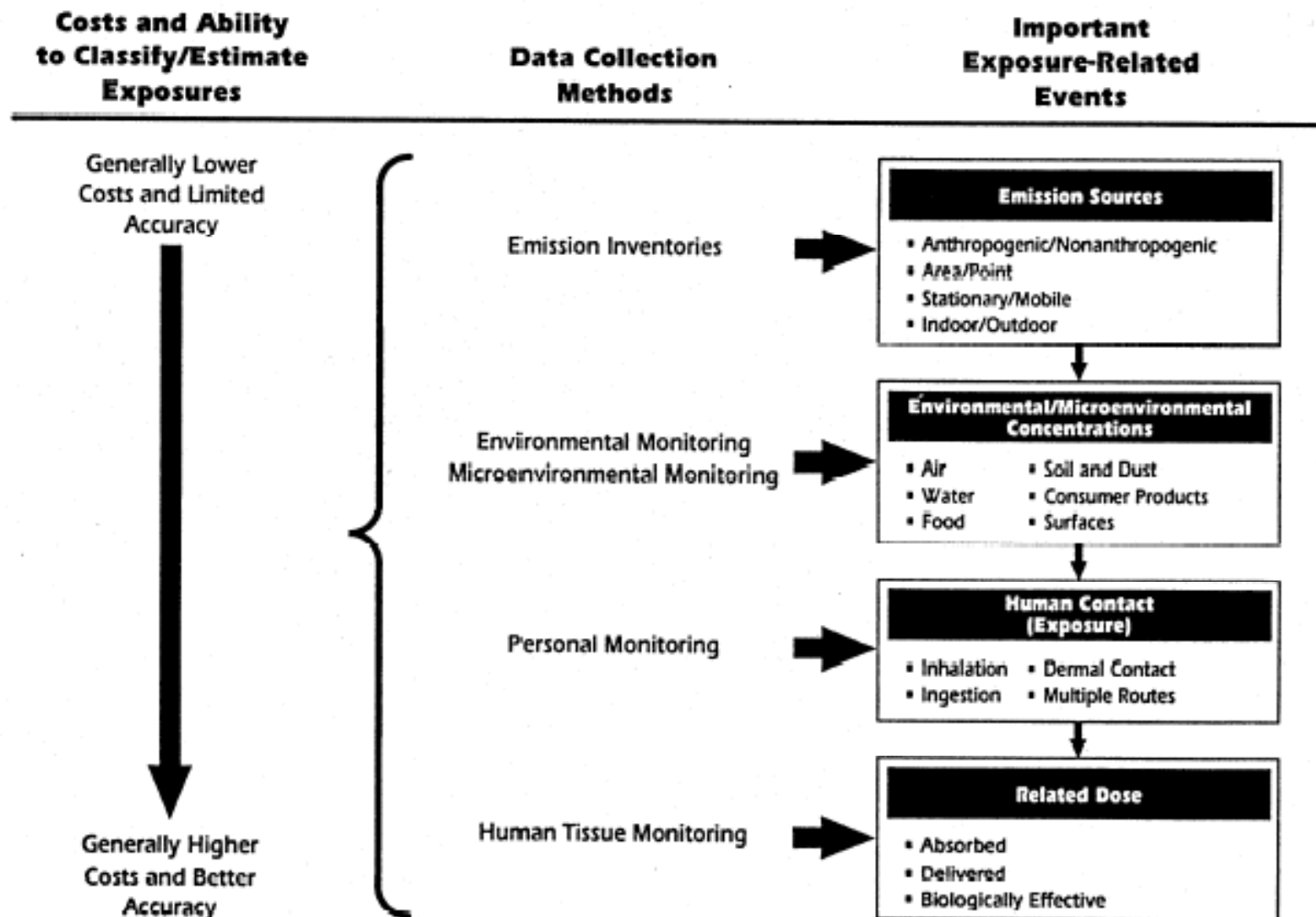
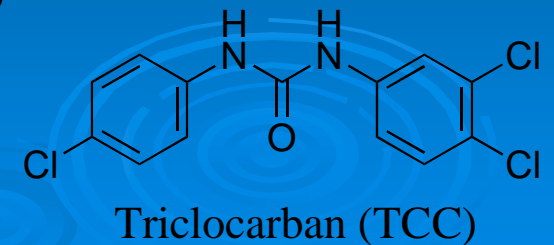
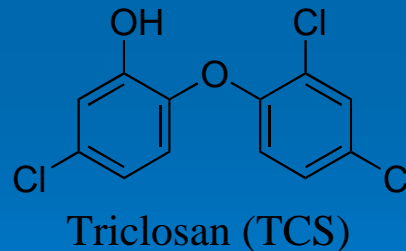


FIGURE 3. A comparison of costs and ability to classify/estimate exposures for selected data collection methods (Sexton et al., 1993b).

