Putting it into Practice: Pediatric Environmental Health Training Resource

Endocrine Disrupting Chemicals and Children's Health: Phthalates and Bisphenol A

Children's Environmental Health Network

Author

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"Putting it into Practice: Pediatric Environmental Health Training Resource" made possible by support from the W.K. Kellogg Foundation

Learning Objectives

The overall goals of the workshop are to:

- Educate pediatric providers about two endocrine disrupting chemicals
- Share principles of risk communication with respect to developing environmental health messages

What are Endocrine Disruptors?

- Endocrine disruptors interfere with endocrine system function
- Mimic, block, alter synthesis, metabolism or excretion of hormones
  - Setting off similar chemical reactions in the body
  - Prevent the action of normal hormones
  - Alter the concentrations of natural hormones

Damstra, T. et al. International Programme on Chemical Safety, 2002.


Common products and potential dangers
Water bottles
Some hard-plastic, reusable water bottles are made with a chemical that scientists fear can affect fetal development.
Metal cans
Bisphenol A, an ingredient in epoxy resins that line some food cans, is associated with a higher risk of cancer.
Are our products our enemy?
Chemicals in everyday goods disrupt hormones
Nail polish
Dibutyl phthalate, which is added to some cosmetics, is linked to genital irregularities in infant boys.
Grapes
Vinclozolin, a fungicide used in growing grapes, caused changes in lab rats that span generations.
Plastic wrap
Some plastic films used to keep foods fresh contain phthalates, chemicals that researchers find are showing up in every American's urine.

USA TODAY

Examples of Endocrine Disrupting Chemicals

- Pesticides: DDT/DDE

  (See also the “Pesticides” module*)

- Organohalogens: PCBs, PBDEs, Dioxins

  (See also the “Persistant Organic Pollutants” module*)

- Heavy Metals: Lead, Mercury, Cadmium

  (See also the “Childhood Lead Poisoning” and the “Mercury, Arsenic, and Cadmium Toxicity in Children” modules*)

- Plastics/Plasticizers: Phthalates and BPA

*Additional modules in CEHN’s Pediatric Training Resource

Risk Factors through the Lifespan

Pregnancy	Birth	Infancy	Childhood	Adolescence	Adulthood






Plastics Are Everywhere

Plasticizers impart flexibility and durability

- Phthalates are anti-androgenic
  - 200 million pounds of DEHP was produced in 2002
- Bisphenol A is a weak estrogen
  - 2.3 billion pounds of BPA was produced in 2004

Wargo et al. Environment and Human Health, Inc. 2008.

Plastics Are Everywhere

Baby shampoo study raises chemical concerns

Phthalates found in urine of infants after they were powdered or lotioned

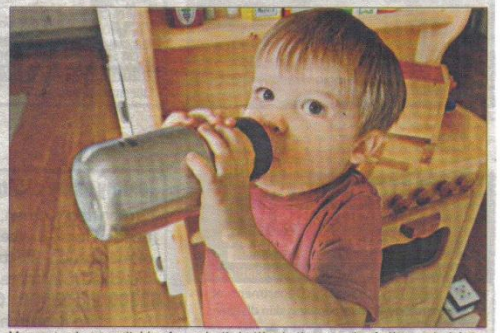
Associated Press

amNY.com/health

Baby bottle danger

Chemical in plastic may be harmful

By Stacy Downs
McClatchy Newspapers



Many parents are switching from plastic bottles to those made of other materials to avoid chemical exposure. (McClatchy Newspapers)

Parents, stores and the entire country of Canada are ditching polycarbonate baby bottles and sippy cups.

That's because the hard plastic that most baby bottles are made from contains the chemical bisphenol-A, which some researchers believe poses health risks.

On Friday, Canada banned BPA, as the chemical is commonly known, from baby bottles and drinking cups, based on a review of worldwide studies. Wal-Mart and other retailers in Canada have removed children's products containing BPA from shelves.

Also last week, Wal-Mart announced plans to stop selling children's products containing BPA by next year in U.S. stores.

"Good," said Aubrey Tsevis, a Blue Springs, Mo., teacher and mother. "It's better to be safe than sorry."

BPA also is found in some pacifiers and teethers.

Studies show a possible link between BPA and cancer, diabetes, hyperactivity and other disorders. Frederick vom Saal, a professor at the University of Missouri-Columbia and one of the key researchers of BPA, says the chemical can cause reproductive problems.

Industry groups for plastics, chemicals, juvenile products and grocery manufacturers maintain that BPA is safe, based on evidence and findings of the Food and Drug Administration.

But last week the National Toxicology Program, an office of the National Institutes of Health, in a draft report expressed concern. The office does not regulate BPA, but its findings are used to set safe exposure limits for chemicals.

In reaction, Sen. Charles Schumer said he would file a bill to ban BPA from baby products, dental sealants and any bottle or container that holds food and drink.

www.nottoopretty.org

What Parents Ask

- How do I know if toys contain phthalates?
- Are bottles with bisphenol A harmful?
- What are the current regulations?
- What health effects should I look for?
- What alternatives can my child use?

Where are Phthalates found?

You could think of them as the sixth basic food group. Oh, you certainly wouldn't eat them, but plastic packaging does help protect our food in many ways. • To help lock in freshness, plastic wrap clings tightly to surfaces. To help lock out moisture, resealable containers provide a strong seal. And plastic wrap helps extend the shelf life of perishable produce, poultry, fish and meats. • To prevent spoilage and contamination, some varieties of plastics help keep air out. While others let air in to help the food we eat stay fresher longer. Plastics also let you see what you're buying, taking the mystery out of shopping. All of which makes them versatile, durable, lightweight and shatter-resistant. • To learn more, call the American Plastics Council at 1.800.777.9500 for a free booklet. Plastics. One part of your diet you may never break.

