EPA
United States Environmental Protection Agency

# A Sustainable Alternative to a Breast Milk Monitoring Program: Using NHANES Serum Data to Predict Breast Milk PBDE Concentrations

Satori A. Marchitti,[1] Judy S. LaKind,[2,3,4] Daniel Q. Naiman,[5]
Cheston M. Berlin,[4] and John F. Kenneke[1]

October 24, 2012

[1]National Exposure Research Laboratory, U.S. EPA; [2]LaKind Associates, LLC; [3]Dept of Epidemiology and Public Health, University of Maryland School of Medicine; [4]Dept of Pediatrics, Milton S. Hershey Medical Center, Penn State College of Medicine; [5]Dept of Applied Mathematics and Statistics, Whiting School of Engineering, Johns Hopkins University.

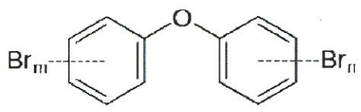
Office of Research and Development
National Exposure Research Laboratory | Ecosystems Research Division | Athens Georgia

EPA United States Environmental Protection Agency

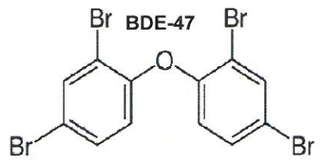
## Polybrominated Diphenyl Ethers (PBDEs)

- Flame retardant compounds used on consumer products
- Levels in humans and wildlife have been increasing
- In animals, PBDE exposures induce embryonic/fetal, neurodevelopmental, reproductive and endocrine toxicities
- Breast milk is the greatest source of PBDE exposure for breastfeeding infants
- Levels in U.S. breast milk are among the highest in the world

**General PBDE Structure**




**BDE-47**



EPA
United States
Environmental Protection
Agency

## Assessing Infant Exposure to PBDEs

***~ Despite the presence of chemicals in breast milk, the preponderance of evidence indicates that breastfeeding confers numerous health benefits on the infant, and may also counter effects associated with prenatal chemical exposure ~***

2

EPA
United States
Environmental Protection
Agency

## Assessing Infant Exposure to PBDEs

***~ Few data exist to quantify exposure levels of environmental chemicals in human milk and the vast majority of current EPA chemical risk assessments do not adequately consider trans-lactational exposure pathways due to the lack of available data and tools necessary to do so ~***

EPA United States Environmental Protection Agency

## Assessing Infant Exposure to PBDEs

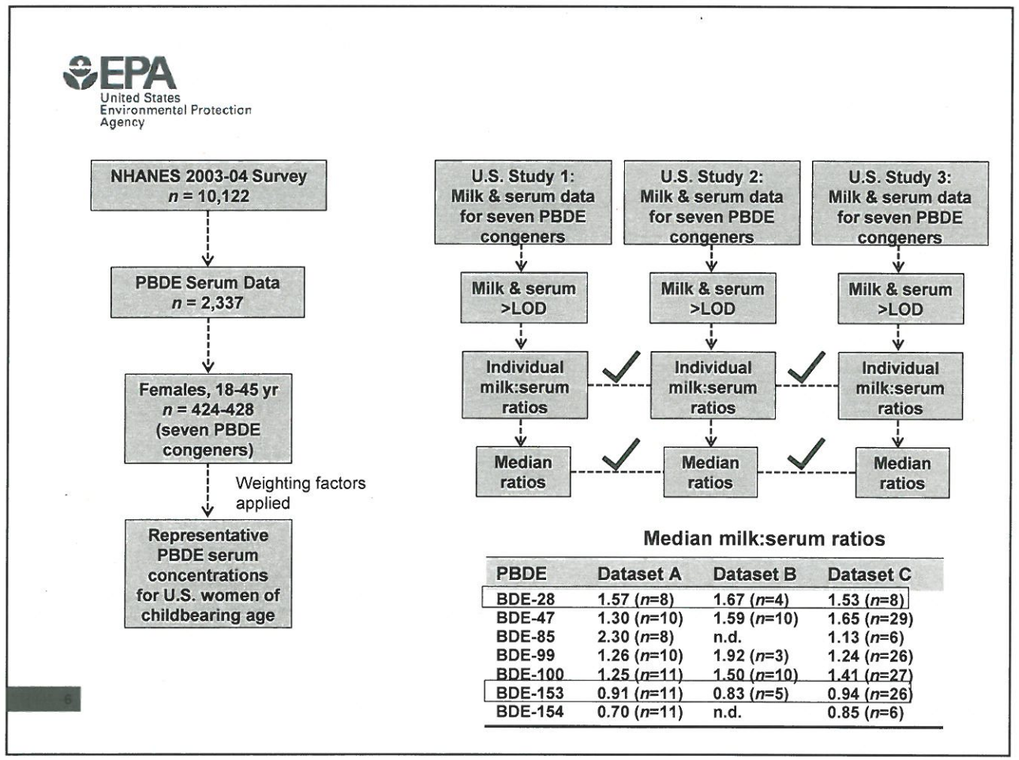
- Representative data on breast milk PBDE concentrations are needed
- Researchers have called for a national breast milk monitoring program
- However, could national serum data be used somehow to predict U.S. breast milk concentrations?
  - Congener-specific PBDE milk:serum relationships need to be understood
  - Prior to 2006, no reliable partitioning data existed for PBDEs
  - Three recent U.S. studies with acceptable data have become available
    - Schecter *et al*. 2006. *Toxicol Environ Chem* 88:319-324
    - Schecter *et al*. 2010. *Chemosphere* 78:1279-1284
    - LaKind *et al*. 2009. *Environ Health Perspect* 117:1625-1631