Triclosan (TCS) and Triclocarban (TCC)

- TCS is a chlorinated aromatic compound with functional groups representative of both phenols and ethers
- TCS is a biocide-has multiple “non-specific” mechanisms of action and numerous cellular targets
- It is an antibacterial used to prevent transmission of disease causing micro-organisms
- TCC is a similarly used antimicrobial additive, less is known about this compound
- TCC co-occurs with TCS: similar properties, method of disposal



List of Products Containing Triclosan

SOAP: Dial® Liquid Soap; Softsoap® Antibacterial Liquid Hand Soap; Tea Tree Therapy™ Liquid Soap; Provon® Soap; Clearasil® Daily Face Wash; Dermatologica® Skin Purifying Wipes; Clean & Clear Oil Free Foaming Facial Cleanser; DermaKleen™ Antibacterial Lotion Soap; Naturade Aloe Vera 80® Antibacterial Soap; CVS Antibacterial Soap, pHisoderm Antibacterial Skin Cleanser, Dawn® Complete Antibacterial Dish Liquid, Ajax® Antibacterial Dish Liquid.

DENTAL CARE: Colgate Total®; Breeze™ Triclosan Mouthwash; Reach® Antibacterial Toothbrush; Janina Diamond Whitening Toothpaste

COSMETICS: Supre® Café Bronzer™; TotalSkinCare Makeup Kit; Garden Botanika® Powder Foundation; Mavala Lip Base; Jason Natural Cosmetics; Blemish Cover Stick; Movate® Skin Lightening Cream HQ; Paul Mitchell Detangler Comb, Revlon ColorStay LipSHINE Lipcolor Plus Gloss, Dazzle

DEODORANT: Old Spice High Endurance Stick Deodorant, Right Guard Sport Deodorant

Queen Helene® Tea Tree Oil Deodorant and Aloe Deodorant; Nature De France Le Stick Natural Stick Deodorant; DeCleor Deodorant Stick; Epoch® Deodorant with Citrisomes; X Air Maximum Strength Deodorant

OTHER PERSONAL CARE PRODUCTS: Gillette® Complete Skin Care MultiGel Aerosol Shave Gel; Murad Acne Complex® Kit, ®; Diabet-x™ Cream; T.Taio™ sponges and wipes, Aveeno Therapeutic Shave Gel.

FIRST AID: SyDERMA® Skin Protectant plus First Aid Antiseptic; Solarcaine® First Aid Medicated Spray; Nexcare™ First Aid, Skin Crack Care; First Aid/Burn Cream; HealWell® Night Splint; 11-1X1: Universal Cervical Collar with Microban

KITCHENWARE: Farberware® Microban Steakknife Set and Cutting Boards; Franklin Machine Products FMP Ice Cream Scoop SZ 20 Microban; Hobart Semi-Automatic Slicer; Chix® Food Service Wipes with Microban; Compact Web Foot® Wet Mop Heads

COMPUTER EQUIPMENT: Fellowes Cordless Microban Keyboard and Microban Mouse Pad

CLOTHES: Teva® Sandals; Merrell Shoes; Sabatier Chef's Apron; Dickies Socks; Biofresh® socks

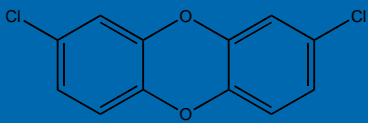
CHILDRENS TOYS: Playskool®: Stack 'n Scoop Whale, Rockin' Radio, Hourglass, Sounds Around Driver, Roll 'n Rattle Ball, Animal Sounds Phone, Busy Beads Pal, Pop 'n Spin Top, Lights 'n Surprise Laptop

OTHER: Bionare® Cool Mist Humidifier; Microban® All Weather Reinforced Hose; Thomasville® Furniture; Deciguard AB Ear Plugs; Bauer® 5000 Helmet; Aquatic Whirlpools; Miller Paint Interior Paint; QVC® Collapsible 40-Can Cooler; Holmes Foot Buddy™ Foot Warmer, Blue Mountain Wall Coverings, California Paints®, EHC AM-Rail Escalator Handrails, Dupont™ Air Filters, Durelle™ Carpet Cushions, Advanta One Laminate Floors, San Luis Blankets, J Cloth® towels. JERMEX mops

Environmental and Human Health Concerns

Degradates

(including chloroform)



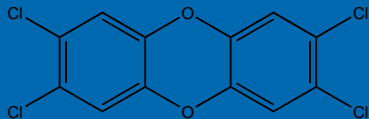
Persistent
Environmental
Contaminant



Cross-resistance
to Antibiotics



Impurities



Triclosan

Bioaccumulation



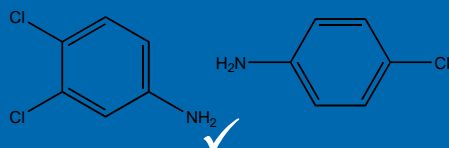
~~Acts as Carcinogen,
Mutagen or
Teratogen~~

Endocrine Disruption



Environmental and Human Health Concerns

Degradates



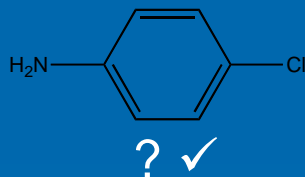
Persistent
Environmental
Contaminant



Cross-resistance
to Antibiotics

?

