



# Introduction to American Academy of Pediatrics (AAP)

The **AAP** is an organization of 67,000 pediatricians committed to the optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults.

The **Council on Environmental Health (COEH)** is the home for Academy members interested in and concerned about children's environmental health and toxic exposures.

# Introduction to AAP's Council on Environmental Health (COEH)

Key activities include:

- Advising the AAP Board of Directors on issues pertaining to environmental health and toxic exposure.
- Council-authored policy statements
  - Ex: air pollution, lead screening, pesticides, radiation disasters, and secondhand smoke.
- Supporting legislative initiatives designed to protect the health of the fetus, infant, and child from environmental agents.
- Developing educational initiatives related to children's environmental health.
- Publishing the Academy landmark Pediatric Environmental Health manual, currently in its third edition.

# Introduction to AAP Statements

TECHNICAL REPORT

American Academy  
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

## Food Additives and Child Health

Leonardo Trasande, MD, MPP, FAAP,<sup>a</sup> Rachel M. Shaffer, MPH,<sup>b</sup> Sheela Sathyanarayana, MD, MPH,<sup>b,c</sup>  
COUNCIL ON ENVIRONMENTAL HEALTH

**POLICY STATEMENT** Organizational Principles to Guide and Define the Child Health Care System  
and/or Improve the Health of all Children

American Academy  
of Pediatrics



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## Food Additives and Child Health

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# What is a “Food Additive?”

Food additives: substances “*the intended use of which results or may reasonably be expected to result, directly or indirectly, in becoming a component or otherwise affecting the characteristics of any food*” (21 USC 321(s) and 21 CFR 170.3)

- Direct: intentionally added to food
  - ex: colorings, flavorings
- Indirect: not intentionally added to foods but reasonably expected to be part of food
  - ex: materials in food packaging & processing equipment



<https://www.istockphoto.com/photo/american-grocery-collection-gm458413271-23870026>



<https://www.npr.org/sections/health-shots/2011/07/22/138606851/eat-enhanced-meat-usda-rule-may-make-it-easier-to-tell>

# Technical Report

Goal: Review evidence of harm to child health from food additives

- Epidemiological & toxicological data
- Exposure data & trends

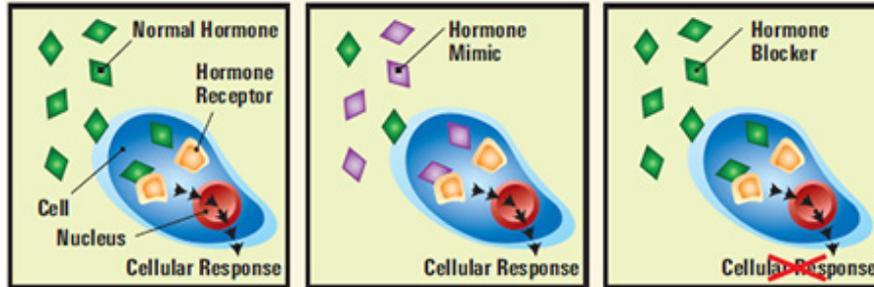
Categories of food additives:

- Indirect: food contact materials, used in packaging or processing
  - Adhesives, coatings, plastics, paperboard
- Direct: deliberately added to food
  - Colorings, flavorings

# Chemical environmental agents and the endocrine system

Endocrine disruptors (EDs) interfere with hormonal signaling

- May mimic, block, or modulate the synthesis, release, transport, metabolism, binding, or elimination of natural hormones



<https://www.niehs.nih.gov/health/topics/agents/endocrine/index.cfm>

- May temporarily or permanently alter feedback loops in the brain, pituitary, gonads, thyroid, and other components of the endocrine system

## Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement

Evanthia Diamanti-Kandarakis, Jean-Pierre Bourguignon, Linda C. Giudice, Russ Hauser, Gail S. Prins, Ana M. Soto, R. Thomas Zoeller, and Andrea C. Gore

Endocrine Section of First Department of Medicine (E.D.-K.), Laiko Hospital, Medical School University of Athens, 11527 Athens, Greece; Department of Pediatrics (J.-P.B.), Centre Hospitalier Universitaire de Liege, 4000 Liege, Belgium; Department of Obstetrics, Gynecology, and Reproductive Sciences (L.C.G.), University of California San Francisco, San Francisco, California 94131; Department of Environmental Health (R.H.), Harvard School of Public Health, Boston, Massachusetts 02115; Department of Urology (G.S.P.), University of Illinois at Chicago, Chicago, Illinois 60612; Department of Anatomy and Cell Biology (A.M.S.), Tufts University School of Medicine, Boston, Massachusetts 02111; Biology Department (R.T.Z.), University of Massachusetts, Amherst, Massachusetts 01003; and Division of Pharmacology and Toxicology (A.C.G.), The University of Texas at Austin, Austin, Texas 78712