EPA United States Environmental Protection Agency

## Study Objectives

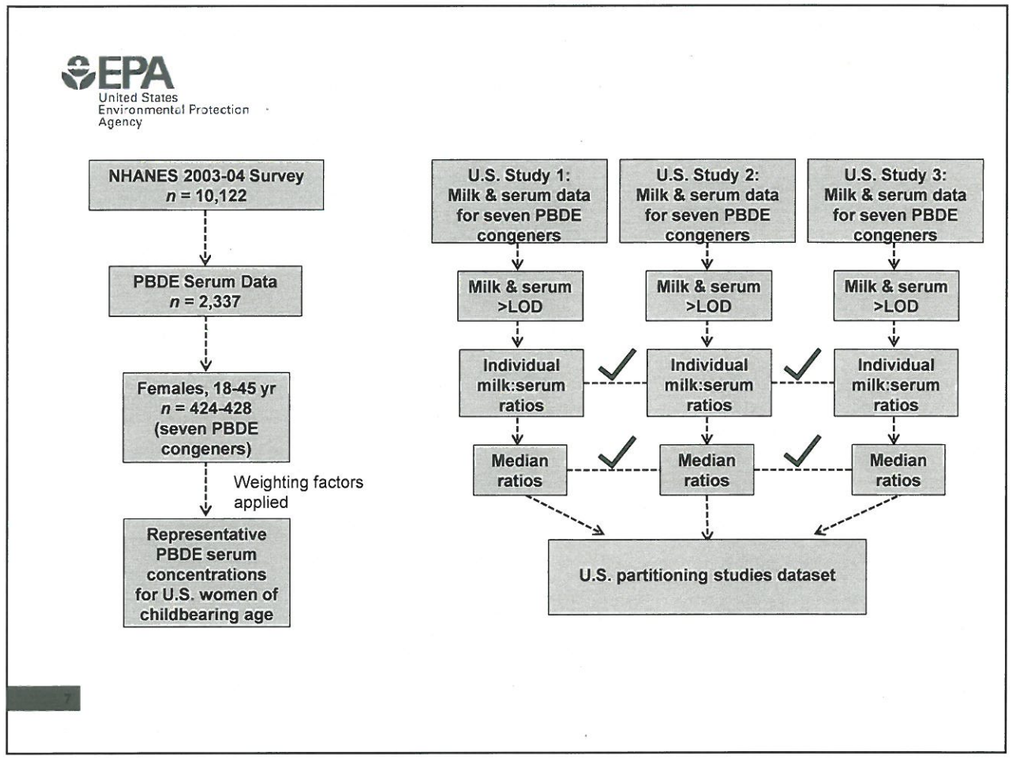
1. Develop congener-specific PBDE partitioning models
2. Apply these models to nationally representative NHANES serum data to predict breast milk PBDE concentrations in the U.S. population

