

NTP Activities on Bisphenols

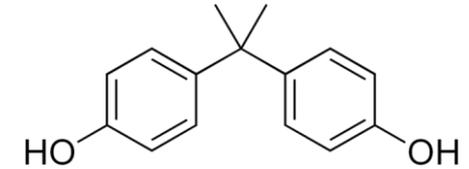
Nigel Walker, PhD, DABT
National Institute of Environmental Health
Sciences

NTP Board of Scientific Counselors Meeting
June 20, 2018



Bisphenol-A (BPA)

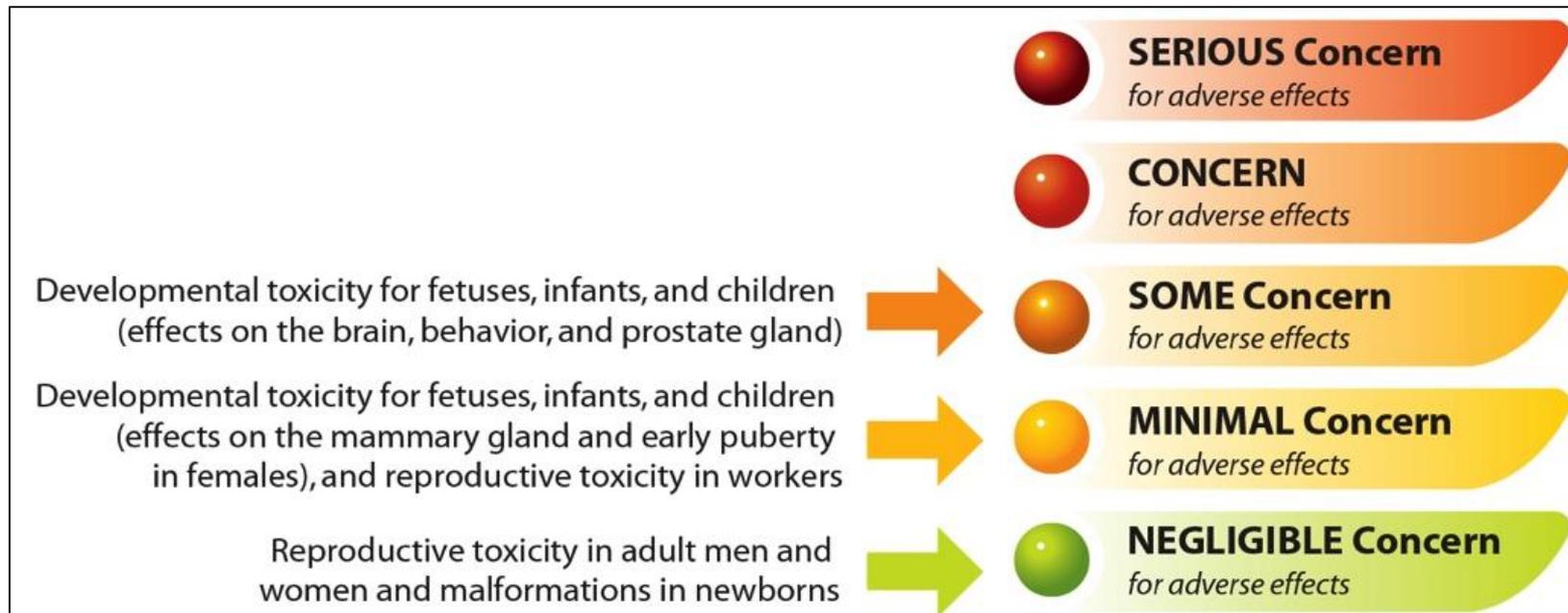
- Chemical widely used to make polycarbonate plastics and epoxy resins
- Widespread low exposure (<1 $\mu\text{g}/\text{kg}$ body weight (bw)/day) from migration of small amounts into foods from food contact materials
- Considerable debate over risk posed by “low level” exposure
- Guideline studies conducted under Good Laboratory Practices (GLP) show no effects of concern at “low doses”
- Academic “investigative” studies report that BPA induces a variety of effects in a variety of model systems at low exposures





