

For our Environment

Umwelt   
Bundesamt

## Supply chain substitution workshop on thermal papers

# "The endocrine potential of Bisphenol A substitutes in environmentally relevant uses like thermal papers"

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## Aim of the Research Project

- Project was part of a national environmental research plan in 2016
- Project was funded by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety and performed on behalf of the Federal Environment Agency

### Aims of the project:

- Identification of environmentally relevant BPA substitutes based on uses
- Assessment of the endocrine potential of these substitutes based on available data and newly performed *in vitro* assays

# Identification of environmentally relevant substitutes of BPA

## Literature and patent review

- Identification of **93** substances that are known to function as BPA substitutes in various products and uses
- Substances can be grouped according to “bisphenolic compounds”, “bisphenol free compounds”, “phenol free compounds” and “natural compounds”
- Selection of “environmentally relevant” uses  $\Rightarrow$  entry path into environmental media
  - ✓ Uses in thermal papers
  - ✓ Uses in textiles
  - ✓ Uses in water pipes
  - ✓ Uses in anti fouling agents
  - ✓ Uses in outdoor epoxy resins

# Identification of environmentally relevant substitutes of BPA

## 44 environmentally relevant substitutes to be further analysed

Bishphenol A Alternative, Abbreviation	Chemical name	Cas-No.
BPF - para	Bisphenol F - para (4,4'-methylenediphenol)	620-92-8
BPC	Bisphenol C (2,2-Bis(4-hydroxy-3-methylphenyl)propane)	79-97-0
MBHA	Methyl bis(4-hydroxyphenyl)acetate	5129-00-0
BisOPP-A; Bisphenol PH	Bisphenol PH ( 2,2-Bis(2-hydroxy-5-biphenyl)propane, 2,2-Bis(4-hydroxy-3-phenylphenyl)propane, 2,2-{5,5'-Bis[1,1'-(biphenyl)-2-ol]}propane, 5,5'-(1-Methylethylidene)bis[(1,1'-biphenyl)-2-ol], 5,5'-Isopropylidenedi-2-biphenylol )	24038-68-4
BPAP	Bisphenol AP (4,4'-(1-Phenylethylidene)bisphenol)	1571-75-1
PHBB	Benzyl 4-hydroxybenzoate	94-18-8
BPS	4,4'-Sulfonyldiphenol	80-09-1
2,4-BPS	2,4'-DIHYDROXYDIPHENYL SULFONE	5397-34-2
TGSA	Bis(3-allyl-4-hydroxyphenyl)sulfone	41481-66-7
BPS-MAE	Propenyloxy)phenylsulphonyl]phenol bis(4-hydroxyphenyl)sulfone monoallyl ether	97042-18-7
BPS-MPF	p-[p-benzyloxyphenyl]sulfonyl]phenol	63134-33-8
D-8	4-(4-isopropoxyphenylsulfonyl)phenol	95235-30-6
D-90; BPSIP	4-hydroxyphenyl 4-isopropoxyphenylsulfone	191680-83-8
DD-70	oxybis[2-chloroethane)	93589-69-6
Pergafast 201	Benzenesulfonamide 4-methyl-N-[[[3-[[[4-methylphenyl)sulfonyl]oxy]phenyl]amino]carbonyl]-	232938-43-1

