



**Environmental sources of polybrominated diphenyl ether (PBDE) and organophosphorus (OP) flame retardants and risk of breast cancer in young women: Early results from a population-based Ontario study**

*Occupational and Environmental Health (OEH) seminar series*

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 & Occupational Cancer Research Centre  
 & Associate Professor, Dalla Lana School of Public Health,  
 University of Toronto

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Emerging Contaminants 2 (2016) 204–219



Contents lists available at ScienceDirect

**Emerging Contaminants**

journal homepage: <http://www.keaipublishing.com/en/journals/emerging-contaminants/>



Review article

**A review of the role of emerging environmental contaminants in the development of breast cancer in women**



Shabana Siddique <sup>a,\*</sup>, Cariton Kubwabo <sup>b</sup>, Shelley A. Harris <sup>a,c,d</sup>

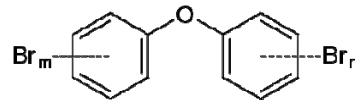
<sup>a</sup> Prevention and Cancer Control, Cancer Care Ontario, 620 University Avenue, Toronto, ON, Canada  
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- alkylphenols (APs)
- bisphenol A (BPA)
- parabens
- perfluoroalkyl substances (PFASs)
- phthalates
- synthetic musks
- triclosan
- polybrominated diphenyl ethers (PBDEs)

Towards a cancer-free workplace

## Polybrominated Diphenyl Ethers (PBDEs)



- Class of brominated flame retardants
- Used in a wide range of industrial and consumer products since 1970's to meet flammability standards for:
  - textiles, insulation, polyurethane foam, carpets, furniture, plastics, electrical appliances/equipment
- PBDEs can be released from products during manufacture, while in use and after disposal

Towards a cleaner, safer world

## Sources of Flame Retardants



Electronics,  
Appliances,  
Plastics,  
Textiles,  
Carpets, etc.

<https://flameretardants.americanchemistry.com/Electrical-Electronic-Equipment/Flame-Retardants-Fire-Safety-Tools-for-Electronics.pdf>

Towards a cleaner, safer world

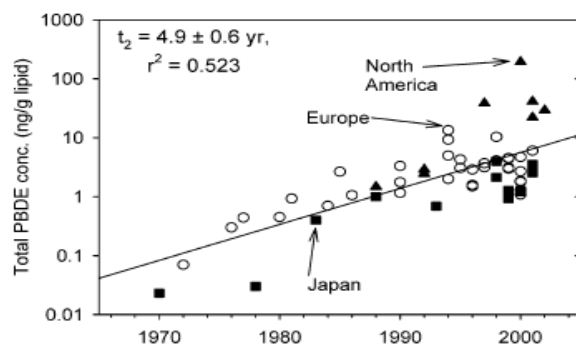
## Why focus on PBDEs?



- **Ubiquitous environmental pollutants**
  - Increasing levels in the environment, especially North America
  - Have contaminated the food chain
    - High concentrations found in fish (salmon, trout, mackerel)
    - **Premenopausal breast cancer** in women associated with consumption of **Great Lakes fish** (McElroy, 2004)
- **Endocrine disruptors**
  - Metabolites act as **pseudoestrogens**
- Classified as a “possible human carcinogen” by U.S. Environmental Protection Agency
- **Exposure through dust, air, dermal contact and diet**

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## PBDEs in human blood, milk, tissue (ng/g lipid)



*2003-2008  
stopped new use  
in EU & North  
America*

FIGURE 1. Total PBDE concentrations ( $\Sigma$ PBDE) in human blood, milk, and tissue (in ng/g lipid) shown as a function of the year in which the samples were taken; see Table 2. The three symbol types indicate the location from which the samples were collected. The overall regression is shown.

Hites RA, 2004.  
Environ Sci Technol 38, 945-956.

Towards a cancer-free workplace

The screenshot shows the website for China Market Research Reports. The header includes the company logo, a search bar, and an email address: sales@chinamarketresearchreport.com. A navigation menu lists various industry sectors: Automotive & Transportation, Business & Financial Services, Consumer Goods, Energy & Power, Food & Beverage, IT & Telecommunication, and Life Sciences. The breadcrumb trail indicates the current page is: Home >> Materials & Chemicals >> Report Detail. The main heading is "Global and China Flame Retardant Industry Report, 2014-2016". Below this are three tabs: "Report Description", "Table of Contents", and "Inquire for Discount". The "Report Description" tab is active, showing a synopsis: "Flame retardant is a general term for the substances that prevent and reduce flammability of fuels or delay their combustion. Over the past 30 years, flame retardant and flame-resisting materials have played an important role in reducing losses of life and property caused by fire disasters. In 2005-2013, the market volume of global flame retardant grew at a CAGR of about 4.2%, to 2.055 million tons in 2013." A red-bordered box on the right contains the text: "Organophosphorus Flame Retardants (OPFRs)". Below the synopsis is a quote: "With obvious advantages like environmental friendliness and safety, organophosphorus flame retardant is gradually substituting for halogen flame retardant ....in 2013 alone, the market volume of organophosphorus flame retardant reached some 620 kt, accounting for 30% of the global total." At the bottom left is the URL: http://www.researchinchina.com/Htmls/Report/2014/7904.html. At the bottom right is the logo for "Towards a cancer-free workplace".