Plastics. An Important Part Of Your Healthy Diet.

American Plastics Council®

PLASTICS MAKE IT POSSIBLE.™

Visit us at http://www.plasticsresource.com

Where are Phthalates found? (continued)

Product	Phthalate	Metabolite
Foods Toys Medical supplies	DEHP: di-(2-ethylhexyl) phthalate	MEHP: mono-(2-ethylhexyl) phthalate MEOHP: Mono(2-ethy-5-oxolhexyl) phthalate MEHHP: Mono(2-ethyl-5-hydroxyhexyl) phthalate MECPP: Mono(2-ethy-5-carboxypentyl) phthalate
Toys	DINP: di-isononyl phthalate DIDP: di-isodecyl phthalate DNOP: Di-*n*-octylphthalate	MINP: monoisononyl phthalate MCIOP: mono(carboxy-isooctyl) phthalate MOINP: mono(oxoisononyl)phthalate MHINP: mono (hydroxy-isononyl)phthalate MIDP: monoisodecyl phthalate MnOP: :mono-n-octyl phthalate

Where are Phthalates found? (continued)

Product	Phthalate	Metabolite
PVC, vinyl floors, cosmetics	BBzP: benzyl butyl phthalate DEHP: di-(2-ethylhexyl) phthalate	MBzP: monobenzyl phthalate MEHP: mono-(2-ethylhexyl) phthalate MEOHP: Mono(2-ethy-5-oxolhexyl) phthalate MEHHP: Mono(2-ethyl-5-hydroxyhexyl) phthalate MECPP: Mono(2-ethy-5-carboxypentyl) phthalate
Cosmetics: nail polish and perfumes	DEP: diethyl phthalate DBP: dibutyl phthalate DMP: dimethyl phthalate	MEP: monoethyl phthalate MBP: monobutyl phthalate

Centers for Disease Control (CDC) 4th Report on Human Exposures

Geometric Means of Phthalates (ug/g creatinine) by age			
PHTHALATE	6-11yo	12-19yo	20yo+
mBzP	35.8	16.6	11
mEHP	3	2.07	2.14
mEOHP	26.6	14.6	12.4
mEHHP	39	21.2	18.8
mEP	96.9	168	197
mBP	38.4	20	18.3
miBP	6.94	3.4	3.3

Phthalates Findings

- Animal studies demonstrate that the male reproductive tract is particularly sensitive to the anti-androgenic effects of phthalates

Summary of Findings

In animal studies there is evidence of:

- Adverse birth outcomes
- Reproductive toxicity
- Male reproductive tract particularly sensitive

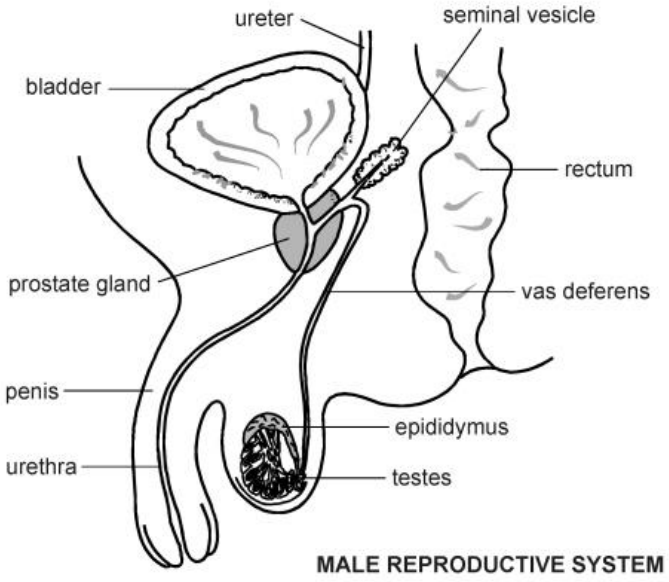
Human studies:

- Alterations in hormone levels
- Male Infertility
- Asthma, puberty and body size
- Prenatal exposure and
  - decreased anogenital distance
  - neurodevelopment