Impurities



Triclocarban

Bioaccumulation

? ✓

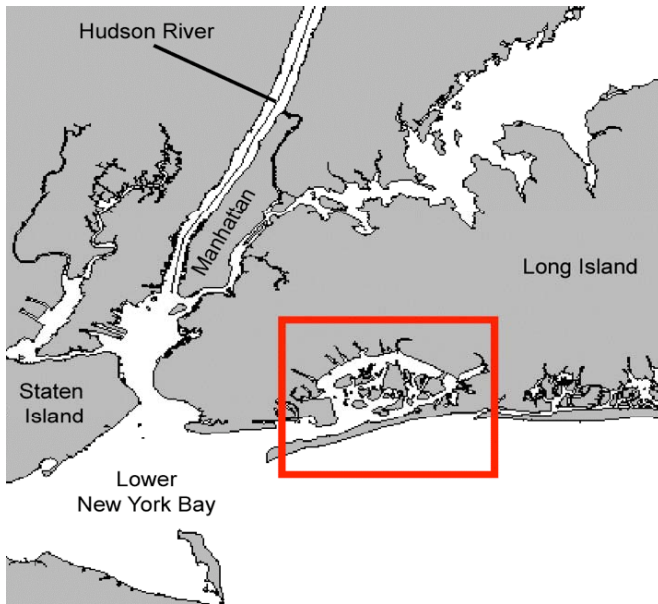
Acts as Carcinogen,
Mutagen or
Teratogen
(Indirectly through metabolites) ?