Historical NTP Context

- National Toxicology Program (NTP) Monograph (2008)
- Evaluated the available scientific literature about the possible effects of BPA on human development and reproduction
- Conclusions





Some Bisphenol Analogs/Derivatives

- Widespread exposure to a variety of chemicals with similarity to BPA
- Detected in foodstuffs, house dust, river and lake sediment, personal care products, and thermal paper
- Detected in human biological specimens
- Several chlorinated and brominated derivatives of BPA are used as flame retardants
- In contrast to BPA, most are poorly understood with respect to potential toxicity

Structure	Abbreviation (CASRN)	Detection	Structure	Abbreviation (CASRN)	Detection
	BPS (80-09-1)	blood ⁸⁸ , food ⁹² , dust ⁸⁹ , sediment ⁹¹ , receipts ^{6; 7; 90; 140} , urine ^{162; 163}		2,4-BPS (5397-34-2)	receipts ¹⁴⁰
	4,4-BPF (620-92-8)	food ^{14; 52; 92} , dust ⁸⁹ , sediment ⁹¹ , receipts ¹⁴⁰ , urine ^{162; 163} , PCP ¹⁵ , municipal sewage sludge ¹²⁷		BPS-MAE (97042-18-7)	receipts ¹⁴⁰
	BPAP (1571-75-1)	food ⁹² , dust ⁸⁹ , sediment ⁹¹ , receipts ¹⁴⁰		TGSA (41481-66-7)	receipts ¹⁴⁰
	BPAF (1478-61-1)	food ⁹² , dust ⁸⁹ , sediment ⁹¹ , municipal sewage sludge ¹²⁷		BPS-MPE (63134-33-8)	receipts ¹⁴⁰
	BPB (77-40-7)	food ^{23-25; 51; 52; 92} , dust ⁸⁹ , sediment ⁹¹ , blood ^{19; 20} , urine ²²		BPC (79-97-0)	receipts ¹⁴⁰
	BPP (2167-51-3)	food ⁹² , dust ⁸⁹		BPPH (24038-68-4)	receipts ¹⁴⁰
	BPZ (843-55-0)	food ^{14; 92} , sediment ⁹¹ , PCP ¹⁵		DD-70 (93589-69-6)	receipts ¹⁴⁰
	D-8 (95235-30-6)	blood ¹³⁴ , receipts ¹³⁴		D-90 (191680-83-8)	receipts ¹⁴⁰
	2,2-BPF (2467-02-9)	resins ¹¹		BTUM (151882-81-4)	receipts ¹⁴⁰
	BPE (2081-08-5)	municipal sewage sludge ¹²⁷		MBHA (5129-00-0)	receipts ¹⁴⁰
	TMBPA (5613-46-7)	polycarbonate resin ⁷⁹		Pergafast 201 (232938-43-1)	receipts ¹⁴⁰
	BDP (5945-33-5)	flame retardant		UU (321860-75-7)	receipts ¹⁴⁰



- Bisphenols are an exemplar for multiple issues being addressed by NTP and NIEHS
 - What is “endocrine disruption”
 - How do we effectively assess hazards posed by compounds that cause “endocrine disruption”
 - What is low dose?
 - Shape of the dose response and evidence for non-monotonicity of effects across the dose range
 - How to integrate academic investigative research with regulatory guideline complaint research for decision making
 - How to assess hazards for classes of structurally/functionally related compounds
 - How to rapidly assess hazard of “replacements” for commodity chemicals that are shown to be toxic in model systems



- CLARITY-BPA Research Program: Peer Review of Core Study and Next Steps

-

-

-

- Evaluation of Bisphenol Analogues

-

-



- CLARITY-BPA Research Program: Peer Review of Core Study and Next Steps
 - How do we effectively assess hazards posed by compounds that cause “endocrine disruption”
 - Shape of the dose response and evidence for non-monotonicity of effects across the dose range
 - How to integrate academic investigative research with regulatory guideline complaint research for decision making
- Evaluation of Bisphenol Analogues
 - How to assess hazards for classes of structurally related compounds
 - How to rapidly assess hazard of “replacements” for commodity chemicals that are shown to be toxic in model systems