**Organophosphorus Flame Retardants (OPFRs)**

*“With obvious advantages like environmental friendliness and safety, organophosphorus flame retardant is gradually substituting for halogen flame retardant ....in 2013 alone, the market volume of organophosphorus flame retardant reached some 620 kt, accounting for 30% of the global total.”*

<http://www.researchinchina.com/Htmls/Report/2014/7904.html>

The screenshot shows the website for the Ontario Environment and Health Study (OEHS). The header includes a navigation menu: HOME, ABOUT, HOUSEHOLD SAMPLING, TEAM, RESOURCES, CONTACT. The logo for OEHS is prominently displayed, along with the text "Ontario Environment and Health Study". Below the logo is a banner image of a forest with the text "CONTACT US". The main content area contains the following text: "Please feel free to contact our Project Coordinator Lidija Latifovic with any questions you may have." "Ontario Environment and Health Study" "620 University Avenue" "Toronto, ON M5G 2L7" "Phone: 416-971-9800 ext. 3305" "Toll Free: 1-855-355-3908" "Send Email". At the bottom right, there is a copyright notice: "Ontario Environment and Health Study | © 2012" and a navigation menu: "Home | About | FAQ | Team | Resources | Contact Us". A red-bordered box at the bottom right contains the text: "Towards a cancer-free workplace".

Exposure to Emerging Environmental Contaminants and Risk of Breast Cancer in Young Women: A Case-Control Study using Biomarkers of Exposure. CCSRI, \$842,000 2011-2017

<http://oehs.ca/>

## OEHS – Case Control Study

### Primary Objective:

1. To evaluate the associations between **lipid-adjusted serum concentrations of PBDEs** and the risk of **incident breast cancer** in young women, aged 18-44 years.

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## OEHS – Case Control Study

### Secondary Objectives:

1. To evaluate the relative contribution of different sources to lipid-adjusted PBDE serum concentrations:
  - **Dietary exposures** (fish consumption, meat, poultry, dairy), **environmental** (household) and **occupational exposures**
2. To collect collect and store **serum** and **morning urine samples for future biomarker studies** of exposure, susceptibility or effect and the risk of breast cancer in premenopausal women (ie: Biobank)

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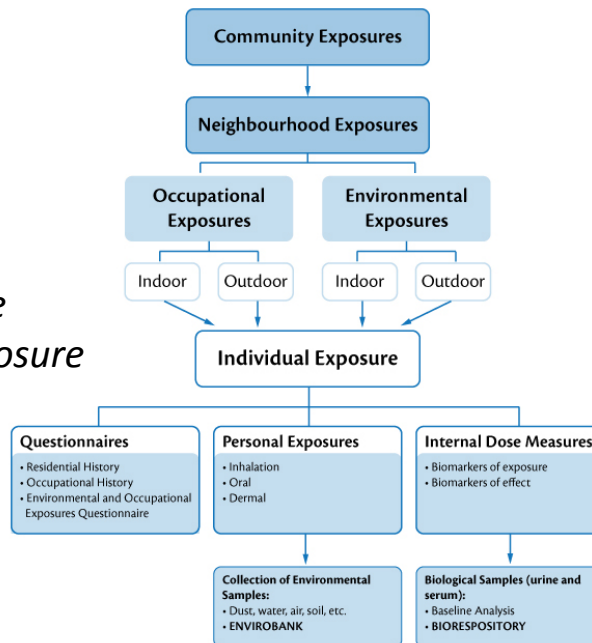
# OEHS – Case Control Study

- Cases: n=350
  - **Population-based:** identified from the **Ontario Cancer Registry (OCR)** 2013-2015
  - Aged **18-44 years**
  - Pathology-confirmed primary breast cancer diagnosis
- Controls: n=350
  - **Population-based:** identified using random-digit dialing (RDD) by the Institute for Social Research (ISR) at York University
  - Frequency-matched within 5-year age groups

Research in context-free methodology



*A comprehensive approach to exposure assessment*



# OEHS – Data Collection



Two web-based questionnaires:

## 1. Environmental Questionnaire

- Lifetime residential history: age /type of home, type of **heating, ventilation**, renovations
  - Cleaning: frequency of **vacuuming, dusting**, carpet cleaning
  - **Furniture types**: age/type of mattress, presence of foam pillows, other foam furniture
- **Occupational history**: computer repair, recycling facilities, hours spent on a computer
- Transportation: vehicle use, airplane travel
- A typical day: hours spent on work/home/travel/sleep

## 2. Diet Questionnaire

Research in progress

Ontario Environment and Health Study

Examining how environmental, dietary, and lifestyle factors affect the risk of breast cancer in young women

This is a controlled study. You need a valid token to participate.  
If you have been issued a token, please enter it in the box below and click continue.

Token

[Continue](#)

OEHS  
Ontario Environment and Health Study

Ontario Environment and Health Study

\* What kind of mattress do you sleep on?  
Choose one of the following answers

Coil spring/pocket spring

Regular foam (polyurethane)

Memory foam (visco-elastic)

Latex foam

Don't know

# OEHS – Data Collection



Two web-based questionnaires:

## 1. Environmental Questionnaire

## 2. Diet Questionnaire

- Modified full-diet Block 2005 FFQ to estimate **usual food and supplement intake** over 12 months about **2 years ago**
- Modifications geared towards improved PBDE assessment:
  - Reviewed all animal foods
  - Modified questions and nutrient database to distinguish **meat** and **chicken** or **turkey sources**, **oily fish**, and **fish oil supplements**