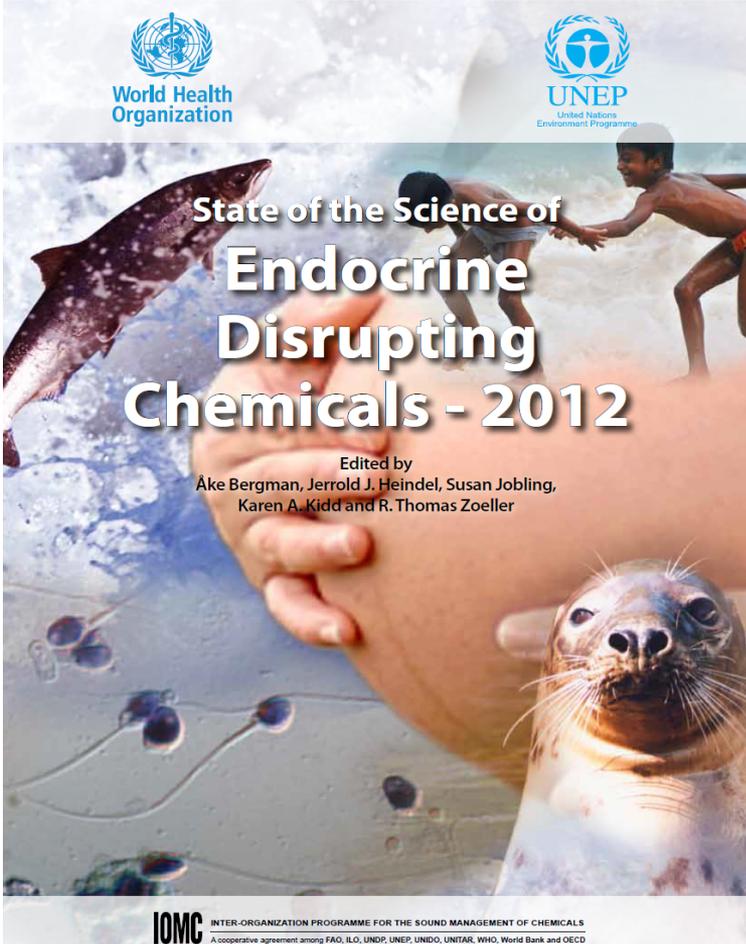
There is growing interest in the possible health threat posed by endocrine-disrupting chemicals (EDCs), which are substances in our environment, food, and consumer products that interfere with hormone biosynthesis, metabolism, or action resulting in a deviation from normal homeostatic control or reproduction. In this first scientific statement of The Endocrine Society, we present the evidence that endocrine disruptors have effects on male and female reproduction, breast development and cancer, prostate cancer, neuroendocrinology, thyroid, metabolism and obesity, and cardiovascular endocrinology. Results from animal models, human clinical observations, and epidemiological studies converge to implicate EDCs as a significant concern to public health. The mechanisms of EDCs involve divergent pathways including (but not limited to) estrogenic, antiandrogenic, thyroid, peroxisome proliferator-activated receptor  $\gamma$ , retinoid, and actions through other nuclear receptors; steroidogenic enzymes; neurotransmitter receptors and systems; and many other pathways that are highly conserved in wildlife and humans, and which can be modeled in laboratory *in vitro* and *in vivo* models. Furthermore, EDCs represent a broad class of molecules such as organochlorinated pesticides and industrial chemicals, plastics and plasticizers, fuels, and many other chemicals that are present in the environment or are in widespread use. We make a number of recommendations to increase understanding of effects of EDCs, including enhancing increased basic and clinical research, invoking the precautionary principle, and advocating involvement of individual and scientific society stakeholders in communicating and implementing changes in public policy and awareness. (*Endocrine Reviews* 30: 293–342, 2009)



World Health  
Organization



UNEP  
United Nations  
Environment Programme



# State of the Science of Endocrine Disrupting Chemicals - 2012

Edited by  
Åke Bergman, Jerrold J. Heindel, Susan Jobling,  
Karen A. Kidd and R. Thomas Zoeller

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS  
A cooperative agreement among FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD



# Indirect Food Additives

Chemical	Food-Related Use	Health Concerns
<b>Bisphenols</b> (Bisphenol-A & related compounds)	<ul style="list-style-type: none"><li>• Polycarbonate plastic containers</li><li>• Polymeric epoxy resins for food &amp; beverage cans</li></ul>	<ul style="list-style-type: none"><li>• Endocrine disruption</li><li>• Obesogenic activity</li><li>• Neurodevelopmental disruption</li></ul>
<b>Phthalates</b>	<ul style="list-style-type: none"><li>• Clear plastic food wrap</li><li>• Plastic tubing &amp; storage containers for food production</li><li>• Food manufacturing equipment</li></ul>	<ul style="list-style-type: none"><li>• Endocrine disruption</li><li>• Obesogenic activity</li><li>• Oxidative stress</li><li>• Cardiotoxicity</li></ul>
<b>Perfluoroalkyl chemicals</b> (PFCs)	<ul style="list-style-type: none"><li>• Grease-proof paper and paperboard</li></ul>	<ul style="list-style-type: none"><li>• Immunosuppression</li><li>• Endocrine disruption</li><li>• Obesogenic activity</li></ul>
<b>Perchlorate</b>	<ul style="list-style-type: none"><li>• Antistatic agent in food packaging</li><li>• Contamination from food manufacturing cleaning products</li></ul>	<ul style="list-style-type: none"><li>• Thyroid hormone disruption</li></ul>

# Direct Food Additives

Chemical	Food-Related Use	Health Concerns
<b>Nitrates/nitrites</b>	<ul style="list-style-type: none"><li>• Preservative</li><li>• Color enhancer</li></ul>	<ul style="list-style-type: none"><li>• Carcinogenicity</li><li>• Thyroid hormone disruption</li></ul>
<b>Artificial food coloring</b>	<ul style="list-style-type: none"><li>• Coloring</li></ul>	<ul style="list-style-type: none"><li>• Potential effects on neurobehavioral outcomes; (ex: exacerbation of attention-deficit/hyperactivity disorders)</li></ul>

# Policy Statement

## Goals:

- Review regulatory system for food additives
- Provide guidance for pediatricians to incorporate into clinical visits
- Propose reforms to current regulatory process



<https://www.helpsystems.com/blog/network-monitoring-government-agencies-areas-focus>

# Regulatory Framework for Food Additives



## Federal Food, Drug, and Cosmetic Act (FFDCA) (1938)

- Gave authority to US Food and Drug Administration (FDA) to oversee safety of food, drugs, medical devices, & cosmetics

## FFDCA Food Additive Amendment (1958)

- Established food additives regulatory program
- Definition of “food additives”
- Exemption for substances *Generally Recognized as Safe (GRAS)*

## Food and Drug Administration Modernization Act of 1997 (1997)

- Created approval process for food contact substances (FCS)

# Does the current regulatory system ensure food safety?

Most food additives have not been tested

- Neltner et al. 2013 study on 3941 direct food additives
  - 63.9% had no oral toxicology data
  - 93.3% had no reproductive toxicology data

Reasons for shortcomings

1. Extensive use of “GRAS” designation
2. Limitations to FDA authority & procedures



<https://www.foodsafetynews.com/2014/04/report-identifies-chemicals-quietly-added-to-food-under-gras/>

# Key Loophole: “GRAS”

Generally Recognized as Safe (GRAS): substances “*generally recognized, among experts qualified by scientific training and experience to evaluate the safety as having been adequately shown...to be safe under conditions of their intended use*” (21 USC 321(s))

- No opportunity or legal obligation for FDA or public review
- Intended for limited use, but now widespread (~1000 chemicals)
- Extensive conflict of interest in GRAS designations
  - Manufacturers or consultants can self-designate products as “GRAS”

# Limitations to FDA authority & procedures

- No authority to obtain data or re-assess safety of chemicals already on the market
- No consideration of cumulative or synergistic effects
- Outdated toxicological testing recommendations may not be sufficiently protective for children
  - Testing guidelines based on estimated daily exposure, without consideration of body weight
  - Limited/no evaluation of neurobehavioral or endocrine endpoints

# Recommendations for Pediatricians & Patients

- Prioritize consumption of fresh or frozen fruits & vegetables
- Avoid processed meats, especially during pregnancy
- Avoid microwaving food or beverages in plastics
- Avoid putting plastics in dishwasher
- Avoid plastics with recycling codes 3 (phthalates), 6 (styrene), and 7 (bisphenols)
- Encourage hand-washing before handling foods
- Wash all fruits & vegetables that cannot be peeled