Endocrine Disruption

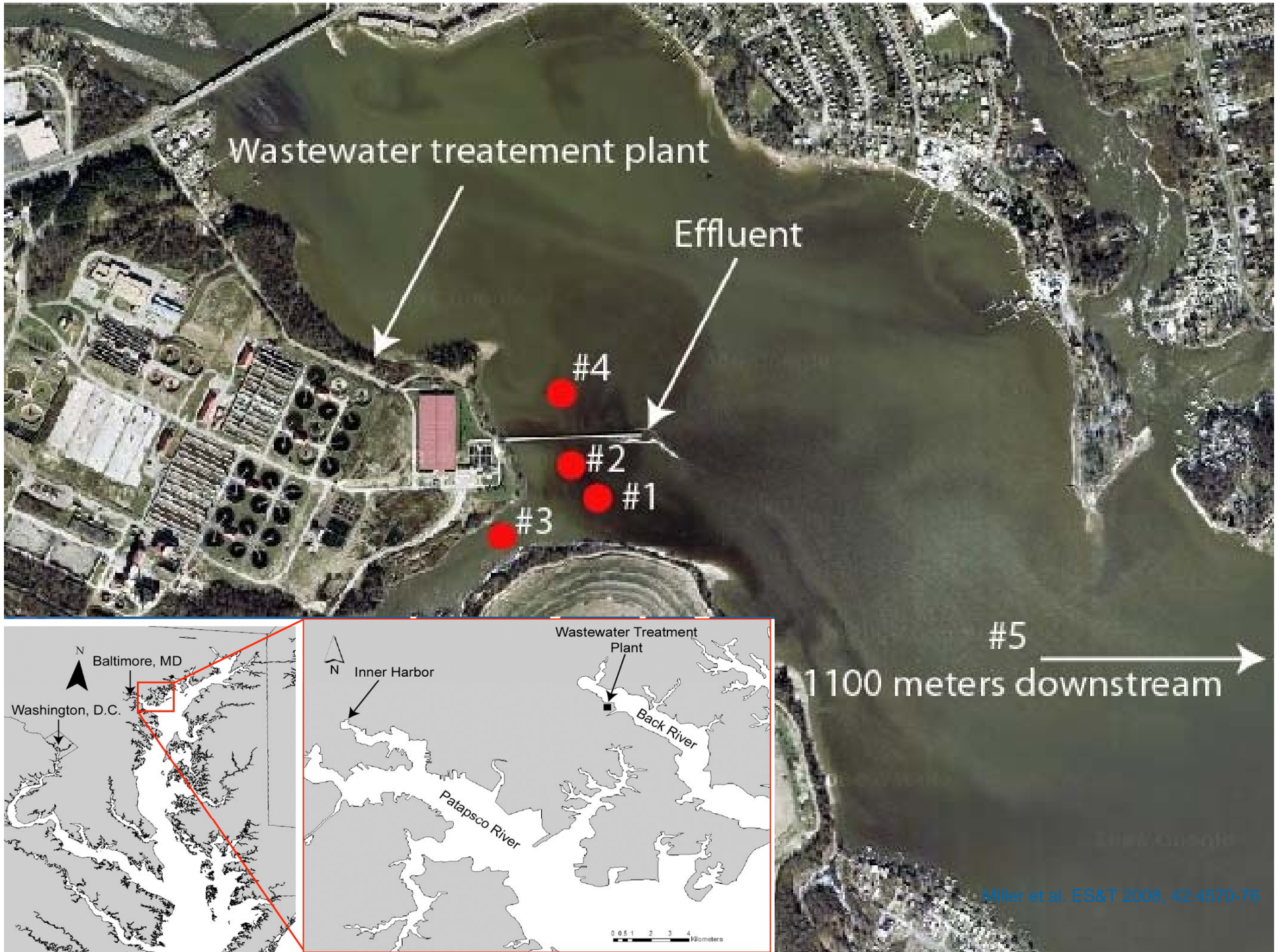


Wastewater Treatment Plants are Principal Sources of Antimicrobials in the U.S. Environment

- Activated sludge WWTP
- 600 ML/D (180 MGD)
- Population served: 1.3 M

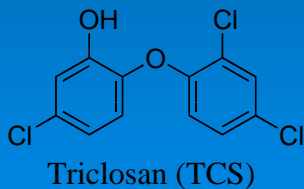
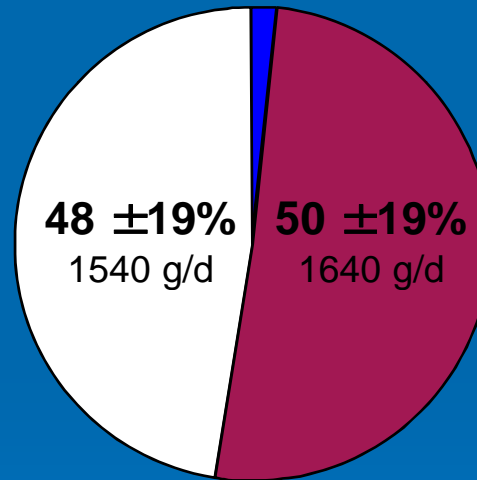


Environmental Persistence: Empirical Evidence



Fate of Triclosan in Activated Sludge WWTP

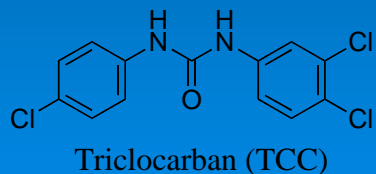
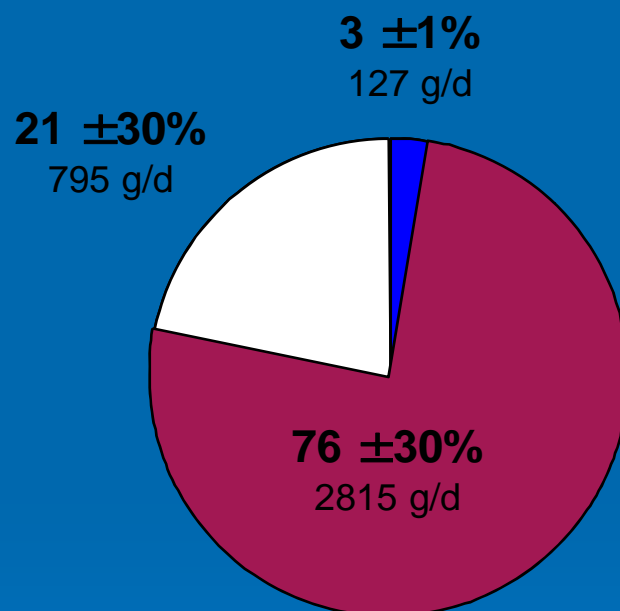
$2 \pm 1\%$
55 g/d



- Mass in effluent
- Mass in sludge
- Mass transformed/lost

Heidler & Halden Chemosphere 66(2):362-9 (2007)

