Potential Designated Chemicals

p,p'-Bisphenols and Diglycidyl Ethers of p,p'-Bisphenols

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Purpose of agenda item

- Panel deliberation on potential designation of the group:

  "p,p'-Bisphenols and diglycidyl ethers of p,p'-bisphenols"

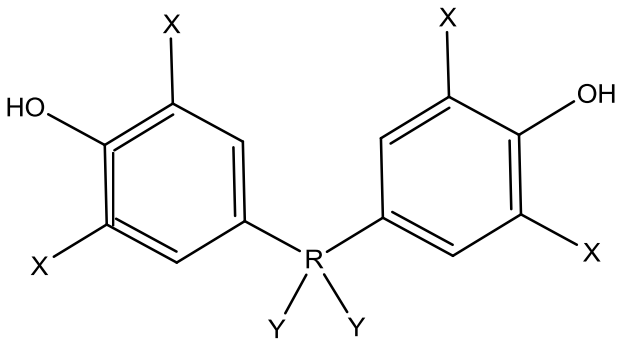
Designated chemicals

- Chemicals that can be considered for biomonitoring
- Chemicals are designated based on:
  - Inclusion in CDC's National Reports on Human Exposure to Environmental Chemicals program
  - Recommendations by the Scientific Guidance Panel for Biomonitoring California

Background

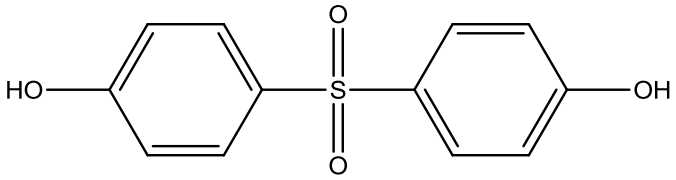
- March 2012 SGP Meeting
  - Preliminary screening table was presented on bisphenol A (BPA) substitutes and structurally-related compounds
- July 2012 SGP Meeting
  - Interim update on additional screening of BPA substitutes and structurally related compounds

p,p'-Bisphenols and diglycidyl ethers of p,p'-bisphenols

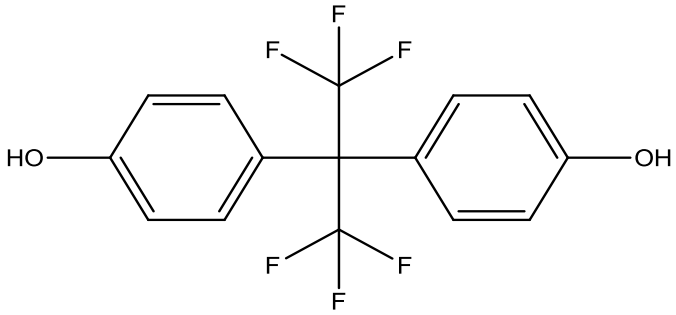


Representative structure of a p,p'-bisphenol

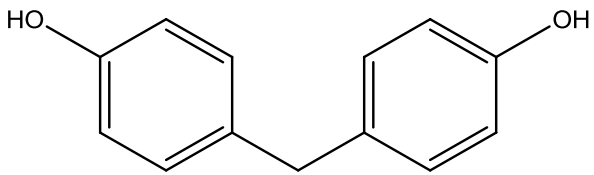
Bisphenol S (BPS)



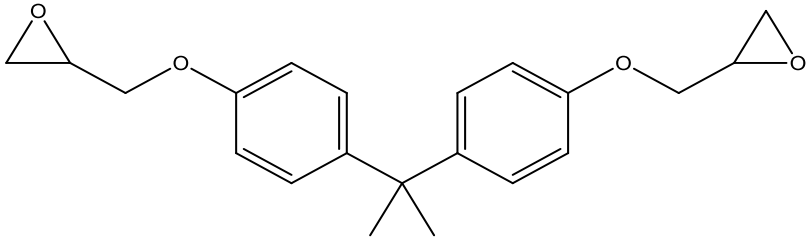
Bisphenol AF (BPAF)



Bisphenol F (BPF)



Bisphenol A diglycidyl ether (BADGE)



Why consider these chemicals as a group?