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# OEHS – Data Collection



## 2. Diet Questionnaire: examples of modifications

- New items and sub-questions added
  1. **Fish:** ready-to-eat vs. white/lean vs. dark/oily
    - Different fish types (i.e. wild vs farmed)
  2. **Meat products and liver:** poultry vs. animal
    - Different types of products (i.e. hot dogs, white vs. dark chicken, fried liver vs. paté)
  3. **Fish oil supplements vs. non-fish Omega3s**
    - 8 different types of fish oil supplements

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**NutritionQuest** The questions have been locked because the questionnaire has been submitted. Stop Survey

WELCOME | ABOUT YOU | BREAKFAST TYPE FOODS | FRUIT | VEGETABLES | BEANS/SOUP/PASTA | MEATS | FISH/SEAFOOD | BREADS/EGGS/SPREADS | NUTS/GRANOLS/SEEDS/EGG | BEVERAGES | GENERAL QUESTIONS | VITAMINS | FINAL QUESTION | YOUR RESULTS

BACK NEXT

What single vitamins (not part of multiple vitamins) did you take fairly regularly over 12 months, about TWO YEARS AGO?

**Cod liver or other fish oils, including mixed with non-fish oils**

How often did you take cod liver or other fish oil supplements, including any mixed with non-fish oils?

Didn't take **A few days per month** 1-3 days per week 4-6 days per week Every day

For how many years?

Less than 1 Year **1 Year** 2 Years 3-4 Years 5-6 Years 10+ Years

What type of fish oil did you usually take? Mark **one**.

**Cod liver** Halibut Krill Menhaden Salmon Seal Shark Other fish or mixed Don't know

---

**NutritionQuest** The questions have been locked because the questionnaire has been submitted. Stop Survey

WELCOME | ABOUT YOU | BREAKFAST TYPE FOODS | FRUIT | VEGETABLES | BEANS/SOUP/PASTA | MEATS | FISH/SEAFOOD | BREADS/EGGS/SPREADS | NUTS/GRANOLS/SEEDS/EGG | BEVERAGES | GENERAL QUESTIONS | VITAMINS | FINAL QUESTION | YOUR RESULTS

BACK NEXT

About TWO YEARS AGO, how often on average, did you eat the following over 12 months?

**Dark or oily fish, like salmon, mackerel, herring, sardines, trout**

How often did you eat dark or oily fish, cooked by any method, or canned?

Never **A few days per year** Once per month 2-3 times per month Once per week 2 times per week 3-4 times per week 5-6 times per week Every day


How much did you eat, on the days you ate it?

**1/4 cup** 1/2 cup 1 cup 2 cups

Which dark or oily fish did you usually eat? Mark those you ate most often (up to 3). If you ate just one kind most often, just mark one choice.

Anchovy  Bass, Sea bass  Herring, Kippers  Mackerel  Salmon  Sardines  Trout  Other dark or oily fish

Was the dark or oily fish you ate usually wild or farmed? Mark **only one**.

 **Journal of Food Composition and Analysis**  

Available online 11 December 2017  
In Press, Accepted Manuscript ?

Original research article

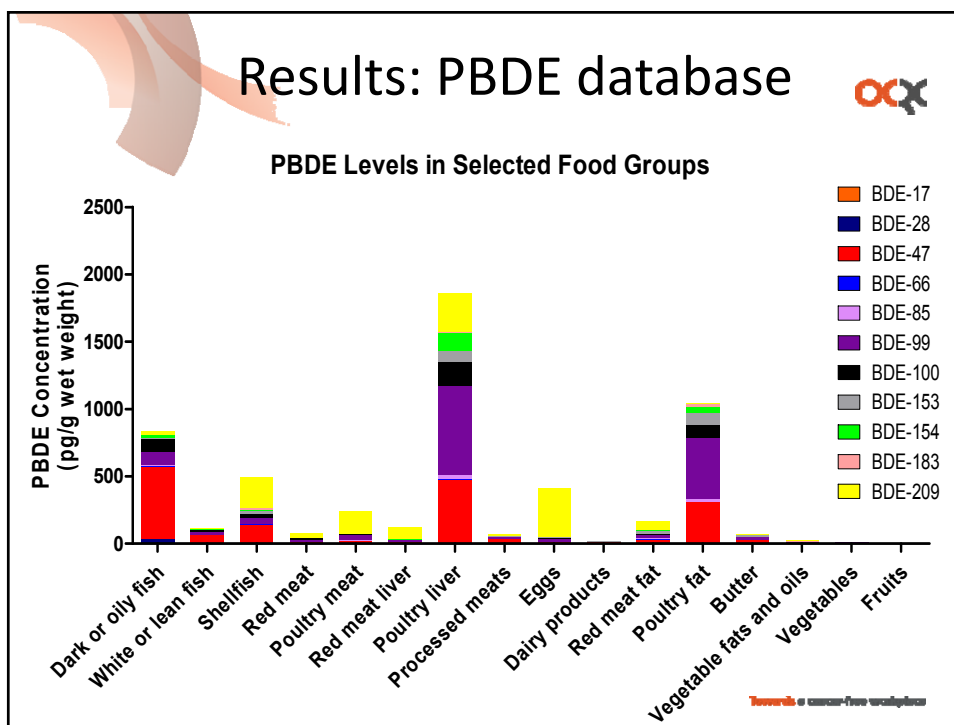
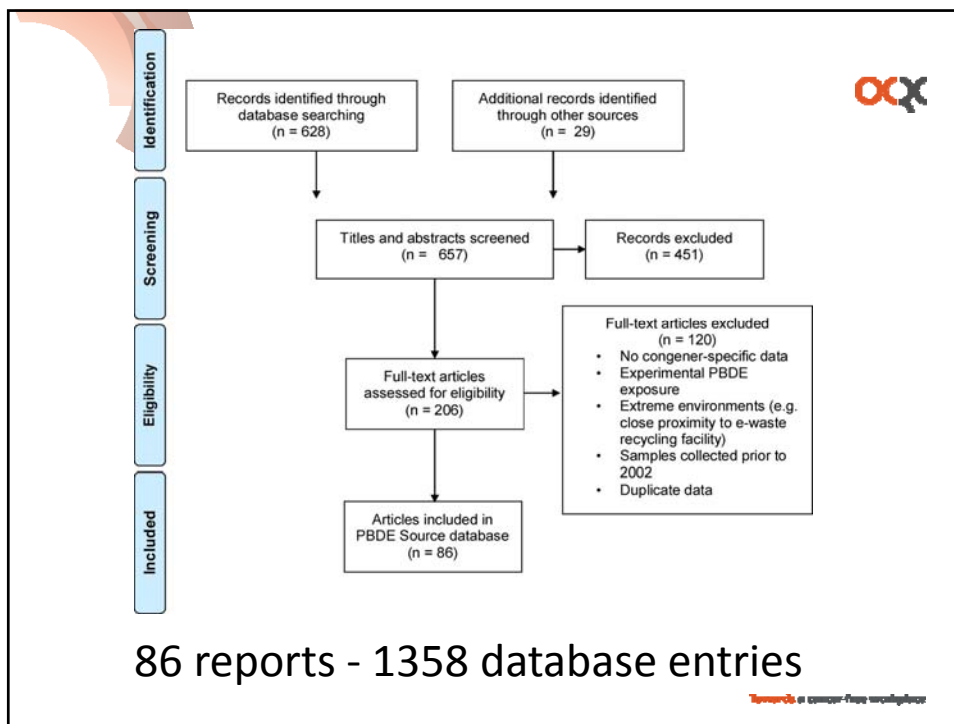
**A global database of polybrominated diphenyl ether flame retardant congeners in foods and supplements**