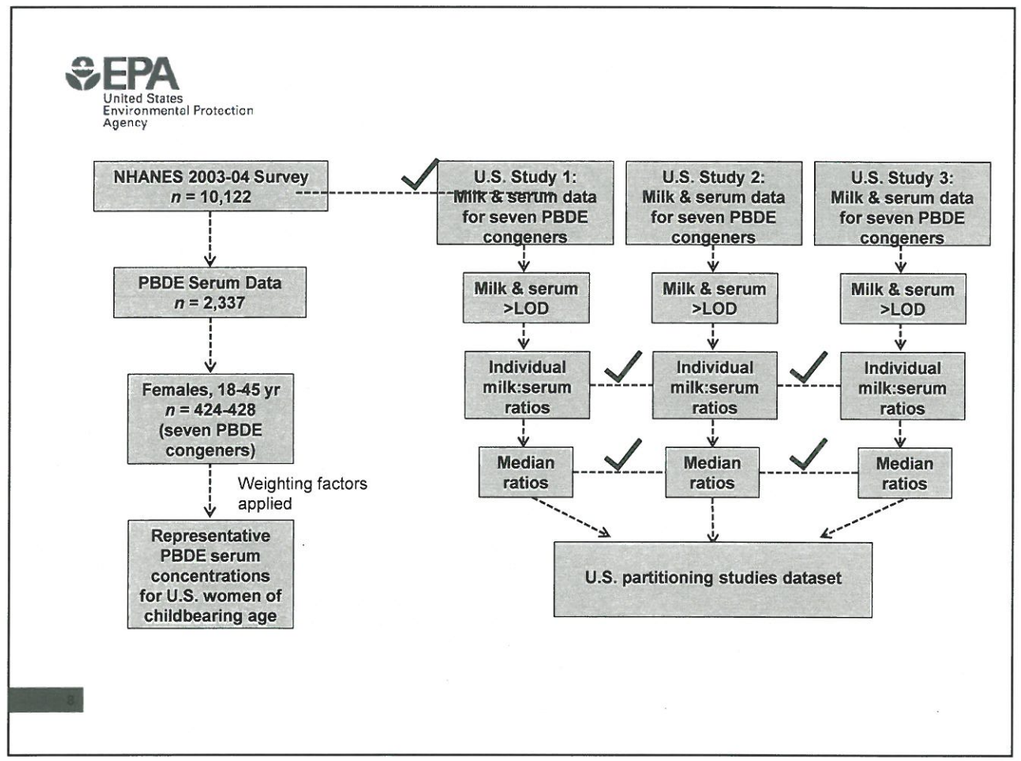
**PBDE milk:serum models + U.S. NHANES serum data** → **Predicted U.S. breast milk PBDE concentrations**




**Median milk:serum ratios**

| PBDE | Dataset A | Dataset B | Dataset C |
|---|---|---|---|
| BDE-28 | 1.57 (*n*=8) | 1.67 (*n*=4) | 1.53 (*n*=8) |
| BDE-47 | 1.30 (*n*=10) | 1.59 (*n*=10) | 1.65 (*n*=29) |
| BDE-85 | 2.30 (*n*=8) | n.d. | 1.13 (*n*=6) |
| BDE-99 | 1.26 (*n*=10) | 1.92 (*n*=3) | 1.24 (*n*=26) |
| BDE-100 | 1.25 (*n*=11) | 1.50 (*n*=10) | 1.41 (*n*=27) |
| BDE-153 | 0.91 (*n*=11) | 0.83 (*n*=5) | 0.94 (*n*=26) |
| BDE-154 | 0.70 (*n*=11) | n.d. | 0.85 (*n*=6) |