Phthalates Syndrome

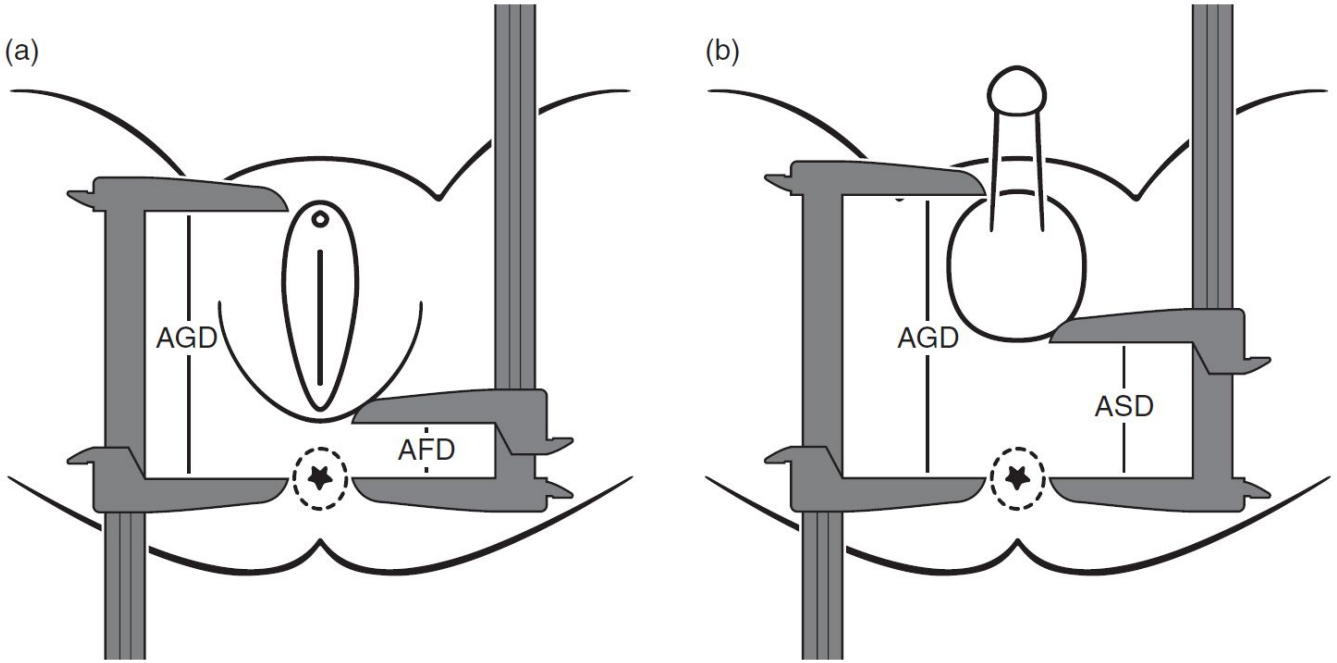
Anti-Androgen Effects

- Hypospadias
- Undescended Testes
- Fetal Germ Cell Effects
- Infertility
- Decreased Anogenital Distance



Foster PMD, Int J Androl, 2006.

Anogenital Distance n=169



Sathyanarayana et al. Int J of Androl, 2009.

Decreased anogenital distance is a measure of anti-androgen exposure n=85

Table 5. Mean (median) phthalate monoester metabolite levels by AGI category.

Monoester metabolite	AGI category [mean (median; ng/mL)]		
	Long[a] ($n = 17$)	Intermediate[b] ($n = 43$)	Short[c] ($n = 25$)
MBP	13.1 (11.5)	22.2 (13.1)	38.7 (24.5)
MBzP	10.6 (6.6)	15.1 (7.7)	25.8 (16.1)
MEP	124 (47.1)	592 (112)	1,076 (225)
MiBP	2.3 (1.5)	3.3 (2.1)	7.7 (4.8)

[a]Long, AGI ≥ 75th percentile of expected AGI. [b]Intermediate, 25th percentile ≤ AGI < 75th percentile of expected AGI. [c]Short, AGI < 25th percentile of expected AGI.

Anogenital Distance is normally twice as long in males as in females

Swann et al. Environ Health Perspect, 2005.

Phthalates & Testicular Descent in Humans n=85

AGD Category	Percent with Incomplete Testicular Descent
Short	20.0%
Intermediate	9.5%
Long	5.9%

P<0.001

Swan SH et al. Environ Health Perspect, 2005.

Postnatal Exposures

Phthalates in breast milk and serum hormone levels in male offspring, n=130

- **Adverse effect on Leydig cell function**:
  - Elevated LH levels
  - decreased free testosterone
  - elevated LH:free testosterone ratio
- **Indirect sign of reduced androgen activity:**
  - Increased SHBG

Main et al. Environ Health Perspect, 2006.

Phthalates Exposures in Infants

Measured phthalates in 163 infants (2-28 mos) born in 2000–2005

- **Lotion** predictive of monoethyl phthalate and monomethyl phthalate concentrations
- **Powder** of monoisobutyl phthalate
- **Shampoo** of monomethyl phthalate
- More products used= higher exposure

Sathyanarayana et al, Pediatrics, 2008.

Prenatal Exposures

3rd Trimester maternal phthalates and neonatal behavior in NYC (n=295)

- NYC Pregnancy Cohort assessed Brazelton Neonatal Behavioral Assessment Scale (BNBAS)
- Among girls, there was a significant linear decline in adjusted mean orientation score with increasing high molecular weight phthalate metabolites (B=-0.37, p=0.02)
- Strong linear decline in adjusted mean Quality of Alertness score (B=-0.48, p<0.01)

Engel et al. Neurotoxicology, 2009.

Prenatal Phthalates Exposures and Child Neurodevelopment (n=188)

- Same cohort with f/u visits between 4-9 years of age, BRIEF and BASC administered.
- Evidence of dose-response effect of Prenatal LMW Phthalate Exposure on behavioral problems in childhood.
- Patterns of association overlap with domains affected in childhood Conduct Disorder and ADHD clinical groups.
- Limitations: Small sample size (n=188), Needs to be replicated in independent cohorts.
- If replicated, preventive measures to reduce exposure during pregnancy may be warranted.

Engel et al. Environ Health Perspect, 2010.