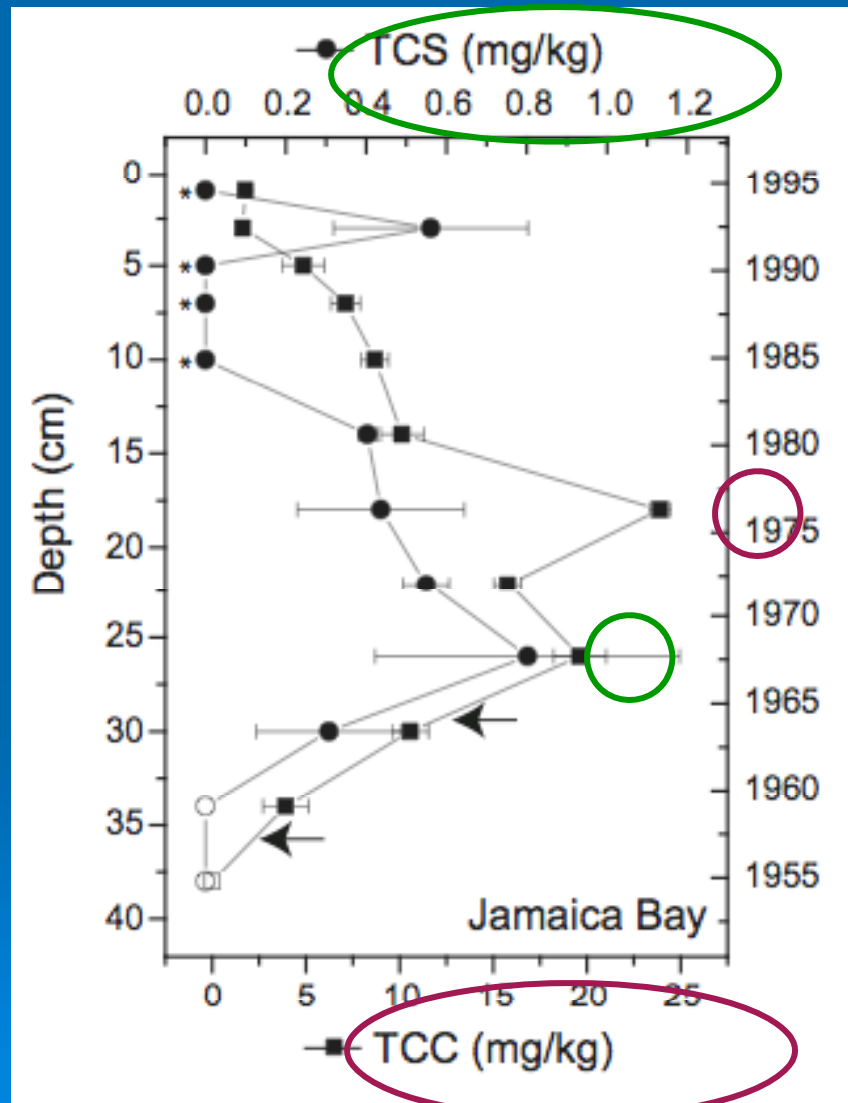
Fate of Triclocarban During Activated Sludge Treatment



- Mass in effluent
- Mass in sludge
- Mass transformed/lost

Heidler et al. *ES&T* 40:3634-9 (2006)

Occurrence of Antimicrobials in Estuarine Sediments



Early decreases attributable to improvements in treatment technology as a result of the Clean Water Act

Environmental Occurrence and Human Exposure Data

Occurrence:

- Environmental occurrence widespread in both aquatic and terrestrial environments (review in Chalew & Halden, 2009)

Human exposure studies:

- Women reporting greater personal care product use show higher levels of TCS and/or metabolites in plasma and milk (Allmyr et al. 2006)



- National Health and Nutrition Examination Survey (NHANES) detected TCS levels in $\frac{3}{4}$ of samples, levels increased with age and higher socioeconomic status (Calafat et al. 2008)