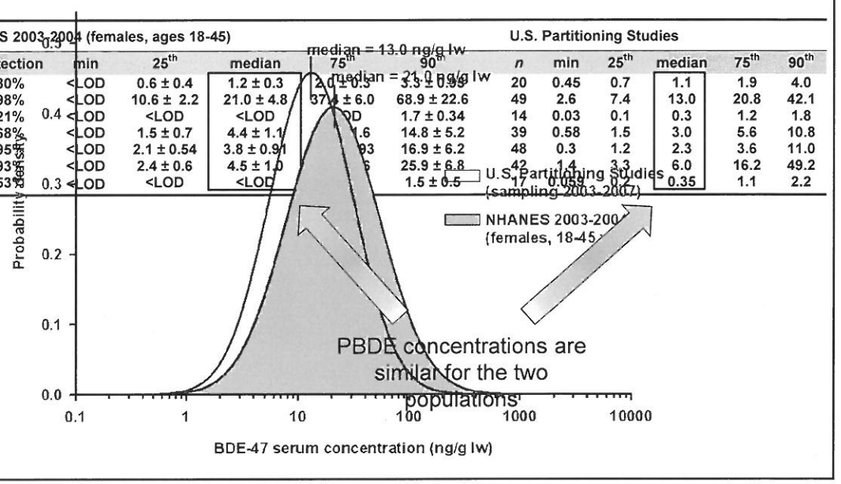

EPA
United States
Environmental Protection
Agency
NHANES 2003-04 Survey
n = 10,122
PBDE Serum Data
n = 2,337
Females, 18-45 yr
n = 424-428
(seven PBDE
congeners)
Weighting factors
applied
Representative
PBDE serum
concentrations
for U.S. women of
childbearing age
U.S. Study 1:
Milk & serum data
for seven PBDE
congeners
U.S. Study 2:
Milk & serum data
for seven PBDE
congeners
U.S. Study 3:
Milk & serum data
for seven PBDE
congeners
Milk & serum
>LOD
Milk & serum
>LOD
Milk & serum
>LOD
Individual
milk:serum
ratios
Individual
milk:serum
ratios
Individual
milk:serum
ratios
Median
ratios
Median
ratios
Median
ratios
U.S. partitioning studies dataset


EPA
United States
Environmental Protection
Agency
NHANES 2003-04 Survey
n = 10,122
PBDE Serum Data
n = 2,337
Females, 18-45 yr
n = 424-428
(seven PBDE
congeners)
Weighting factors
applied
Representative
PBDE serum
concentrations
for U.S. women of
childbearing age
U.S. Study 1:
Milk & serum data
for seven PBDE
congeners
U.S. Study 2:
Milk & serum data
for seven PBDE
congeners
U.S. Study 3:
Milk & serum data
for seven PBDE
congeners
Milk & serum
>LOD
Milk & serum
>LOD
Milk & serum
>LOD
Individual
milk:serum
ratios
Individual
milk:serum
ratios
Individual
milk:serum
ratios
Median
ratios
Median
ratios
Median
ratios
U.S. partitioning studies dataset

United States Environmental Protection Agency

**Representative PBDE serum concentrations for U.S. women of childbearing age** ✓ **U.S. partitioning studies dataset**

| | U.S. NHANES 2003-2004 (females, ages 18-45) | | | | | | | U.S. Partitioning Studies | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PBDE | *n* | Detection | min | 25th | median | 75th | 90th | *n* | min | 25th | median | 75th | 90th |
| BDE-28 | 424 | 80% | <LOD | 0.6 ± 0.4 | 1.2 ± 0.3 | 2.0 ± 0.5 | 3.5 ± 0.99 | 20 | 0.45 | 0.7 | 1.1 | 1.9 | 4.0 |
| BDE-47 | 431 | 98% | <LOD | 10.6 ± 2.2 | 21.0 ± 4.8 | 37.4 ± 6.0 | 68.9 ± 22.6 | 49 | 2.6 | 7.4 | 13.0 | 20.8 | 42.1 |
| BDE-85 | 428 | 21% | <LOD | <LOD | <LOD | <LOD | 1.7 ± 0.34 | 14 | 0.03 | 0.1 | 0.3 | 1.2 | 1.8 |
| BDE-99 | 425 | 68% | <LOD | 1.5 ± 0.7 | 4.4 ± 1.1 | 8.6 | 14.8 ± 5.2 | 39 | 0.58 | 1.5 | 3.0 | 5.6 | 10.8 |
| BDE-100 | 434 | 95% | <LOD | 2.1 ± 0.54 | 3.8 ± 0.91 | 6.93 | 16.9 ± 6.2 | 48 | 0.3 | 1.2 | 2.3 | 3.6 | 11.0 |
| BDE-153 | 434 | 93% | <LOD | 2.4 ± 0.6 | 4.5 ± 1.0 | 8.6 | 25.9 ± 6.8 | 42 | 1.4 | 3.3 | 6.0 | 16.2 | 49.2 |
| BDE-154 | 432 | 53% | <LOD | <LOD | <LOD | 0.9 | 1.5 ± 0.5 | 17 | 0.053 | 0.2 | 0.35 | 1.1 | 2.2 |