Phthalates Legislation

- **European Union 2005**
  - 3 banned in all toys/child-care products
  - 3 banned in toys/child-care products that can be mouthed

- **California Phthalates Ban 2009**
  - 6 phthalates banned in toys/child-care products
  - prohibits manufacture, sale, and distribution

Consumer Product Safety Improvement Act of 2008

- Federal legislation: mandatory third party safety testing and certification of all toys and products marketed to children <12 years old
- It includes a ban on phthalates in toys and children's products: DEHP, DBP and BBP
- Interim ban on the use of three other phthalates: DINP, DIDP and DnOP

European Union 2003

- Phthalates DEHP, DBP and BBP are all prohibited from use in cosmetics due to their classification as substances that are potentially carcinogenic, mutagenic or reproductive toxicants.

California Safe Cosmetics Act of 2005

- Manufacturers that sell over $1 million a year in personal-care products
- Report any products containing a chemical that is either a carcinogen or a reproductive or developmental toxic agent.
- Phthalates: DEHP and DBP

EPA Action Plan 2009

- Coordinated approach with the Consumer Product Safety Commission (CPSC) and the Food and Drug Administration (FDA)

- Intends to initiate action to address the
  - Manufacturing
  - Processing
  - Distribution in commerce and/or use

What Can You Do to Reduce Phthalates Exposures?

Precautionary Approach:

- Eat fresh foods
- Avoid use in microwave
- Avoid use in dishwasher
- Wet mop and dust frequently
- Seek phthalates free labels
- Keep it simple, less is more
- www.cosmeticsdatabase.org

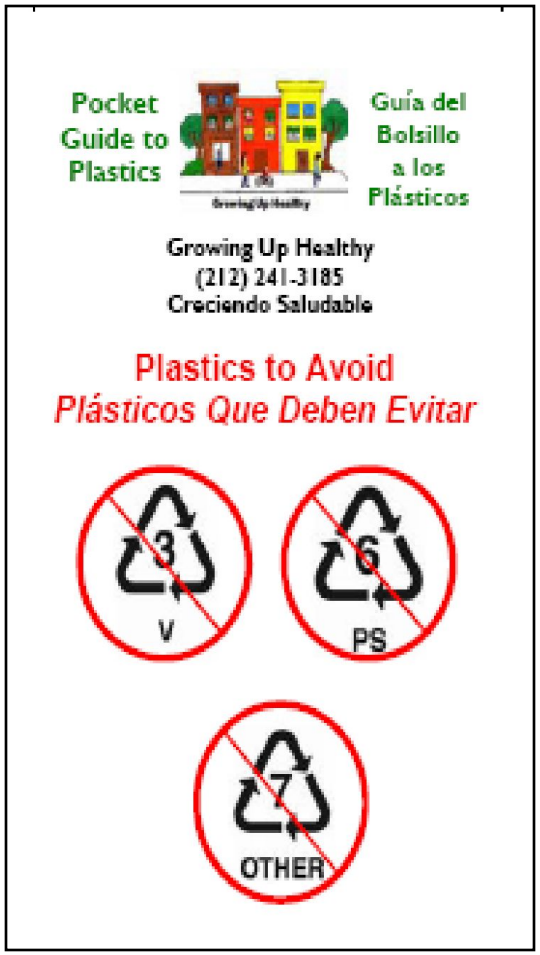
Look to recycling labels

#3 plastics can contain phthalates

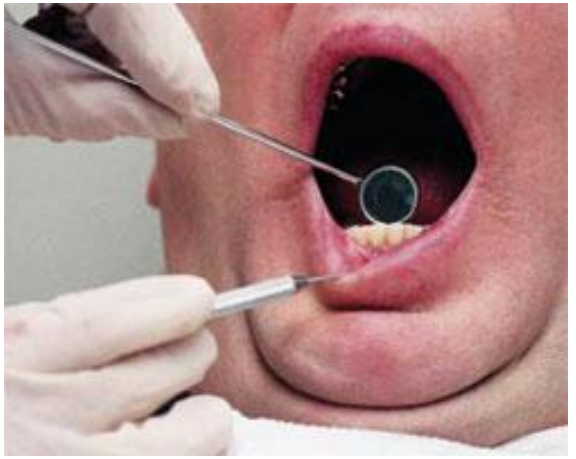
Pocket Guide to Plastics

Front of card

Back of card



Bisphenol A (BPA)



BPA Exposures are Widespread

- NHANES 2003-2004 Calafat et al.
  - US population ages 6-85 years (n=2517)
  - BPA present in 93% of population
  - Children 6-11 years (n=217)
    - Geometric mean BPA=4.3 ug/gram creatinine
    - Children >6 years old ($p < 0.001$) and adolescents ($p < 0.003$) had higher levels than adults

Summary of Findings

BPA is a weak estrogen

- Animal studies:
  - Adverse birth outcomes
  - Male reproductive tract
  - Early pubertal development
  - Increased body size
- Human studies:
  - Prenatal exposure and neurodevelopment
  - Prenatal exposure and wheeze in children
  - Cardiovascular disease, Type 2 Diabetes, Obesity
  - Liver function (GGT, LDH, Alk Phos)
  - Childhood Obesity
  - Cancer classification controversial

Prenatal BPA and early childhood behavior in 2 year olds n=249

- Maternal urine collected from 16-26 weeks
  - Behavioral Assessment System for Children (BASC 2)
- Mean BPA concentration associated with externalizing scores in girls, a measure of aggression and hyperactivity
  - 16 weeks>26 weeks more strongly correlated