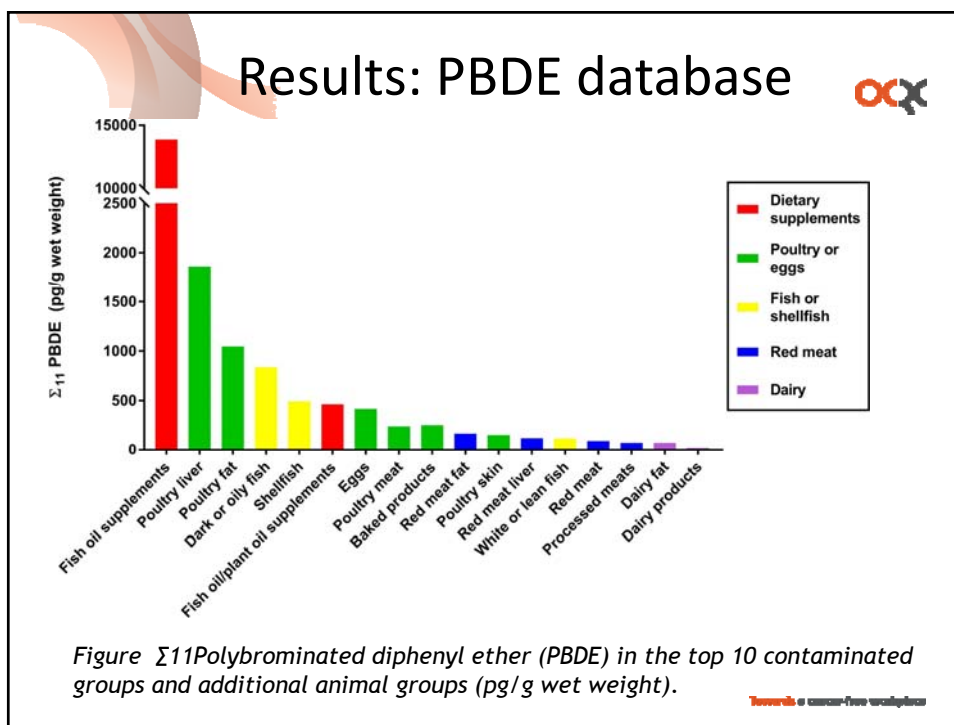
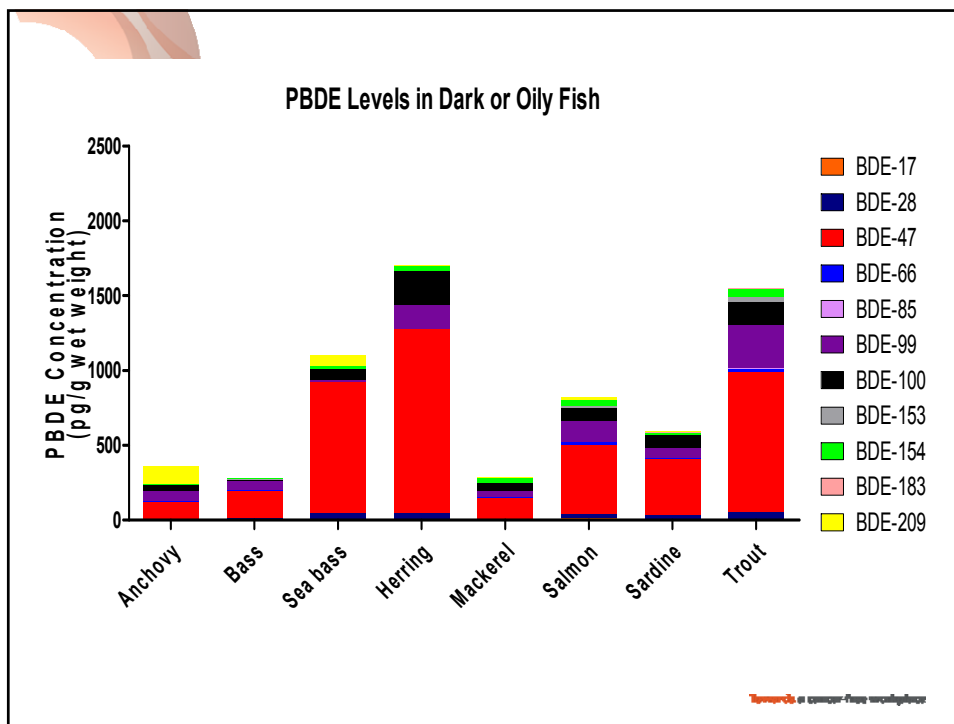
Beatrice A. Boucher<sup>a, b, 1</sup>, Julie K. Ennis<sup>a, b, 1</sup>, Dina Tsirlin<sup>a</sup>, Shelley A. Harris<sup>a, c, d</sup>