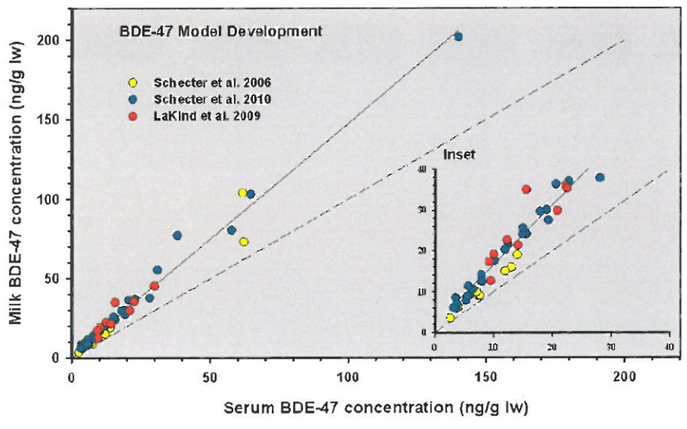
EPA United States Environmental Protection Agency

U.S. partitioning studies dataset

Models | BDE-28 | BDE-47 | BDE-85 | BDE-99 | BDE-100 | BDE-153 | BDE-154

EPA
United States
Environmental Protection
Agency

## PBDE Partitioning Models ($r^2 \geq 0.90$)




11

EPA United States Environmental Protection Agency

**U.S. partitioning studies dataset**

**Models** BDE-28 | BDE-47 | BDE-85 | BDE-99 | BDE-100 | BDE-153 | BDE-154

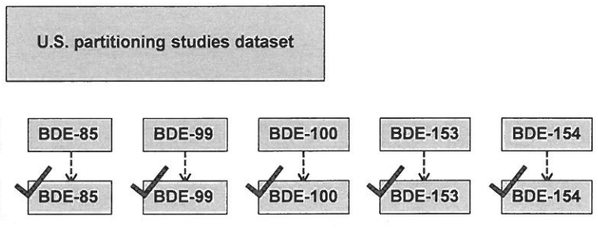
**Linear regression models**

| PBDE | *n* | $y_i' = \beta_1 x_i$ | $r^2$ | $Q^2$ |
|---|---|---|---|---|
| BDE-28 | 20 | $y_i' = 1.41(1.27, 1.55)x_i$ | 0.95 | 0.90 |
| BDE-47 | 49 | $y_i' = 1.46(1.39, 1.53)x_i$ | 0.98 | 0.97 |
| BDE-85 | 14 | $y_i' = 1.32(1.13, 1.51)x_i$ | 0.95 | 0.93 |
| BDE-99 | 39 | $y_i' = 1.40(1.24, 1.56)x_i$ | 0.90 | 0.88 |
| BDE-100 | 48 | $y_i' = 1.26(1.24, 1.28)x_i$ | 1.00 | 1.00 |
| BDE-153 | 42 | $y_i' = 0.93(0.90, 0.96)x_i$ | 0.99 | 0.99 |
| BDE-154 | 17 | $y_i' = 0.84(0.73, 0.95)x_i$ | 0.95 | 0.93 |

**Predicted Breast Milk Concentration ($y_i'$) = [Regression slope ($\beta_1$)] X [U.S. NHANES Serum Concentration ($x_i$)]**