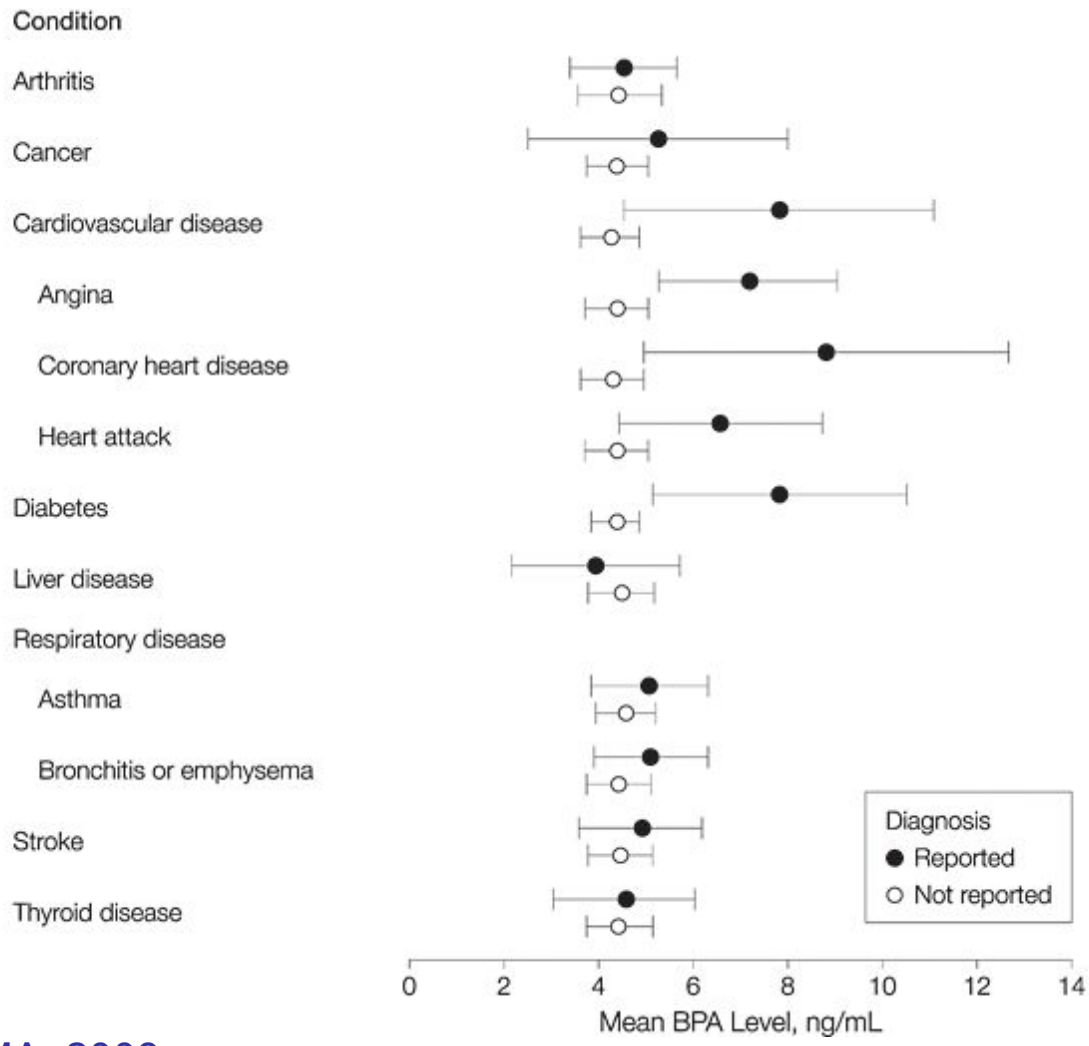
Braun et al, Environ Health Perspect, 2009.

Prenatal Exposure to BPA and child wheeze from birth to 3 yrs

- Cohort of 398 mother-infant pairs and assessed serial maternal BPA and parent-reported child wheeze every 6 months for 3 years.
- Mean prenatal BPA at 16 weeks gestation was associated with increased odds of wheeze in early life 6 months to 3 years

Spanier et al, Environ Health Perspect, 2012.

Estimated Mean BPA Concentrations in Relation to Reported Diseases and Conditions, N=1455



Lang, I. A. et al. JAMA, 2008.

JAMA

BPA in dental sealants

- BPA released from dental resins through enzymes in the saliva
  - Detectable in saliva for up to 3 hours
  - % absorbed is unknown
  - Bis-GMA resins preferred over bis-DMA
- Rub sealants with pumice stone at time of placement and gargle x 30 seconds
- Recommend continued use of sealants, though avoid in pregnancy

Fleisch et al, Pediatrics, 2010.

BPA Legislation

- Canada BPA ban effective 2008
  - prohibits the importation or sale of BPA in bottles and food packaging for infants and newborns
  - 2010 Update: Canada to list BPA as 'toxic‘
- Suffolk County, Long Island, NY 2009
- Chicago, Illinois 2009
- NYS 2010: Bisphenol-A-Free Children and Babies Act
- California 2010: Toxin Free Infants and Toddlers act.
- Voluntary Withdrawal: US Products, Manufacturers, and Major Retailers
- U.S. lawmakers move to ban BPA from food, beverage containers

Suffolk County, Long Island, NY Ban on BPA Hailed in Some Quarters

Ann-Marie Norris for The New York Times
NY TIMES March 13, 2009

What Can You Do to Reduce Phthalates and BPA Exposures?

Parents do the best they can with the information they have at the time…..

What Can You Do to Reduce Phthalates and BPA Exposures?

