Hormonally active contaminants- Interactions and effects on food safety

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Contents

- EDC definition and effects
- Effects of dioxin-like compounds
- TEQ concept and TEF values for dioxin-like compound
- Need of periodic revision process

EDC Definition

(Weybridge, OECD, WHO/IPCS etc. 1997)

”An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny”

Endocrine effects
(WHO/IPCS 2002)

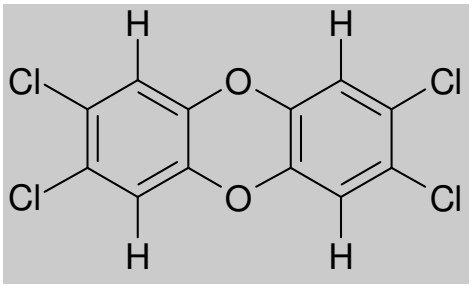
- **Reproduction**
  - →Sperm
  - →Fertility
  - →Sex ratio
  - →Hypospadia, chryptorcidism
  - →Endometriosis
  - →Early puberty
- **Cancer**
  - →Breast cancer
  - →Endometrial cancer
  - →Testis cancer
  - →Prostate cancer
- **Behaviour**
- **Immune system**

http://whqlibdoc.who.int/hq/2002/WHO_PCS_EDC_02.2.pdf

What is a dioxin-like compound?

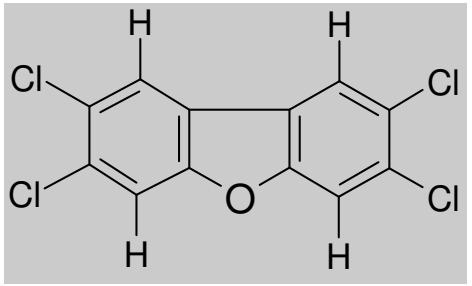
PCDD - polychlorinated dibenzo-*p*-dioxins

2,3,7,8-TCDD (N = 7/75)



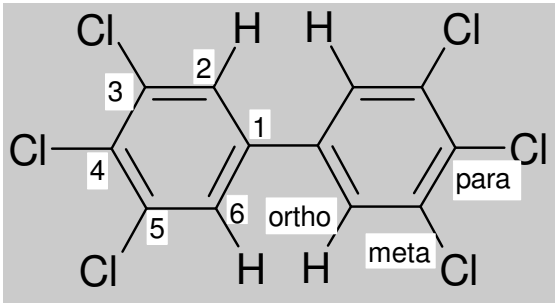
PCDF – polychlorinated dibenzofurans

(N =10/135)