12

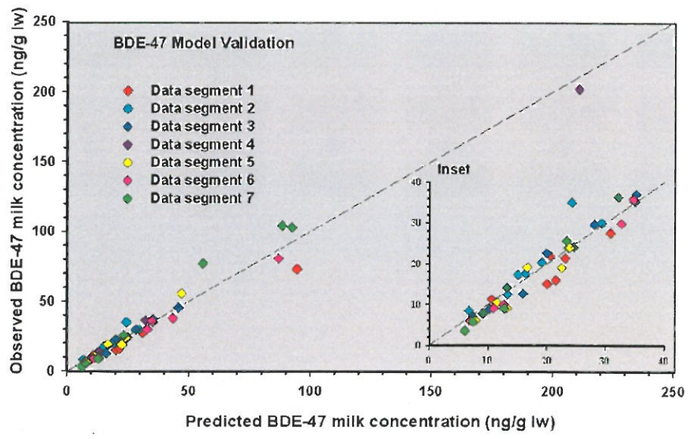
EPA United States Environmental Protection Agency



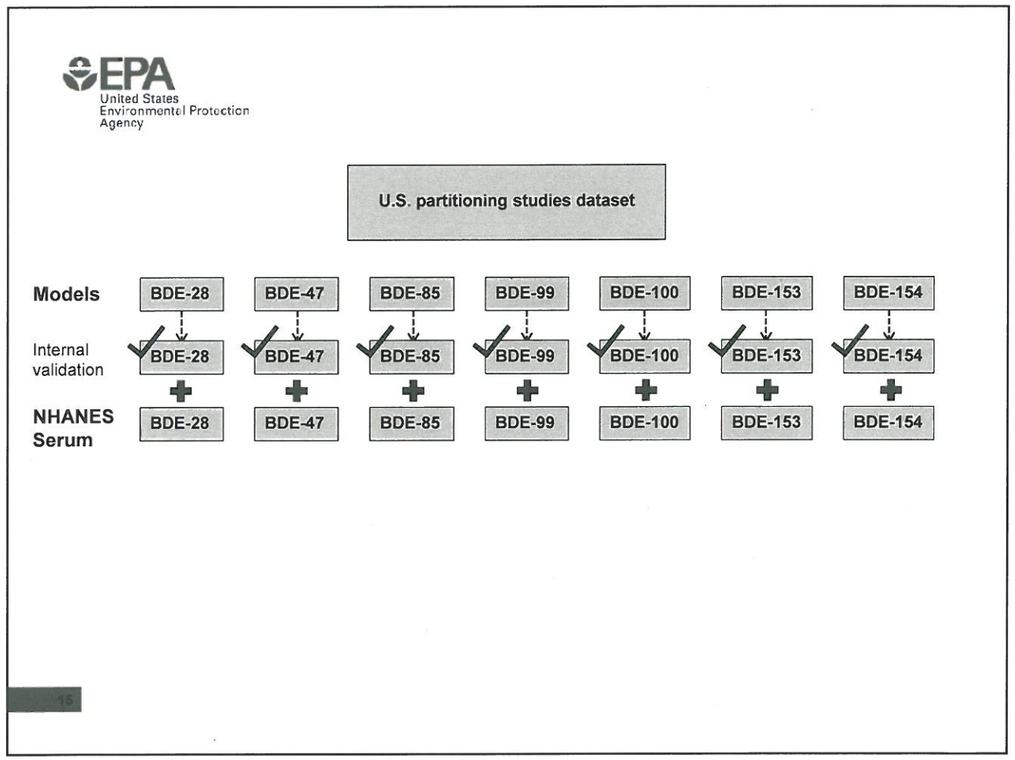

13

EPA United States Environmental Protection Agency

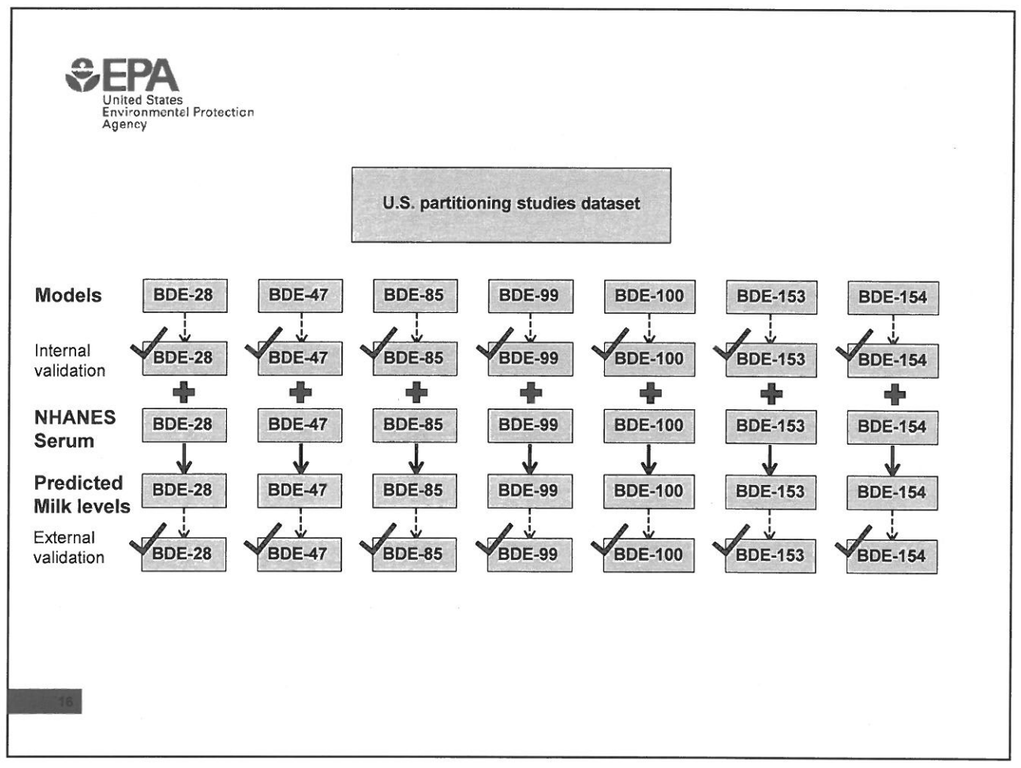
## Model Predictability ($Q^2 \geq 0.90$)



EPA United States Environmental Protection Agency




15


EPA