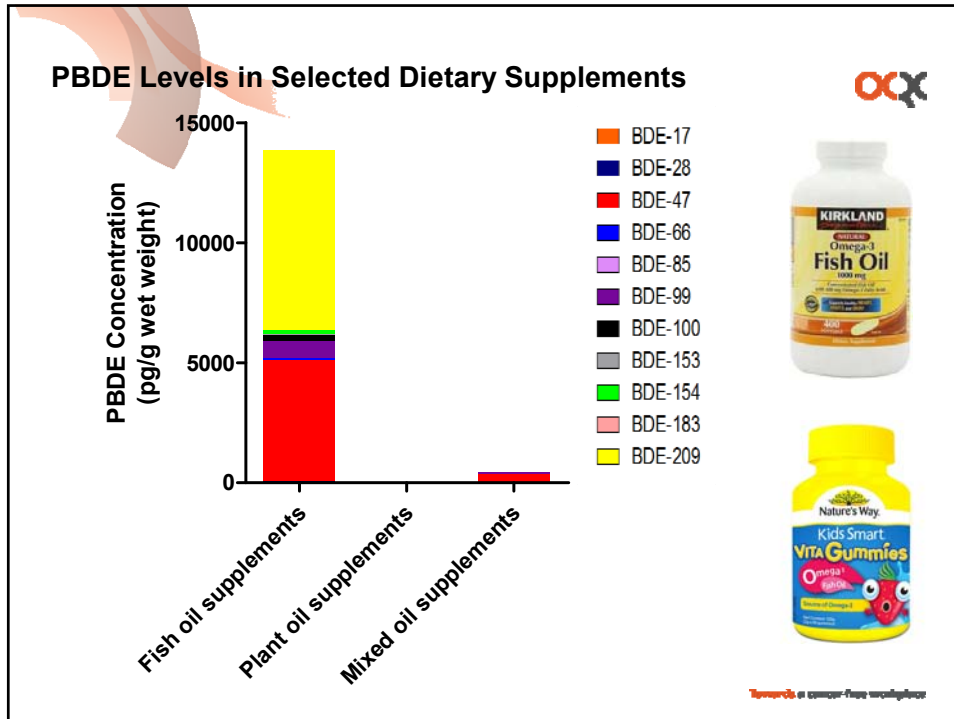
**Search Strategy:**

- Medline 1996 – April 2015
- MeSH terms and keywords: (flame retardants/an [Analysis]; OR halogenated diphenyl ethers/an, ch [Analysis, Chemistry]; OR hydrocarbons, brominated/an, ch [Analysis, Chemistry]; OR pbde) AND (food: OR diet: OR dietary supplements OR fish oils)

 18







## OEHS – Data Collection

### 3. Biological sample collection

- After consent, cases and controls were mailed a **BioKit** containing:
  1. Test tubes, pipettes and containers for sample collection
  2. Participant instructions, a Google maps print out of the 5 closest GDML locations to their home
  3. A set of laboratory instructions
- Collect **60mL of fasting blood** and **90mL of urine**
- Location: **Gamma Dynacare Medical Laboratory (GDML)**