Recent Toxicity Data

➤ In vitro studies

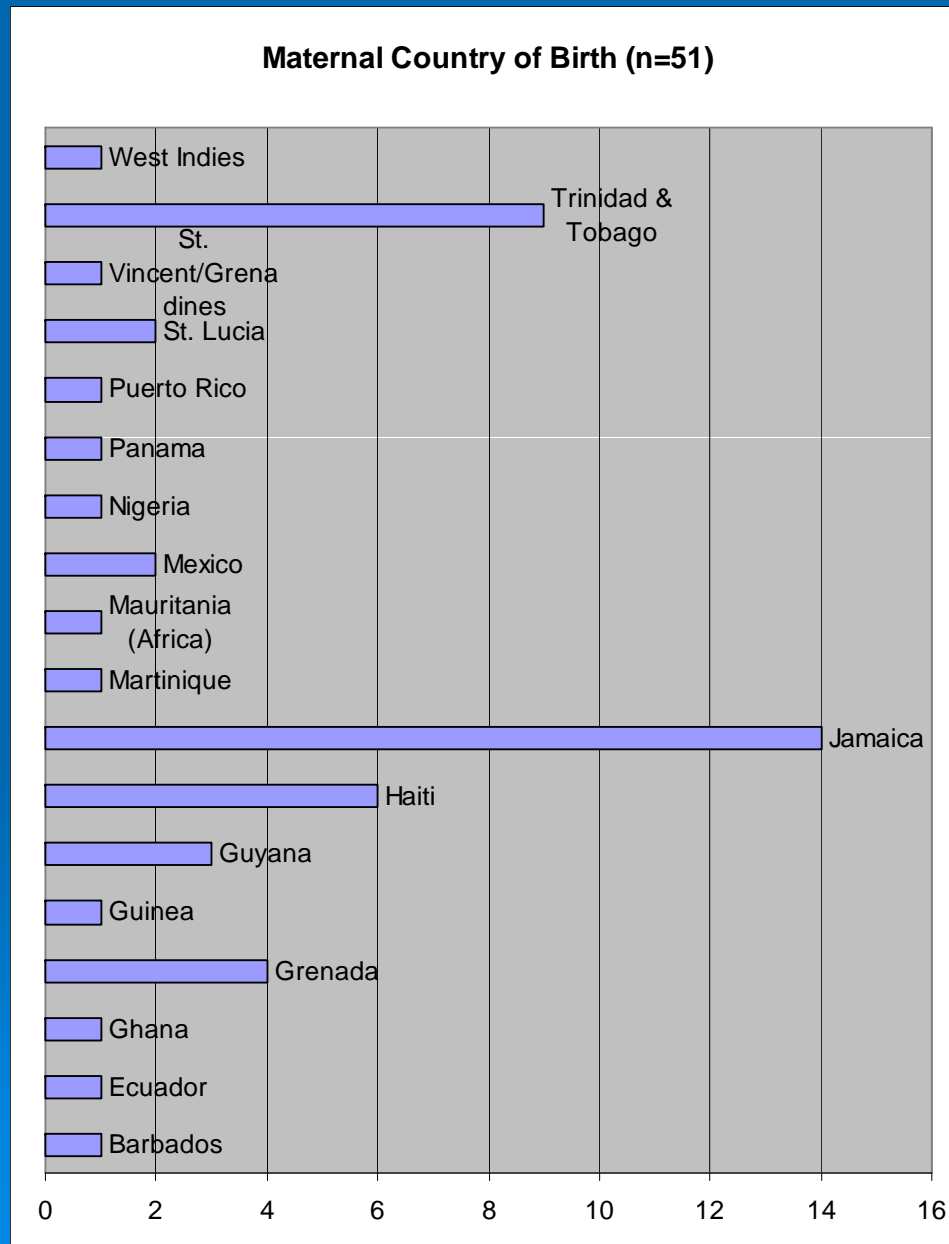
- Ahn et al. (2008): TCC/TCS enhanced the ability of steroid hormones E2 and testosterone to induce ER*- and AR*-dependent reporter gene expression
- Chen et al. (2008): bioactivity of testosterone amplified in presence of TCC, duplicated *in vivo* in male rats

*ER estrogen receptor, AR androgen receptor

SUNY Study Objectives

- 1) To measure the body burden of persistent biocides in pregnant women via analysis of urine, and
- 2) To characterize fetal *in utero* exposure by examining cord blood levels in their newborns

Half SUNY Study Population Born Outside the U.S.



SUNY Methods (1)

- Design:
Hospital-based cross-sectional
- Study population:
Women presenting at prenatal clinic
and returning to SUNY for delivery
 - Study period December 2007-present
- Inclusion criteria:
All singleton births

SUNY Methods (2)

Sample collection:

Biological: umbilical cord blood (serum and plasma),
mother's prenatal urine

Dr. Halden, ASU { – TCC, TCS and metabolites

Dr. Parsons,
Wadsworth Lab { – Metals (Hg, Pb, Cd)