United States
Environmental Protection
Agency
U.S. partitioning studies dataset
Models
Internal validation
NHANES Serum
Predicted Milk levels
External validation
BDE-28
BDE-47
BDE-85
BDE-99
BDE-100
BDE-153
BDE-154
16

EPA United States Environmental Protection Agency

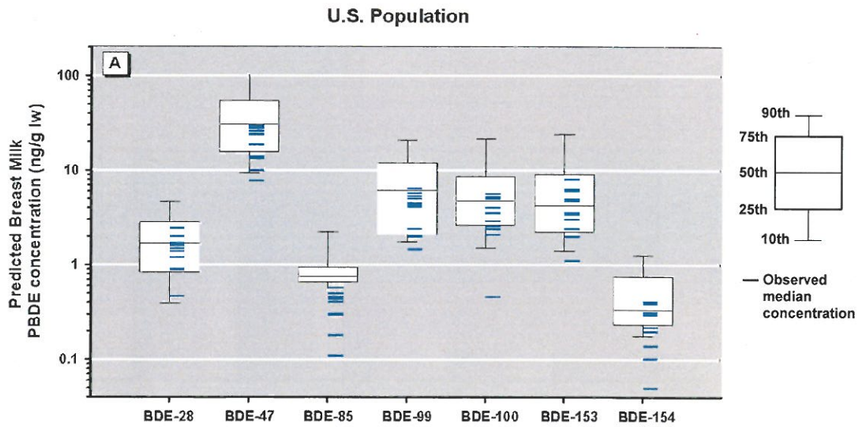
# Predicted Breast Milk PBDE Concentrations