- Provide families with evidence based information so that they may make informed decisions about what is best for their family
- In the absence of scientific certainty, err on the side of caution and take a precautionary approach

Precautionary Approach: Alternative Products

Stainless Steel Water Bottles

Bisphenol A free bottles

Precautionary Approach: Alternative Products

Choose alternatives to canned foods: Fresh fruits and vegetables

Consider alternatives to canned infant formulas: Breast is Best!

Select Glass Food Containers

Look to recycling labels

#7 plastics *may* contain bisphenol A

Pocket Guide to Plastics

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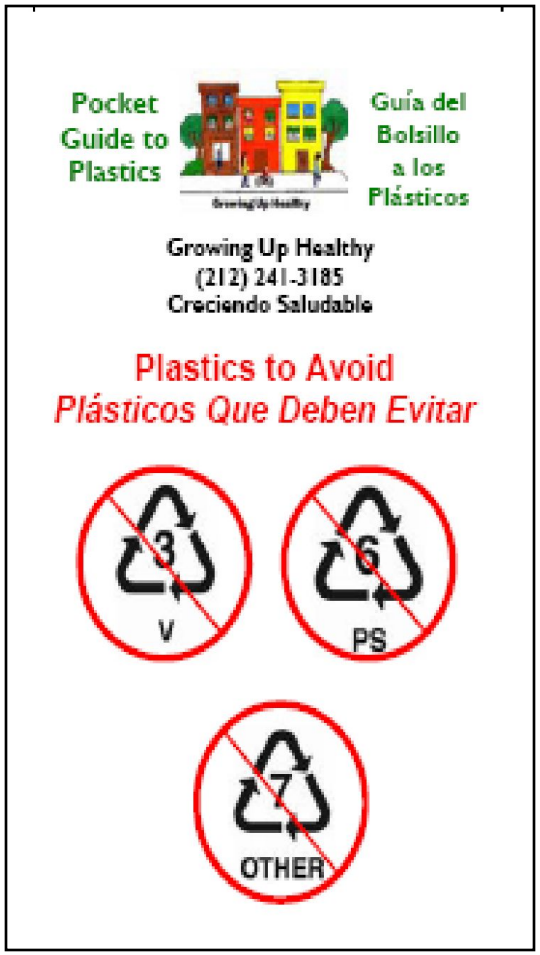
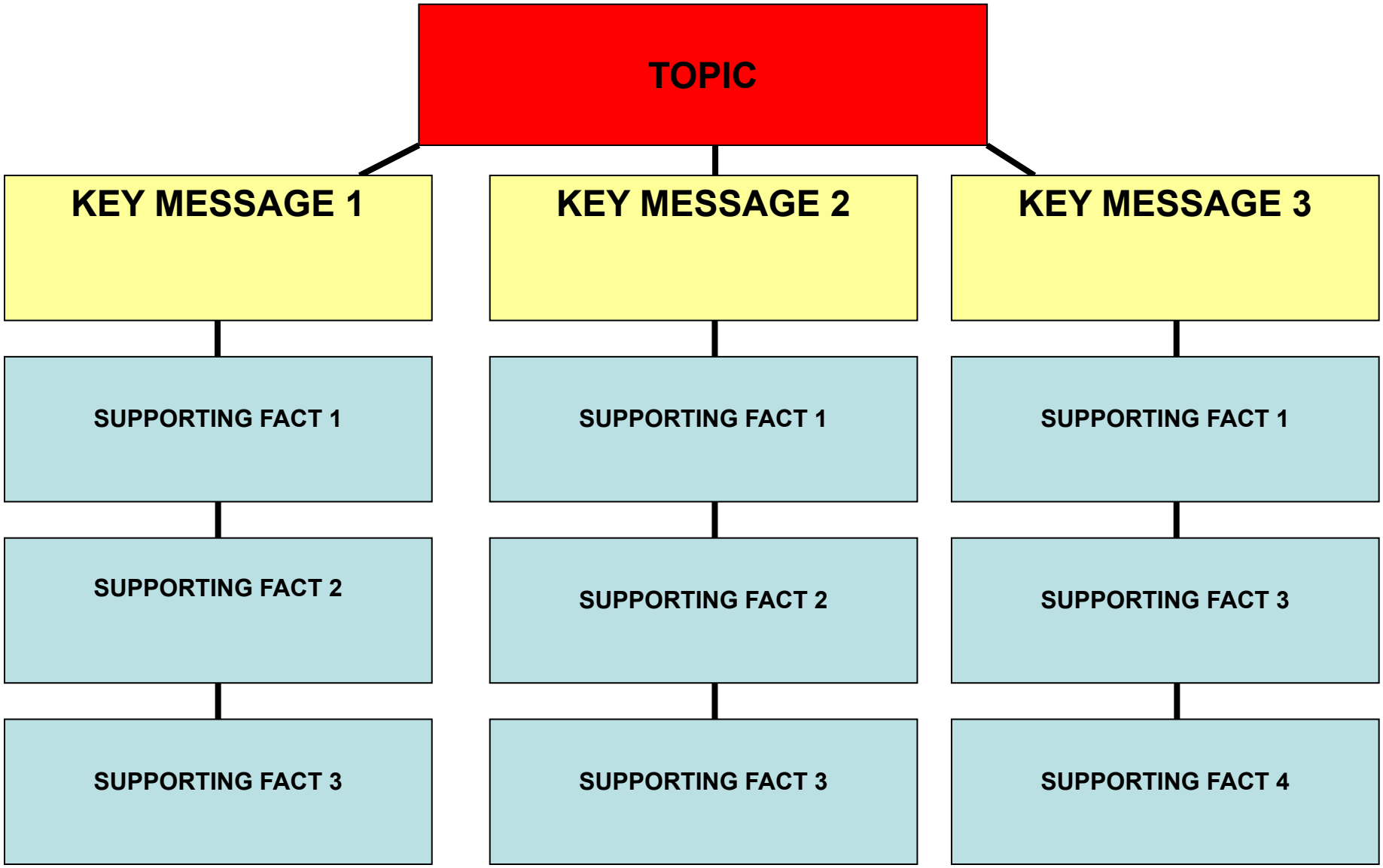