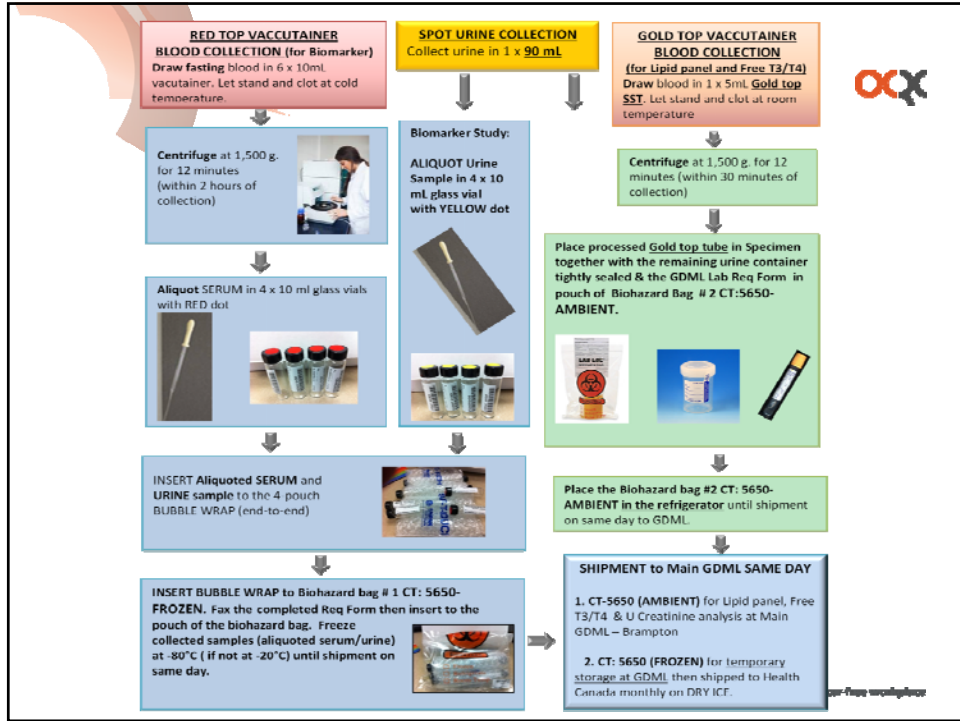


## OEHS BioKit



- GDCML: Collection, processing, analysis, shipment, short term storage





**Gamma-Dynacare Medical Laboratories**  
115 Midair Court, Brampton, ON, L6Y5M3  
TEL: (905) 790-3000 RESULT INQUIRY (905) 790-3030

COLLECTION TIME: 14/01/2014 @ 10:00  
LAB NUMBER: CT00397080  
STATUS: FINAL  
SERVICE DATE: 14/01/2014 @ 18:21  
REPORT DATE: 14/01/2014 @ 22:38

PATIENT: OEHS-CL999L-L  
HEALTH NUMBER: 000000001  
CLIENT: S.A. HARRIS  
DATE OF BIRTH: [REDACTED]  
SEX: F  
AGE: 26  
TORONTO ON  
M5G2L7  
PHONE: (416) 971-9800  
PHONE: (000) 000-0000  
CHART: 26621  
COMMENTS: 20140113 22:00 VISIT:SCREENING

CODES	TEST DESCRIPTION	RESULT	ABN	REFERENCE RANGE
<b>C H E M I S T R Y</b>				
	CHOLESTEROL	4.30		DESIRED: < 5.20 mmol/L
	TRIGLYCERIDES	0.69		< 2.30 mmol/L
	HDL CHOLESTEROL	1.59		F: >=1.30 mmol/L
	LDL CHOLESTEROL CALC.	2.39		mmol/L
	T4 FREE	18.		12 - 22 pmol/L
	FREE T3	5.8	H	2.6 - 5.7 pmol/L
<b>U R I N E C H E M I S T R Y</b>				
	CREATININE R U	31.1	H	F: 2.6 - 20.0 mmol/L



## Challenges Associated with Sample Preparation for the Analysis of PBDEs in Human Serum

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IVANA KOSARAC and CARLTON KUBWABO<sup>1</sup>

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SHELLEY HARRIS

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1) GC/electron ionization-tandem MS method develop to quantify **8 PBDE congeners in human serum**: BDE-28 BDE-47 BDE-85 BDE-99 BDE-100 BDE-153 BDE-154 BDE-183

2) Subset of 120 subjects (60 cases and 60 age-matched controls) assessed for **OPFR exposures** via urinary metabolites: BDCIPP, DPHP, BBOEP, DoCP & DpCP, TCIPPOH, BCIPP, BCEP, Desbutyl TBOEP

Towards a cancer-free workplace

## Results: demographic and health-related characteristics of OEHS participants



Characteristic	Cases (n=305)		Controls (n=144)	
	N	(%)	N	(%)
Age (years)				
Mean (SD)	39.70	(4.41)	38.33	(4.54)
20 years and younger	0	-	1	(0.69)
>20 to 30 years	12	(3.93)	6	(4.17)
>30 to 40 years	130	(42.62)	85	(59.03)
>40 to 45 years	163	(53.44)	52	(36.11)
Education				
Elementary School	0	(0.0)	1	(0.7)
High School	33	(10.8)	8	(5.6)
Trade or technical school	11	(3.6)	2	(1.4)
Non-university diploma	71	(23.3)	47	(32.6)
University, below Bachelor's	6	(2.0)	6	(4.2)
Bachelor's degree	123	(40.3)	55	(38.2)
Graduate degree	61	(20.0)	25	(17.4)
Marital Status				
Married or living with partner	246	(80.7)	120	(83.3)
Divorced	10	(3.3)	6	(4.2)
Widowed	1	(0.3)	0	(0.0)
Separated	6	(2.0)	4	(2.8)
Single or never married	42	(13.8)	14	(9.7)

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## Associations with selected characteristics, all models adjusted for age



Characteristic	Cases (n=305)	Controls (n=144)	OR	(95% CI)
Body mass index (BMI) - 2 years ago				
Mean (SD)	24.73	26.29	0.95	(0.92, 0.98)
Normal: 18.5 to <25	181	66	1.00	
Below 18.5	15	2	2.88	(0.63, 13.04)
35 to <30	70	41	0.61	(0.37, 0.98)
30 and above	39	34	0.40	(0.23, 0.69)
Smoking status				
Never (<100 cigarettes)	197	101	1.00	
Ever	106	38	1.38	(0.88, 2.15)
Dietary alcohol intake (grams)				
Mean (SD)	9.08	5.86	1.02	(1.00, 1.04)
≤Q1	60	35	1.00	
Q1 to Q2	60	35	1.11	(0.61, 2.03)
Q2 to Q3	70	34	1.22	(0.68, 2.20)
Q3≥	105	34	1.81	(1.02, 3.22)
Parity: number of live births				
None	92	20	1.00	
1	52	18	0.47	(0.22, 1.00)
2	111	66	0.27	(0.14, 0.50)
3 or more	50	40	0.18	(0.09, 0.37)