# Identification of environmentally relevant substitutes of BPA

Bishphenol A Alternative, Abbreviation	Chemical name	Cas-No.
BTUM	4,4'-bis(N-carbamoyl-4-methylbenzenesulfonamide)diphenylmethane	151882-81-4
UU	Urea-urethane Compound	321860-75-7
BPF - ortho	2,2'-Methylenediphenol (Bisphenol F - ortho)	2467-02-9
Biphenyl-4-ol	4-phenylphenol	92-69-3
	4-tert-Butylphenol	98-54-4
DMP-OH	Dimethyl 4-hydroxyphthalate	22479-95-4
	3,5-di-ter-butylsalicylic acid	19715-19-6
	Zinc 3,5-bis(alpha-methylbenzyl)salicylate	53770-52-8
silane/silicone polymer, diverse chemicals with an organic moiety, a hydrolyzable group, and a spacer (either aryl or alkyl chain)	octamethylcyclotetrasiloxane (D4)	
silane/silicone polymer, diverse chemicals with an organic moiety, a hydrolyzable group, and a spacer (either aryl or alkyl chain)	decamethylcyclopentasiloxane (D5)	
CBDO	2,2,4,4-Tetramethyl-1,3-cyclobutanediol	3010-96-6
Isosorbide		652-67-5
Tannin, biobased		
Linseed oil		
BPS alternative:	acid hydroxy benzene disulfonic acid polymer	
Alpha® free (Vitamin C)	vitamin C (Ascorbinsäure)	
Polyurethane resin		
Polyurethane resin		
Polyamide		
BPZ (Bisphenol Z)	4,4'-Cyclohexylidenbisphenol	843-55-0
HPP	4-cumylphenol	599-64-4
Lignocellulosic material from cedar, eucalyptus, bamboo		9005-53-2
n-Alkyl Diphenolate (DPA) Diglycidyl Ethers	Diphenolic acid (DPA); 4,4-Bis(p-hydroxyphenyl)pentanoic acid	126-00-1
Cardanol	3-[(8Z,11Z)-pentadeca-8,11,14-trienyl]phenol	37330-39-5
Tritan Coploymer aus di-methylterephthalate (DMT), 1,4-cyclohexanedimethanol (CHDM) und 2,2,4,4-tetramethyl-1,3-cyclobutanediol (TMCD)	di-methylterephthalate (DMT), 1,4-cyclohexanedimethanol (CHDM), und 2,2,4,4-tetramethyl-1,3-cyclobutanediol (TMCD)	120-61-6, 105-08-8, 3010-96-6
BHPF	9,9-Bis(4-hydroxyphenyl)fluorene	3236-71-3

# Assessment of the ED potential of the selected substitutes

## 1. Literature review

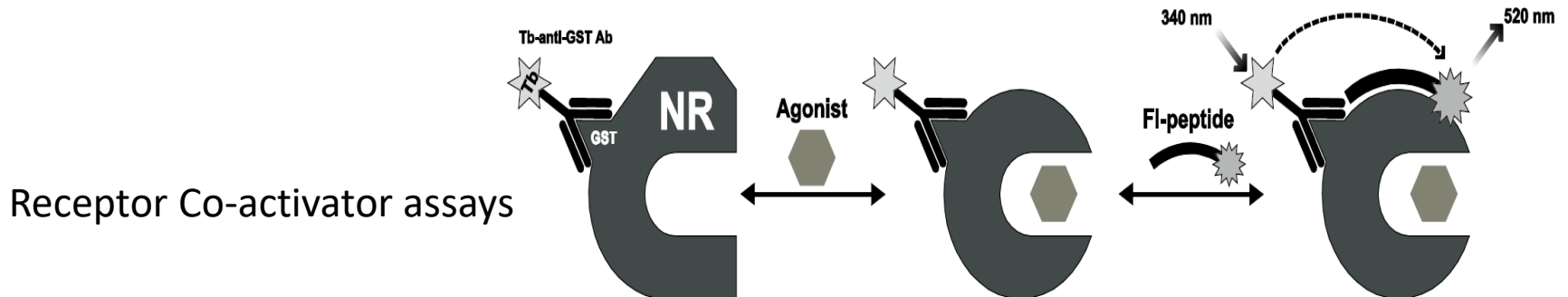
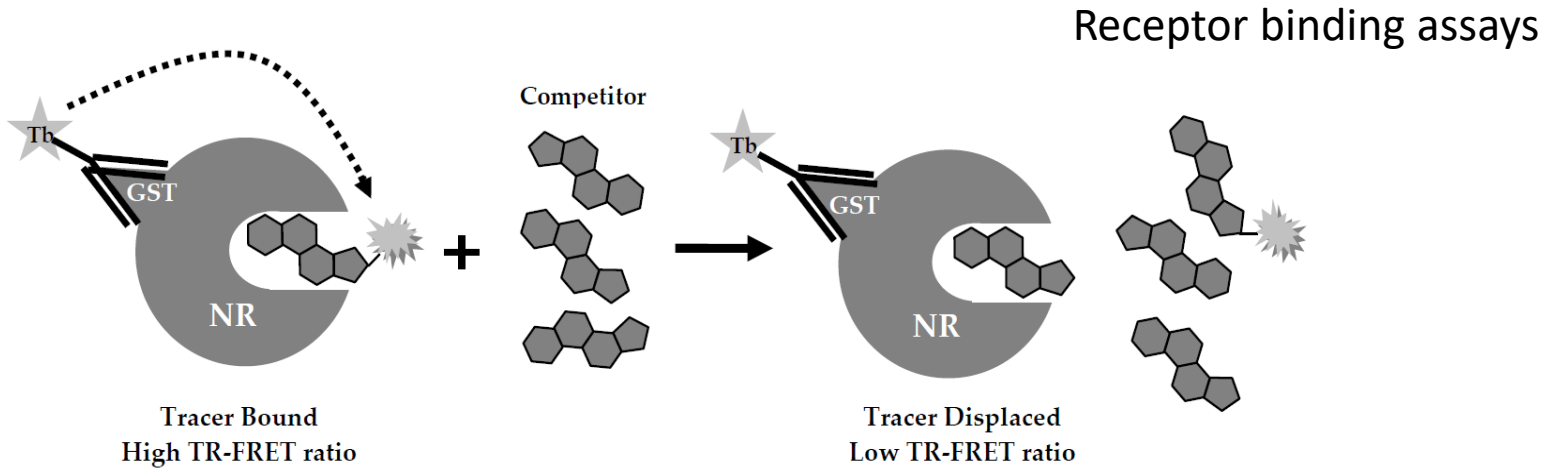
- Modes of Action included in the search
  - ✓ Estrogenic and anti-estrogenic activity
  - ✓ Androgenic and anti-androgenic activity
  - ✓ Interference with the thyroidal pathways