Key Risk Communication Lessons

- It is important to craft clear and concise messages in advance using straightforward language.
- Develop 3 key messages maximum with 3 supporting facts for each key message
  - Define the Exposure
  - Explain What is Known About Potential Health Effects
  - Provide Action Items for Families

Message Map


TOPIC
KEY MESSAGE 1
KEY MESSAGE 2
KEY MESSAGE 3
SUPPORTING FACT 1
SUPPORTING FACT 2
SUPPORTING FACT 3
SUPPORTING FACT 1
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SUPPORTING FACT 3
SUPPORTING FACT 1
SUPPORTING FACT 3
SUPPORTING FACT 4

Key Messages

Endocrine Disrupting Chemicals:

Phthalates and Bisphenol A

Key Message 1

Phthalates and bisphenol A are added to every day products because they add flexibility and durability.

Key Message 2

Concerns have been raised about potential for health effects based on animal studies and growing evidence that the US population is universally exposed.

Key Message 3

Given the concerns raised by animal studies and limited human studies, one can take a precautionary approach and choose alternatives.

Endocrine Disrupting Chemicals: Phthalates and Bisphenol A

Key Message 1

Phthalates and bisphenol A are added to every day products because they add flexibility and durability.

SF1

Phthalates are found in foods and food packaging, personal hygiene products (eg cosmetics), medical tubing, children's toys, and vinyl products.

SF2

Bisphenol A is found in hard plastics such as sports bottles, baby bottles, canned goods, and dental sealants.

SF3

These 2 chemicals are of particular concern because they are known to leach from these products resulting in exposure through ingestion, inhalation or dermal absorption.

Key Message 2

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Endocrine Disrupting Chemicals: Phthalates and Bisphenol A

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Key Message 2

Concerns have been raised about potential for health effects based on animal studies and growing evidence that the US population is universally exposed.

SF1

Phthalates and BPA are known to have hormonal activity. For these reasons, they are often referred to as endocrine disruptors.

SF2

The US population is universally exposed with children and adolescents having higher exposure levels than adults.

SF3

Animal studies suggest a potential for impacts on birth outcomes and the male reproductive tract is particularly sensitive. Human studies are assessing links to early puberty, obesity and asthma.

Key Message 3

Given the concerns raised by animal studies and limited human studies, one can take a precautionary approach and choose alternatives.

Endocrine Disrupting Chemicals: Phthalates and Bisphenol A

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Key Message 3

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SF1

Look for phthalates and bisphenol A free products. In the absence of labeling, look to recycling labels, avoid #3, 6 and 7 plastics.

SF2

Avoid heating in microwave and placing in dishwasher since high heat promotes leaching of plasticizers.

SF3

Choose what are known to be safer alternatives, fresh or frozen foods rather than canned, choose glass or stainless steel instead of plastic and encourage breastfeeding.

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Safe Chemicals Act: A Proposal for Chemical Reform

- Bills to overhaul federal toxic chemicals policies are moving through Congress.

- Require that all chemicals be proven safe for children before they can be sold.

Major Concerns: Putting it into Context

Mount Sinai Children's Environmental Health Center

U.S.

- Cigarette and Tobacco Smoke
- Pesticides
- Environmental Asthma Triggers
- Lead
- Mercury in Fish

Worldwide

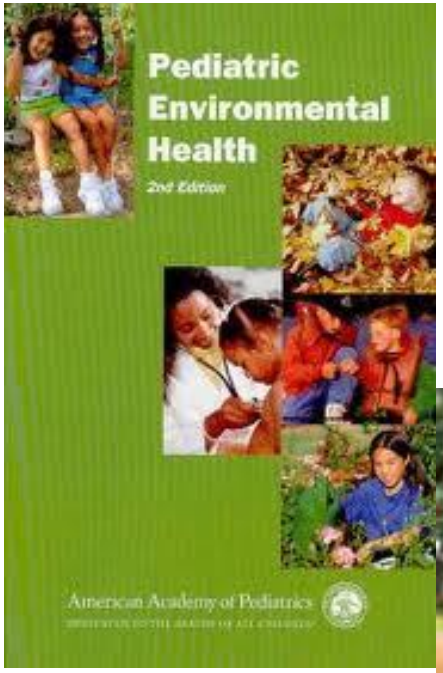
- Clean Water and Air
- Basic Shelter and Housing

Changes You May Wish to Make in Practice

- Participants will have a framework for developing evidence-based health messages for plastics exposure in childhood that are easily comprehensible
- Key principles of risk communication will be utilized in developing these messages
- Participants will utilize existing key resources in children's environmental health

Resources

- AAP Green Book
- AAP Technical Report on Phthalates
- PEHSU fact sheets
- Contemporary Pediatrics Article
- CDC National Report on Human Exposures
  - http://www.cdc.gov/exposurereport/



Resources (continued)