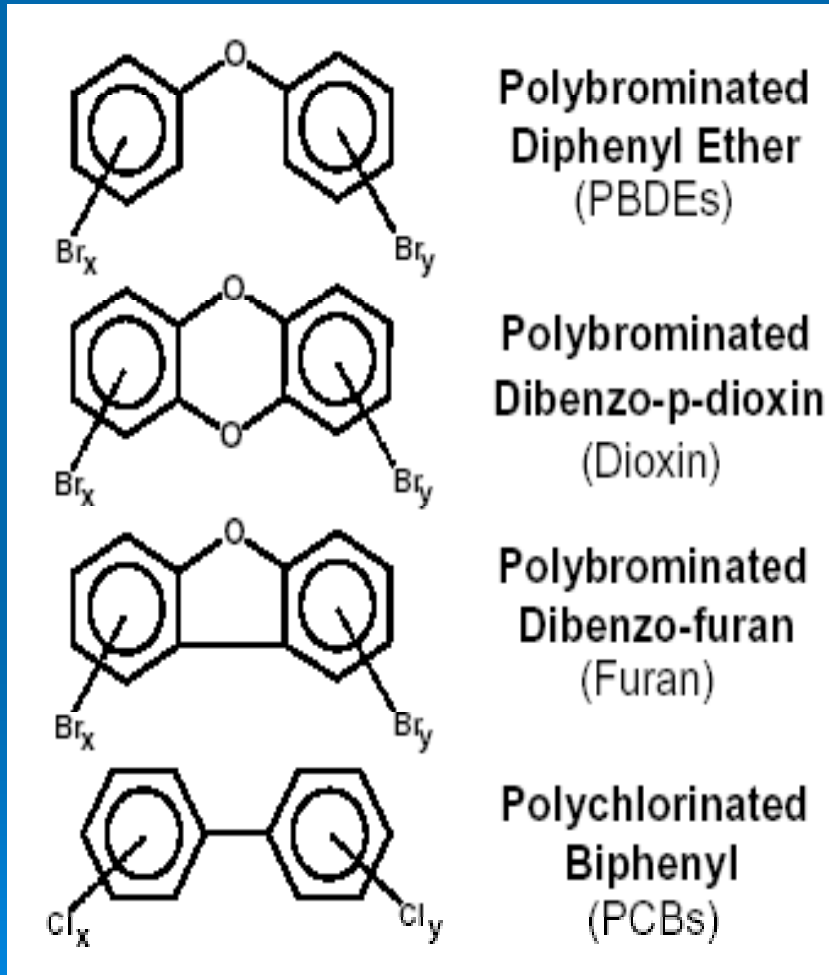
- Questionnaire

- Maternal characteristics
- Product use in the home
- Occupational history
- Fish consumption
- Folk medicine or cultural practices

Medical records:

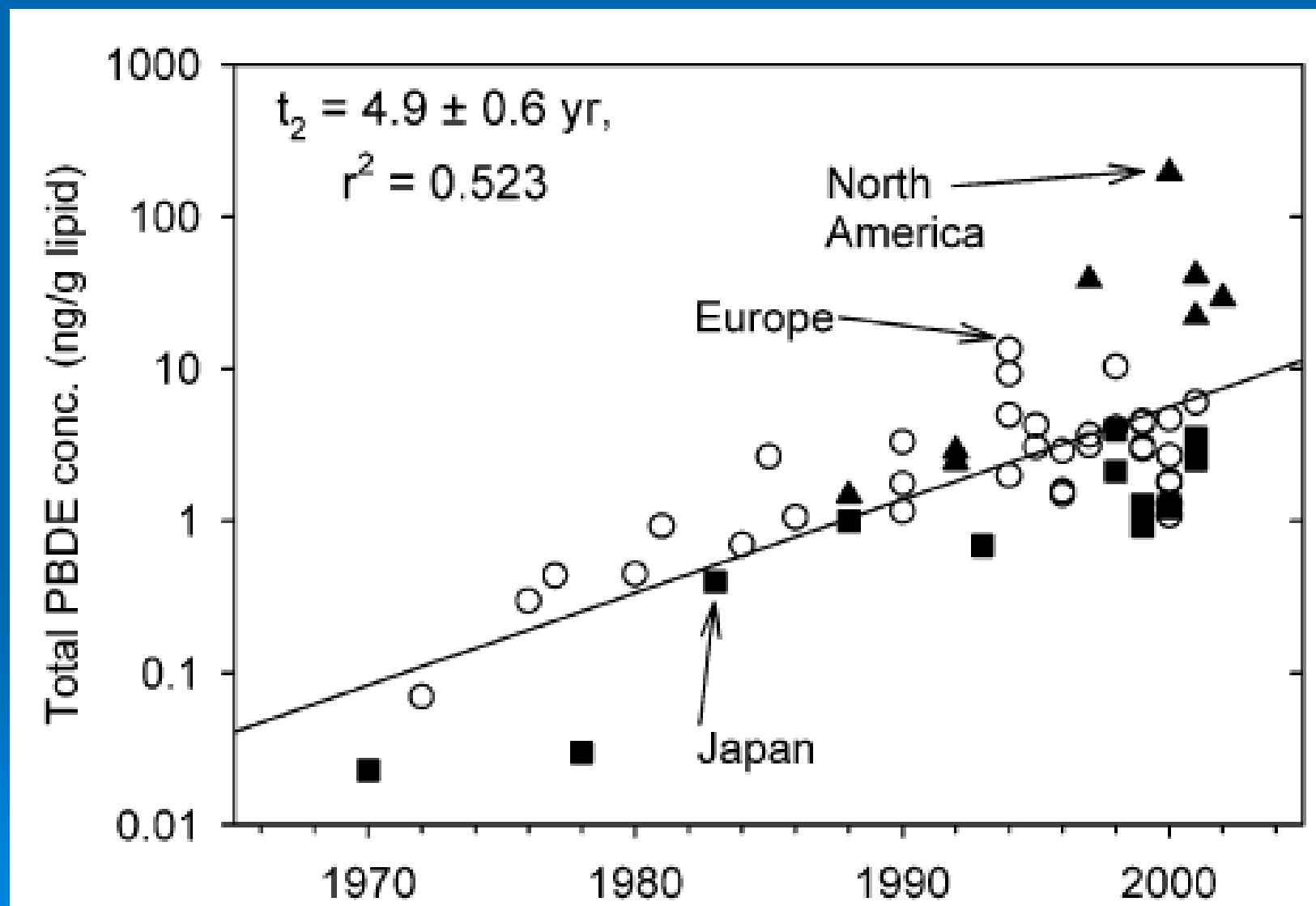
- Maternal and infant information (health and demographic)