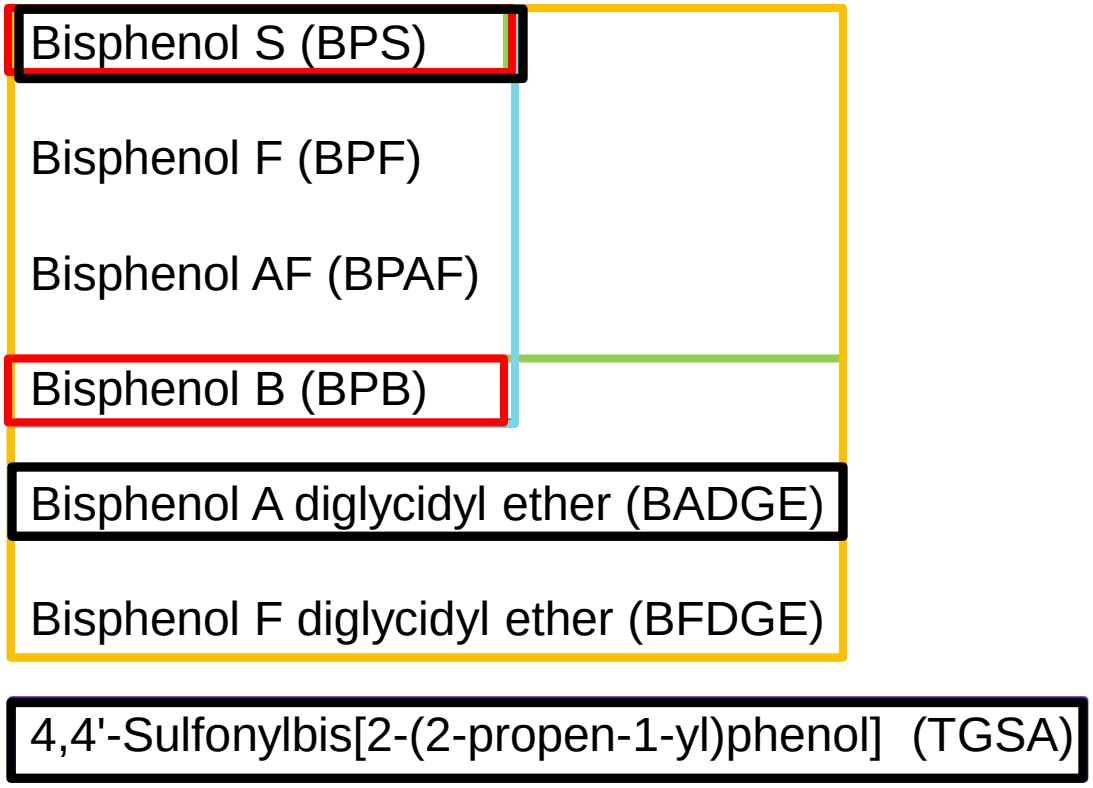
- Facilitate broad laboratory screening of these structurally similar chemicals
- Allow the Program to look for emerging chemicals in this general group

Criteria for Designation

- Exposure or potential exposure
- Known or suspected health effects
- Need to assess efficacy of public health action
- Availability of analytical methods
- Availability of biospecimen samples
- Incremental analytical cost

Highlighted Chemicals

powerpoint animation of boxes not visible in pdf



Over 1 million pounds production/import volume in 2006*

Detected in consumer products

Detected in dust

Detected in biomonitoring studies

In vivo evidence of endocrine activity

In vitro indications of endocrine activity

Other concerns

**US EPA, Toxic Substances Control Act (TSCA) Inventory Update Reporting for 2006*

Exposure or potential exposure

Major uses:

- Protective coatings (e.g., BPF, BPAF, BADGE)
  - For example, linings inside food and beverage containers
- Developers in thermal paper (e.g., BPS, TGSA)
  - For example, in cash register receipts

Other uses include: plastics, dental sealants

Detections in products, dust

Chemical	Consumer Products				Indoor Dust
	Cans	*Canned food*	*Beverages*	*Paper products*	
BPS	√	√		√	√
BPF	√		√		√
BPAF					√
BPB		√	√		√
BADGE*	√	√	√		
BFDGE*	√	√	√		
TGSA	*No studies located*				

√ Indicates detection in one or more samples

* Includes parent compounds and/or derivatives

Biomonitoring studies

- **BPS**
  - 81% of urine samples from New York and seven other countries (China, India, Japan, Korea, Kuwait, Malaysia & Vietnam)
- **BPB**
  - 10% of urine samples (2/20) from volunteers in Portugal
  - ~28% of serum samples (16/58) from endometriotic women in Italy; BPB was not detected in the control group (11 healthy women)
- **BADGE**
  - Saliva of dental patients after application of a dental sealant

(Liao et al., 2012; Cunha et al., 2010; Cobellis et al., 2009; Olea et al., 1996)

Known or suspected health effects

- Positive response in *in vivo* rodent uterotrophic assays (e.g., BPS, BPF, BPAF)
- *In vitro,* numerous bisphenols and some diglycidyl ethers:
  - Bind to hormone receptors (e.g., estrogen receptor [ER])
  - Are active in hormone receptor-mediated reporter gene assays
  - Increase cell proliferation of MCF7 breast cancer cells
- A few of these chemicals exhibit:
  - *In vitro* activity related to adipogenesis
  - Positive responses in some *in vitro* genotoxicity assays

Comparison of *in vivo* with *in vitro* studies

- Yamasaki et al. (2002, 2003, 2004)
- Chemicals positive in the *in vivo* uterotrophic assay in rodents were also active *in vitro*:
  - Binding to estrogen receptor
  - Estrogenic activity in reporter gene assay

Analytical methods

- Biomonitoring California would need to adapt or develop analytical methods
- Reference standards and methods are available for many compounds
- Biospecimen: likely urine
- Analysis of bisphenols and diglycidyl ethers could likely be bundled and run as a panel

Need to assess efficacy of public health action

- Increasing use of some bisphenols is expected for certain applications:
  - For example, TGSA in thermal paper
- For many others, extent of use and exposure is unknown and more information is needed
- Biomonitoring this group of chemicals would help assess extent and level of exposure in California

Options for the Panel

- Consider recommending for designation:
  - "p,p'-Bisphenols and diglycidyl ethers of p,p'-bisphenols" as a group
  - One or more of these chemicals
- Recommend against designating
- Postpone recommendation