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## OEHS Data Collection, Part 4 HOME Study -Diamond Laboratory, University of Toronto/Environment Canada



### NEW FUNDING:

#### **Monitoring and modeling of residential indoor semi volatile organic compounds.** Harris, S.A. (PI) and Diamond, M. (PI)

Health Canada, Water, Air and Climate Change Bureau, CARA project funds.

2014 - 2017, Amount: \$497,100

#### **Monitoring organophosphorus flame retardants in Canadian homes.**

Harris, S.A., (PI) Diamond, M. (PI) and Jantunen, L. (Co-I)

Health Canada, CMP Monitoring and Surveillance Fund.

2014 to 2017, Amount: \$100,000

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## SVOCs?



- SVOCs include: halogenated (bromine and chlorine) organic compounds, phthalates, and phosphorus-containing (OP) flame retardants (FRs)
- The concentration of SVOCs in indoor air is influenced by a number of poorly characterized emission sources:
  - Personal care products
  - Building and decorator materials (wallpaper, flooring type)
  - Electronic equipment, furniture
  - Indoor sinks (carpets, dust)

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## HOME Study Objectives



- Evaluate association between SVOCs, as measured in a variety of media (air, dust, hand wipes...)
  - serum PBDE levels of individuals residing in the household
  - urinary OPFRs
- Investigate whether housing characteristics are predictive of measured SVOCs

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# Methods OEHS Home Study



Figure 2. Equipment set-up in a participant's home



Figure 1. Study process and timeline

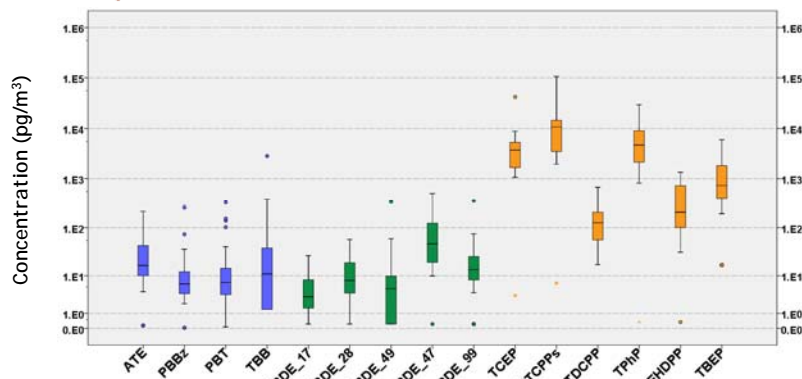
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## BROMINATED AND ORGANOPHOSPHATE FLAME RETARDANTS (BFRS AND OPES) IN HOUSEHOLD AIR IN ONTARIO, CANADA



C. Yang<sup>1,2,3,4</sup>, L.M. Santorelli<sup>2,3,4</sup>, A. Heggen<sup>2,3,4</sup>, L.O. Chenevix<sup>2,3,4</sup>, S. Harris<sup>1,2,3,4</sup>, D. Thériault<sup>2,3,4</sup>, B. Fosse<sup>2,3,4</sup>, R. De La Campa<sup>2,3,4</sup>, H. You<sup>2,3,4</sup>, E. Balle<sup>2,3,4</sup>, M. L. Charbonnet<sup>2,3,4</sup>

<sup>1</sup>Department of Earth Sciences, University of Toronto; <sup>2</sup>Ontario Atmospheric Research, Assessment and Control Program; <sup>3</sup>Department of Applied and Environmental Science, University of Toronto; <sup>4</sup>Canadian Health and Protection, Prevention and Control Centre, Cancer Research Centre, Health Law School, Public Health, University of Toronto; <sup>5</sup>Department of Chemical Engineering, University of Toronto; <sup>6</sup>Department of Chemical Engineering, University of Toronto; <sup>7</sup>Department of Chemical Engineering, University of Toronto

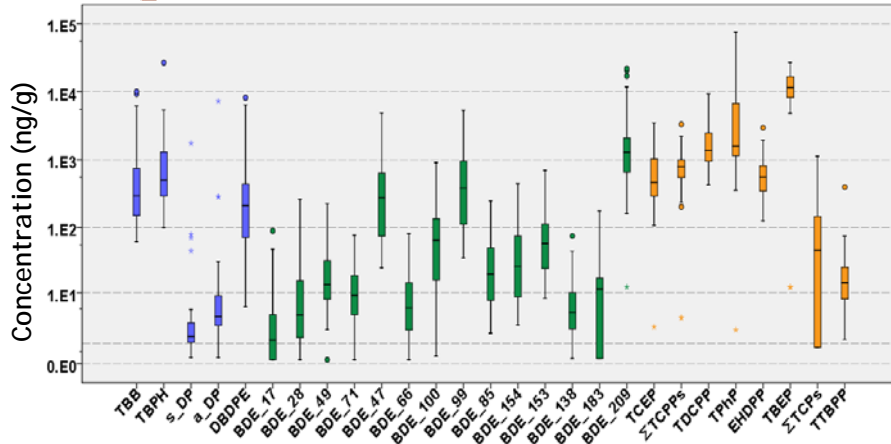


➤ OPFRs > NBRs & PBDEs by ~ 2-3 orders of magnitude (PUF passive)