Background: Organohalogens (PBDEs)



- Benzene rings with halogen atoms (Cl, Fl, Br, I) attached
- Lipophyllic
- Many toxicological endpoints
- Classified by the number of bromine atoms (4 min, 10 max)
- 209 possible congeners
- Toxicology depends on # and position of the bromine atoms

PBDE Temporal and Geographic Trends

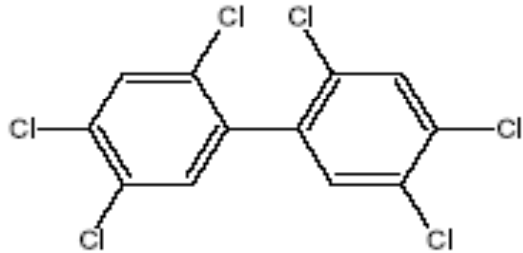


[Hites (2004). *Environ Sci Technol* 38: 945-956.]

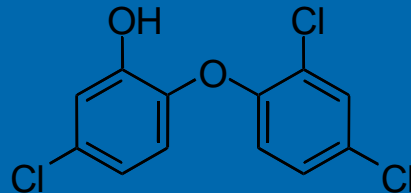
Toxicological Endpoints of PBDEs

- Growth
 - Development
 - Cancer
 - Reproduction
 - Immunological function
 - Endocrine disruption (esp. thyroid)
- } Critical period for fetal brain development beginning 6 weeks
- } Hyperactivity, learning and memory processing

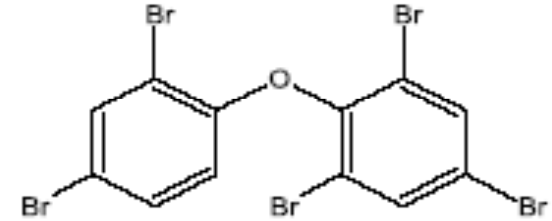
Potential Thyroid Hormone Modulation



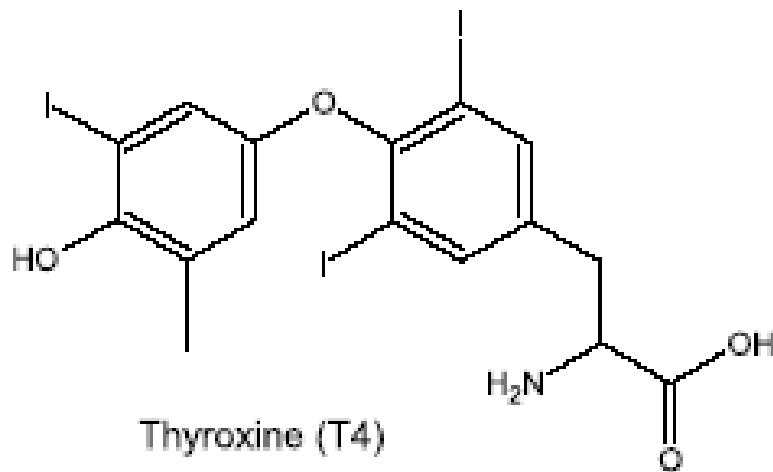
2,2',4,4',5,5'-hexachlorobiphenyl
(PCB-153)



Triclosan (TCS)



2,2',4,4',6-pentabromodiphenylether
(PBDE-100)



Thyroxine (T4)

- Thyroid hormones are critical for normal human brain development
- *Prenatal* exposure to compounds impact thyroid hormones may be particularly detrimental to growth and development

Exposure Data

- Lema et al. (2008) demonstrate alterations of hypothalamic-pituitary-thyroid axis in presence of PBDEs
 - Sensitivity of TH-response to disruption by PBDEs
- Turyk et al. (2008) examined serum of 405 adult male fisherman for PBDEs, PCBs and various hormones
 - PBDEs positively related to T4 and rT3, and inversely related to total T3 and TSH
 - (inconsistent with animal studies showing decreases of T4)

Epidemiologic Data

- Mazdai et al. (2004) examined total PBDEs and TH in 12 maternal-fetal pairs
 - TT4 and FT4, an additive measure
- Herbstman et al. (2008) examined PBDEs and TH in cord blood serum for 297 newborns in The Baltimore Three Study
 - BDE-100 associated with increased odds of low cord TT4
 - BDE-153 associated with increased odds low cord TT4 and FT4

Future directions in the study of human exposure

- Toxicity of co-exposures
- Placental transfer
- Markers of effect (thyroid hormones)
- Epidemiologic data
 - Occupational cohorts
 - Prospective cohorts

Acknowledgements

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 - Dr. Julie Herbstman, Columbia University
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- 