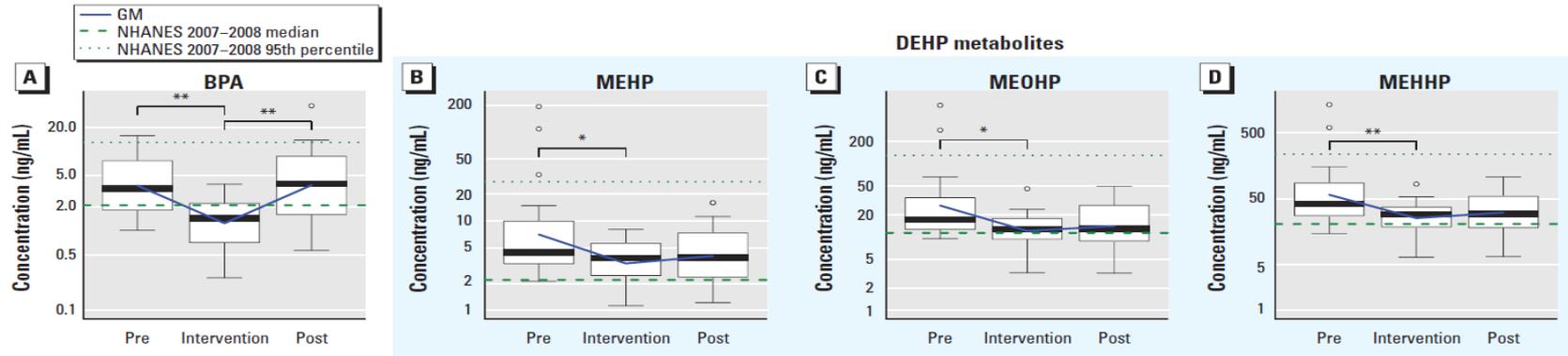


<http://newsroom.ucla.edu/stories/ucla-faculty-voice-pediatricians-need-to-discuss-gun-safety-with-patients>

# Bisphenol and phthalate exposures are preventable

Limiting canned food consumption and avoiding processed foods

- Intervention reduced mean concentrations of BPA by 66% and DEHP metabolites by 53–56%.



Rudel et al EHP 2011

# Recommendations for Government & Policy

## FDA should:

- Revise the “GRAS” process
- Coordinate with other agencies to address existing data gaps
- Establish requirements for prioritization and re-testing of approved chemicals
- Update safety assessment guidelines
  - Ex: endocrine disruption testing, safety factors for children, synergistic & cumulative effects
- Establish requirements for labeling of food additives with little or no toxicity data, and those not reviewed for safety by FDA

## Congress should

- Provide FDA with authority to collect information about food additives (ex: use & toxicity data)
- Provide FDA with dedicated resources to support strengthened agency activities
- Support provisions to ensure transparency and minimize conflict of interest

# Policy action on BPA

BPA banned in baby bottles and sippy cups

- But not in other food uses

# Costs of BPA exposure

12,404 cases of childhood obesity

33,863 cases of newly incident coronary heart disease

Estimated social costs of \$2.98 billion in 2008

Trasande Health Affairs 2014

# Benefits and costs of replacing BPA

- Potential cost of one BPA alternative, oleoresin = \$0.022 per can
  - 100 billion aluminum cans are produced annually
  - 100 billion x \$0.022 = **\$2.2 billion**
- Potential benefit of replacing BPA with lining free of health effects = **\$1.74 billion**
  - Does not include other effects (cognitive, asthma, breast cancer)
- Sensitivity analyses suggest as high as \$13.8 billion

Trasande Health Affairs 2014

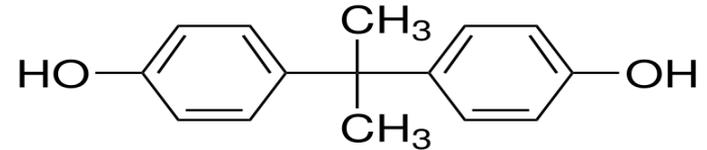
# BPS replacing BPA?