PEHSU
Pediatric Environmental Health Specialty Units

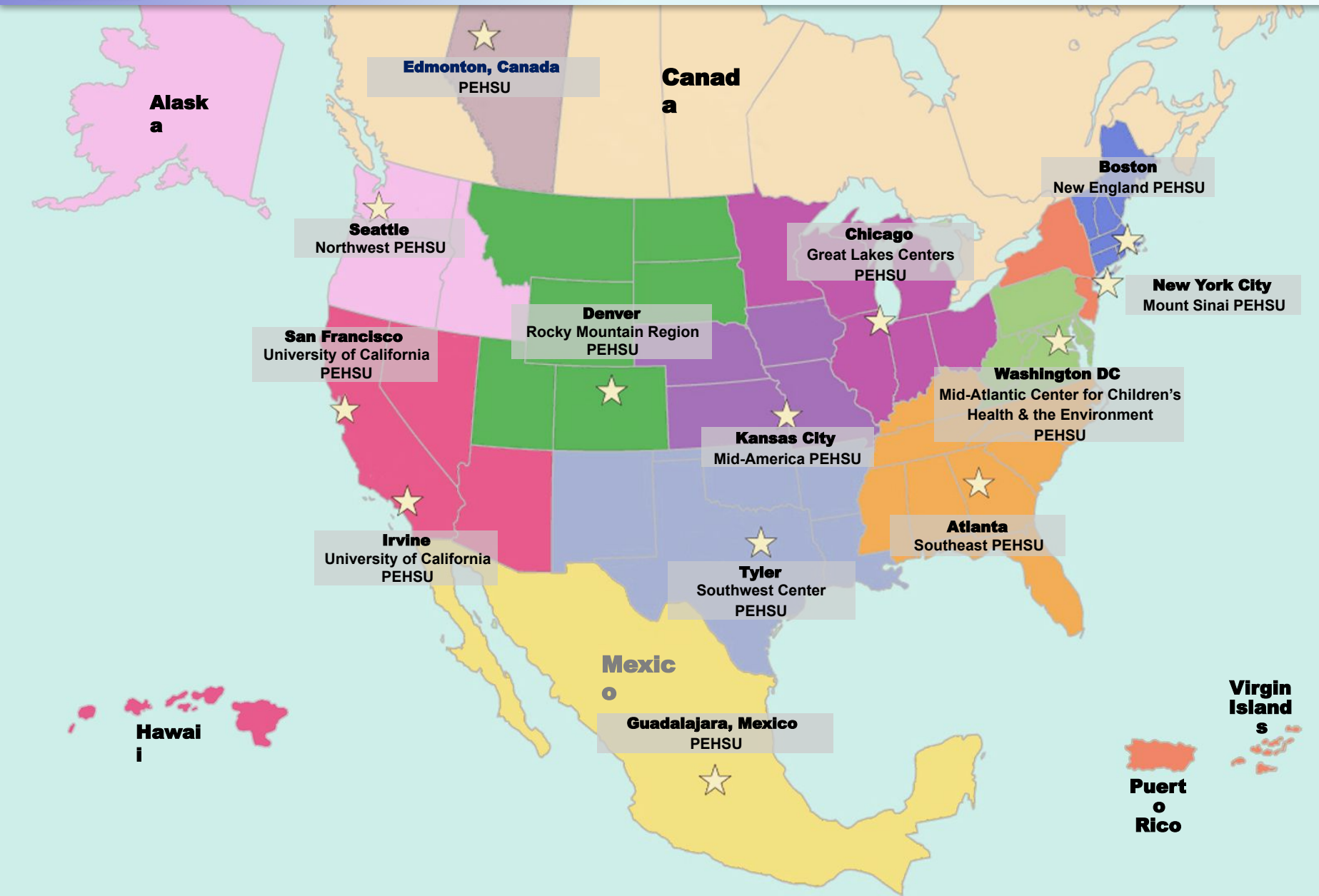
A resource for pediatricians, public health officials, school personnel, parents and others to get questions answered about children's health and the environment

ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

AOEC

Pediatric Environmental Health Specialty Units (PEHSU) In North America



PEHSU Staff

- Environmental Pediatricians
- Allergy Immunologists
- Family Medicine
- EOM Physicians
- Toxicologists
- PEHSU coordinator
- Social Worker
- Industrial Hygienists
- Environmental Pediatrics Fellows

Thank You!

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Acknowledgements

- Drs. Sheela Sathyanarayana, Susan Teitelbaum, Luz Claudio, Joel Forman, Barbara Brenner and Mary Wolff
- AAP COEH District 2 Chapter 3
- National Institute of Environmental Health Sciences
  - NIEHS Grant #2 P01 ES009584 and ES012645
- Environmental Protection Agency
  - EPA Grant #R827039 and #RD831711
- National Cancer Institute
  - NCI Grant #CA93447
- National Center for Research Resources (GCRC)
  - NCRR grant #MO1-RR-00071
- Agency for Toxic Substances and Disease Registry
  - ATSDR Grant #ATU 300014

Acknowledgements

- This material was supported by Association of Occupational and Environmental Clinics and funded under cooperative agreement award 1U61TS000118-03 from the Agency for Toxic Substances and Disease Registry (ATSDR).

- The US Environmental Protection Agency (EPA) supports the PEHSU by providing funds to ATSDR under Inter-Agency Agreement number DW-75-92301301-0.

Neither EPA nor ATSDR endorse the purchase of commercial products/services mentioned.

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