| | | | | BDE-28 | BDE-47 | BDE-85 | BDE-99 | BDE-100 | BDE-153 | BDE-154 | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Predicted U.S. median breast milk PBDE concentrations (ng/g lw)** | | | | | | | | | | | |
| | | | | 1.69 (1.3, 2.0) | 30.61 (23.7, 37.6) | 0.75 (0.75, 0.75) | 6.14 (4.7, 7.6) | 4.79 (3.6, 5.9) | 4.20 (3.3, 5.1) | 0.33 (0.2, 0.5) | This study |
| **Observed U.S. median breast milk PBDE concentrations (ng/g lw)** | | | | | | | | | | | |
| U.S. state | Sample year | *n* | Age range (yr) | | | | | | | | |
| NC | 2004-06 | 303 | 31 ± 5 | 2.0 | 28.0 | 0.5 | 5.0 | 5.0 | 6.0 | 0.3 | Daniels et al. 2010 |
| NH | 2005-06 | 40 | 22-40 | 1.50 | 13.36 | 0.11 | 2.02 | 2.54 | 4.95 | 0.102 | Dunn et al. 2010 |
| MA | 2004 | 38 | 24-45 | 0.47 | 7.69 | <0.46 | 1.46 | <0.46 | 1.1 | 0.05 | Johnson-Restrepo et al. 2007 |
| PA | 2004-06 | 22 | 21-41 | 1.6 | 24.0 | n.d. | 3.8 | 3.6 | 3.4 | 0.3 | LaKind et al. 2008b |
| PA | 2004-05 | 10 | 22-37 | 1.6 | 26.0 | n.d. | 4.55 | 4.0 | 3.5 | 0.4 | LaKind et al. 2009 |
| CA | 2003-05 | 82 | 31 ± 7 | 2.44 | 29.7 | 0.44 | 6.40 | 5.65 | 6.34 | 0.32 | Park et al. 2011 |
| TX | 2002 | 47 | 20-41 | 1.2 | 18.4 | 0.41 | 5.7 | 2.9 | 2.0 | 0.22 | Schecter et al. 2003 |
| TX | 2003 | 11 | NA | 0.9 | 10.0 | 0.18 | 2.0 | 2.1 | 2.4 | 0.14 | Schecter et al. 2006a |
| TX | 2007 | 29 | 26-44 | 1.4 | 24.0 | 0.3 | 4.3 | 3.5 | 8.0 | 0.3 | Schecter et al. 2010 |
| MT, OR, WA | 2003 | 40 | 26-36 | 1.72 | 27.8 | 0.57 | 5.36 | 5.25 | 4.79 | 0.4 | She et al. 2007 |
| MA | 2004-05 | 46 | 19-41 | 0.9 | 13.9 | 0.3 | 2.4 | 2.4 | 3.0 | 0.2 | Wu et al. 2007 |

17

EPA United States Environmental Protection Agency

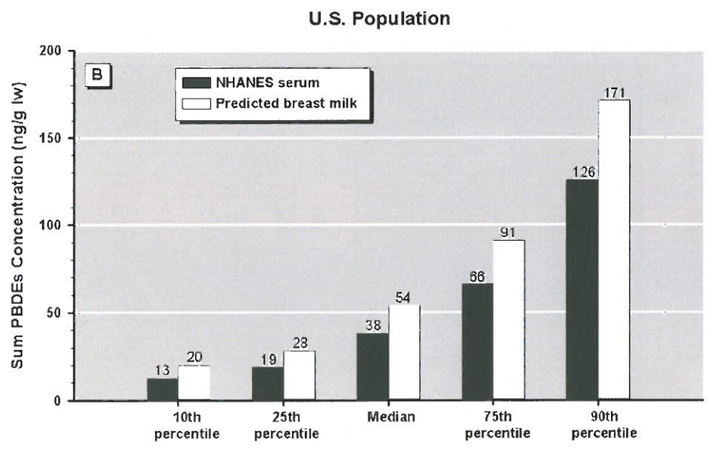
## Predicted Breast Milk PBDE Concentrations




18

EPA United States Environmental Protection Agency

## Predicted Sum PBDEs Breast Milk Concentrations




19

EPA United States Environmental Protection Agency

## Study Conclusions

**Models can predict breast milk PBDE concentrations from serum PBDE concentrations**

**Potential impacts:**
- Exposure and Risk assessment
- Understanding PBDE exposure pathways
- Monitoring temporal trends

**Future Directions:**
- Data are available for other POPs
- A comprehensive tool (QSARS) applicable to other chemicals

20

EPA
United States
Environmental Protection
Agency

# THANK YOU

The views expressed in this presentation are those of the author(s) and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency

Office of Research and Development
National Exposure Research Laboratory | Ecosystems Research Division | Athens Georgia