Emerging evidence suggests replacement of BPA and BPS

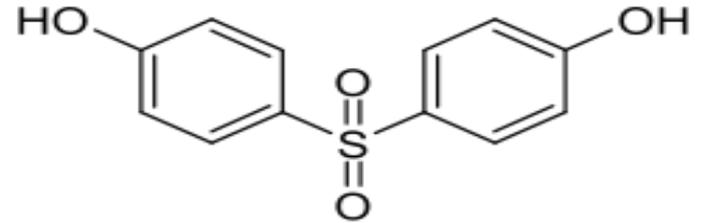
Similar, weak estrogen like BPA

Disrupts signaling of estrogen in animal studies

Does not degrade as easily in seawater



Bisphenol A



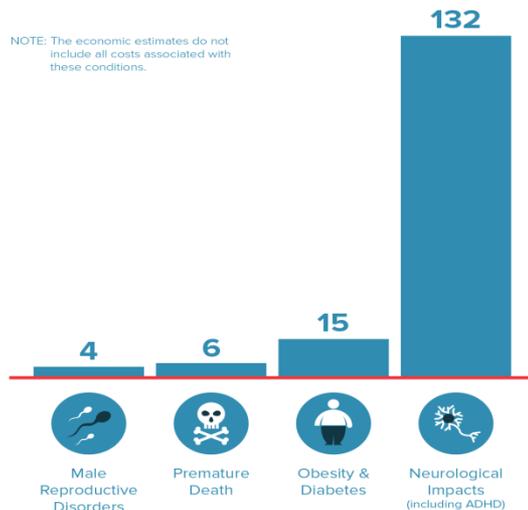
Bisphenol S

Liao et al Environ Sci Technol. 2012 Jun 19;46(12):6860-6.  
Liao et al Environ Sci Technol. 2012 Jun 19;46(12):6515-22.  
Grignard et al Toxicol In Vitro. 2012 Aug;26(5):727-31.  
Vinas and Watson EHP doi:10.1289/ehp.1205826  
Danzl et al Int J Environ Res Public Health. 2009 Apr;6(4):1472-84

## HEALTH EFFECTS FROM ENDOCRINE DISRUPTING CHEMICALS COST THE EU 157 BILLION EUROS EACH YEAR.

This is the tip of the iceberg: Costs may be as high as €270B.

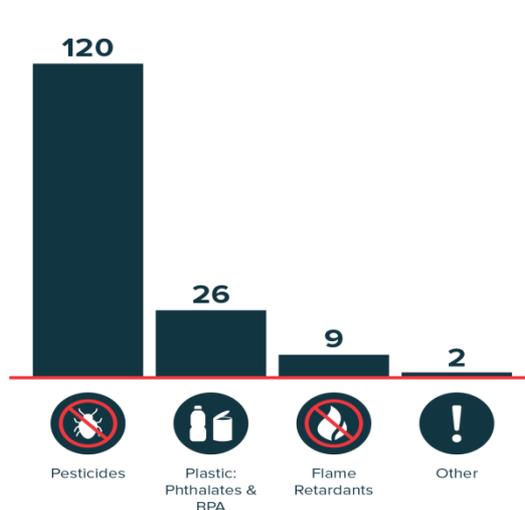
### €157B Cost by Health Effect



#### SOME EDC-RELATED HEALTH OUTCOMES NOT INCLUDED:

- Breast Cancer
- Prostate Cancer
- Immune Disorders
- Female Reproductive Disorders
- Liver Cancer
- Parkinson's Disease
- Osteoporosis
- Endometriosis
- Thyroid Disorders

### €157B Cost by EDC Type



#### SOME EDCs NOT INCLUDED:

- Atrazine
- 2, 4-D
- Styrene
- Triclosan
- Nonylphenol
- Polycyclic Aromatic Hydrocarbons
- Bisphenol S
- Cadmium
- Arsenic
- Ethylene glycol



Endocrine Disrupting Chemicals (EDCs) interfere with hormone action to cause adverse health effects in people.

#### “THE TIP OF THE ICEBERG”

The data shown to the left are based on fewer than 5% of likely EDCs. Many EDC health conditions were not included in this study because key data are lacking. Other health outcomes will be the focus of future research.

See Trasande et al. The Journal of Clinical Endocrinology & Metabolism  
<http://press.endocrine.org/edc>



## Health Effects From Endocrine Disrupting Chemicals Cost The U.S.

**\$340** Billion Annually

Endocrine Disrupting Chemicals (EDCs) interfere with hormone action to cause adverse health effects in people.

### \$340 Billion by Health Effect



**Neurological Conditions**  
(including ADHD)



**Endometriosis & Fibroids**



**Premature Death**



**Obesity & Diabetes**



**Male Reproductive Problems**



### \$340 Billion by EDC Type



**Flame Retardants**



**Plastic, Cans**



**Pesticides**



**Other Mixes of Chemicals**  
(including Teflon-like materials)