Yang et al., BFR 2016

Towards a cancer-free workplace

# Dust Concentrations

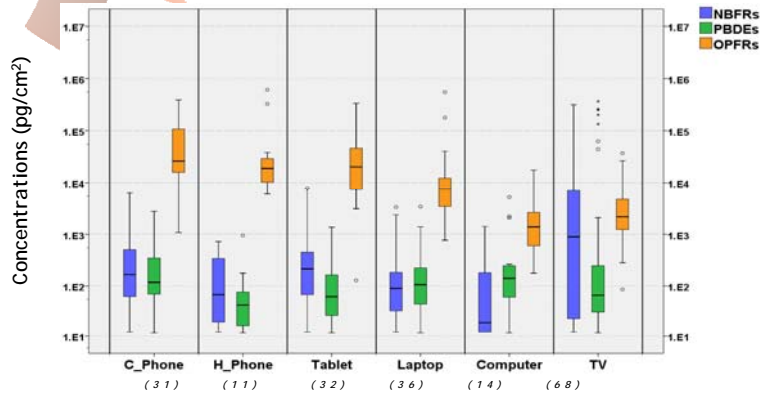


➤ OPFRs ~ 10 times higher than NBRs & PBDEs

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## Handheld

## Non-Handheld

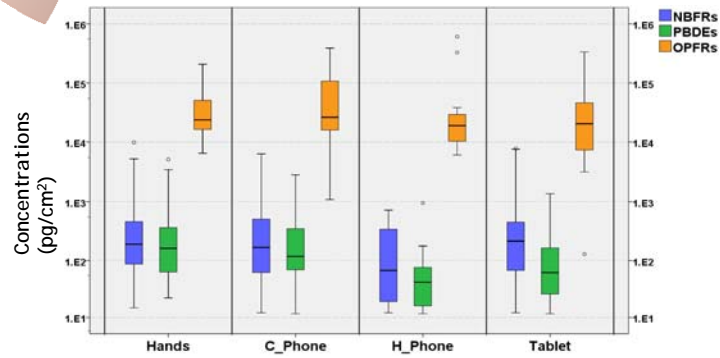


- OPFRs Handheld > non-handheld
- BFRs Handheld ≈ Non-handheld
- Handheld newer than non-handheld?

38

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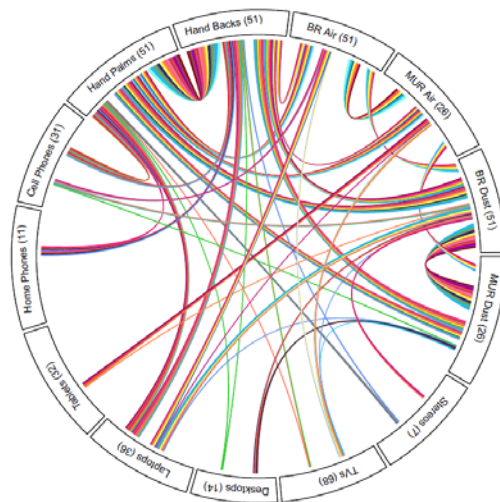
## Hands vs Handheld Devices



- Hands ≈ Handheld devices
- Handheld devices as sources to hands or vice versa?

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## Exposome Globe BFRs, Yang et al., in prep



Cold tone/blueish ribbons represent NBFRs, and warm tone/redish ribbons represent PBDEs.

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05

## Conclusions



- **associations for PBDE exposures** and premenopausal breast cancer risk .....
- elevated breast cancer risk observed in relation to urinary concentrations of **OP flame retardants** ....
- **diet** may be an important contributor to serum PBDE concentrations
- **OPFRs more frequently detected** and in higher concentrations than PBDE congeners in biological samples
- OPFR concentrations far **higher in indoor environments** than PBDEs

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## OEHS Future Directions



- **Diet analysis**
  - PBDEs in foods/supplements
  - Organic foods
- **OEHS Home Study** – predictive modelling of serum (PBDEs) and urinary (OPs) biomarkers
- **Additional analyses funded:**
  - Multimedia Exposure to Replacement Chemicals of Emerging Concern and Selected CMP3 Chemicals (Awarded); PI: Kubwabo, C, Mandy Fisher (Co-PI), Dr. Pat Rasmussen (Co-PI), Harris, S.A. (Co-I) et al. Chemical Management Plan, Health Canada 2017- 2021, Amount: \$600,000.

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## Investigators and Collaborators

### OEHS:

- **Shelley Harris** (PI), Beatrice Boucher, Cariton Kubwabo, Michelle Cotterchio, Julia Knight, Len Ritter, Paul Villeneuve
- **Grad Student/Post Doc/RAs:** **Linda Kachuri, Lidija Latifovic**, Gil Valencia, Brooke Filsinger

### Health Canada Biomonitoring Team:

- **Cariton Kubwabo, Shabana Siddique**  
Kaela Lalonde, Ivana Kosarac

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### PBDE database team:

- **Beatrice Boucher**, Julie Ennis, Dina Tsirlin

### OEHS Home Study Team:

- **Miriam Diamond**, Liisa Jantunen, Congqiao Yang, Joseph Okeme, Dina Tsirlin, Lidija Latofivic, Regina De La Campa; Hung You, Ryan Kulka, Bruce Fraser

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