### Hints for endocrine activity from literature studies for:

BPF-para, BPC, PHBB, **BPS**, Biphenyl-4-ol, TDP, 4-tert-Butylphenol, Octamethylcyclotetrasiloxan (D4), CBDO, Linseed oil, Ascorbic acid, BPZ, HPP, TMBPA and BPFL (BHPF)

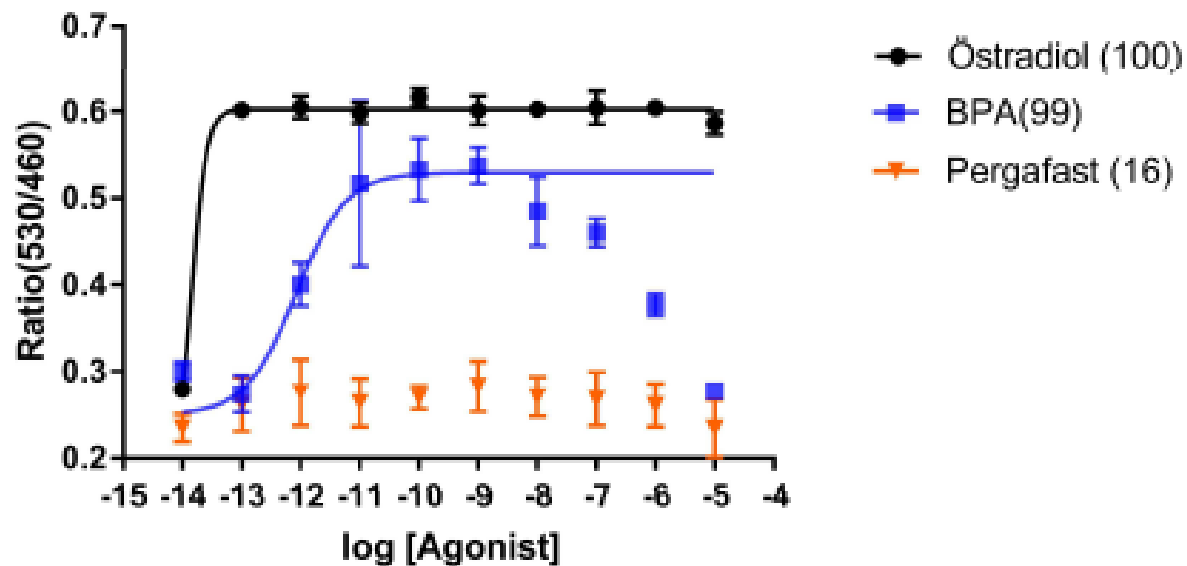
# Assessment of the ED potential of the selected substitutes

## In vitro assays to fill data gaps



# Assessment of the ED potential of the selected substitutes

Example: Estrogen Receptor alpha binding assay





## Summary

- Assessment was based only on available literature data and *in vitro* screening assays
- For assessment 44 environmentally relevant BPA substitutes were systematically selected according to their uses
- In vitro screening assays were performed for estrogenic, androgenic and thyroidal pathways in agonistic and antagonistic mode

## Summary

- All bisphenolic compounds showed activity in estrogen receptor binding assays
- Most of the phenolic compounds also showed some activity in estrogen receptor binding studies
- The relevant substitutes for thermal paper BPS and D8 showed activity in estrogen and androgen receptor binding
- Pergafast was found to be inactive in all test systems used.
- Further properties like persistence or potential for bioaccumulation were not assessed!
- Tentative date for publication of report: April 2019
- Manuscript for peer-reviewed journal currently in preparation

**Thank you for your attention!**

**Umwelt  
Bundesamt**

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