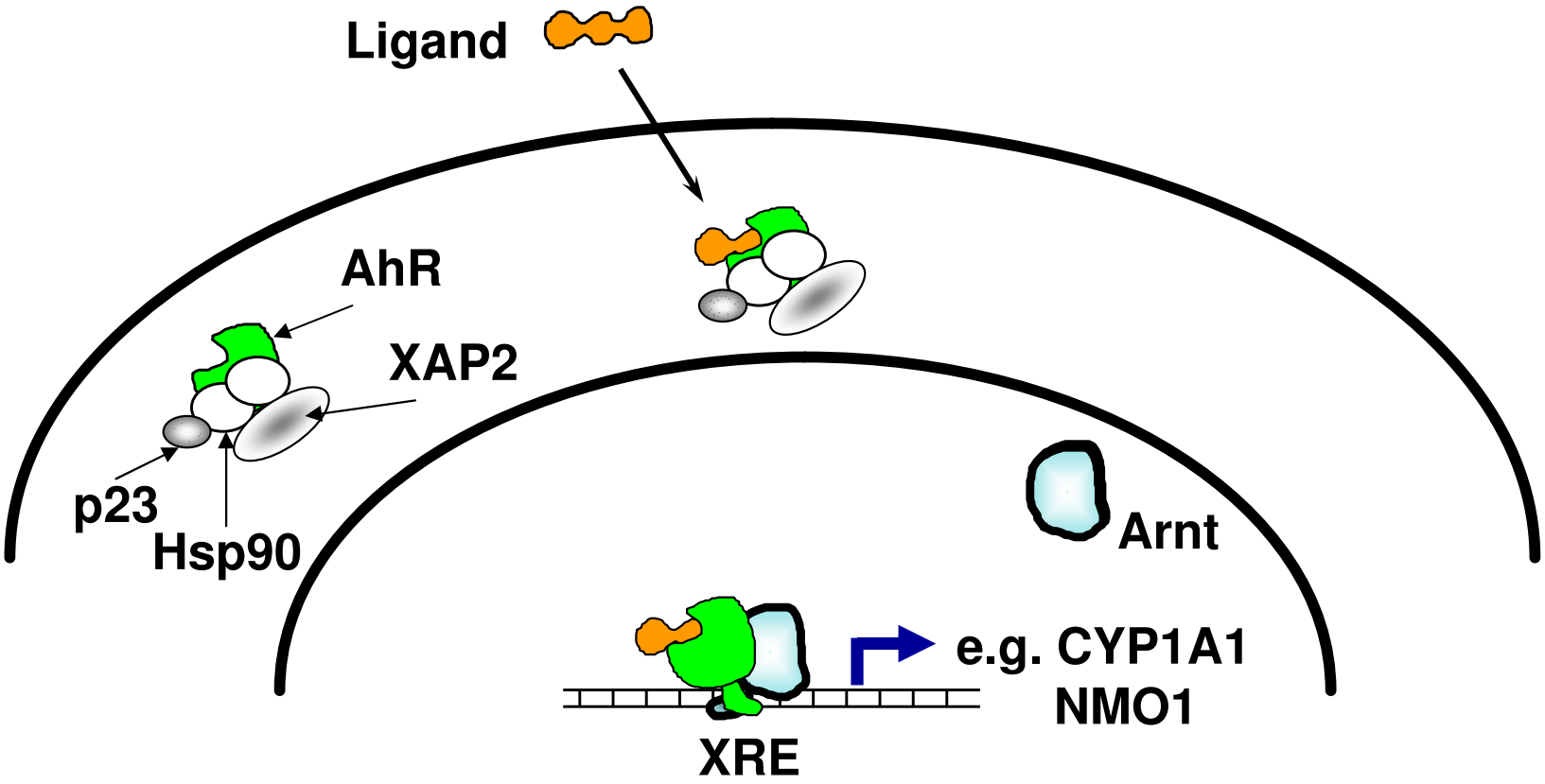


PCB – polychlorinated biphenyls

(N = 12/209)



Common mechanism: Initial step involves ligand-dependent activation of the Ah receptor



AhR + L -> hormones, enzymes, ?? - - -> toxicity

Toxicological profile: From experiments to human disease

Karolinska Institutet

Until the early 1990íes

- Cancer (non genotoxic)
- Reproduction
- Immune system

1990ies - today

- Early (foetal) development
- Neurobehavioral alterations
- Endocrine disruption
  - → Estrogenic/Anti-estrogenic
  - → Thyroid hormones
  - → Retinoid system
  - → More???

Today – Future?

Disease of developmental origin?

- Obesity
- Diabetes
- Cardiovascular diseases
- Bone and tooth abnormalities
- Hearing problems
- More???

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- Need of regular revision process

What is the TEQ-concept?

- A regulatory tool based on the idea that the toxicity of compounds, which share a common mechanism of action, can be added.

- Assumes that differences in toxic potency can be compensated for by assigning TEF-values to individual compounds.

- TEF-values for dioxin-like compounds, are based on experimental data, including potency comparisons with TCDD, and represents an integrated judgement of different biological end-points, where more weight is given to the end-points that are of concern in the risk assessment process

Chemical conc x **TEF** = **TEQ** (toxic conc)

TEQ-concept for dioxin-like compounds

- 1988 – Nordic dioxin TEFs and I-TEFs
- 1990 – first PCB-TEFs
- 1992 – Nordic PCB-TEFs

- 1994 – WHO-TEFs for PCB (Bilthoven 1993)
  → non-, mono- and di-ortho PCB

- 1998 – WHO-TEFs revised (Stockholm 1997)
  → not di-ortho PCB, even birds & fish

- 2006 – WHO-TEFs revised (Geneva 2005)
  → logaritmic scale, contamination of mono-orth PCB

WHO-TEFs 2006 (van den Berg *et al.* 2006)

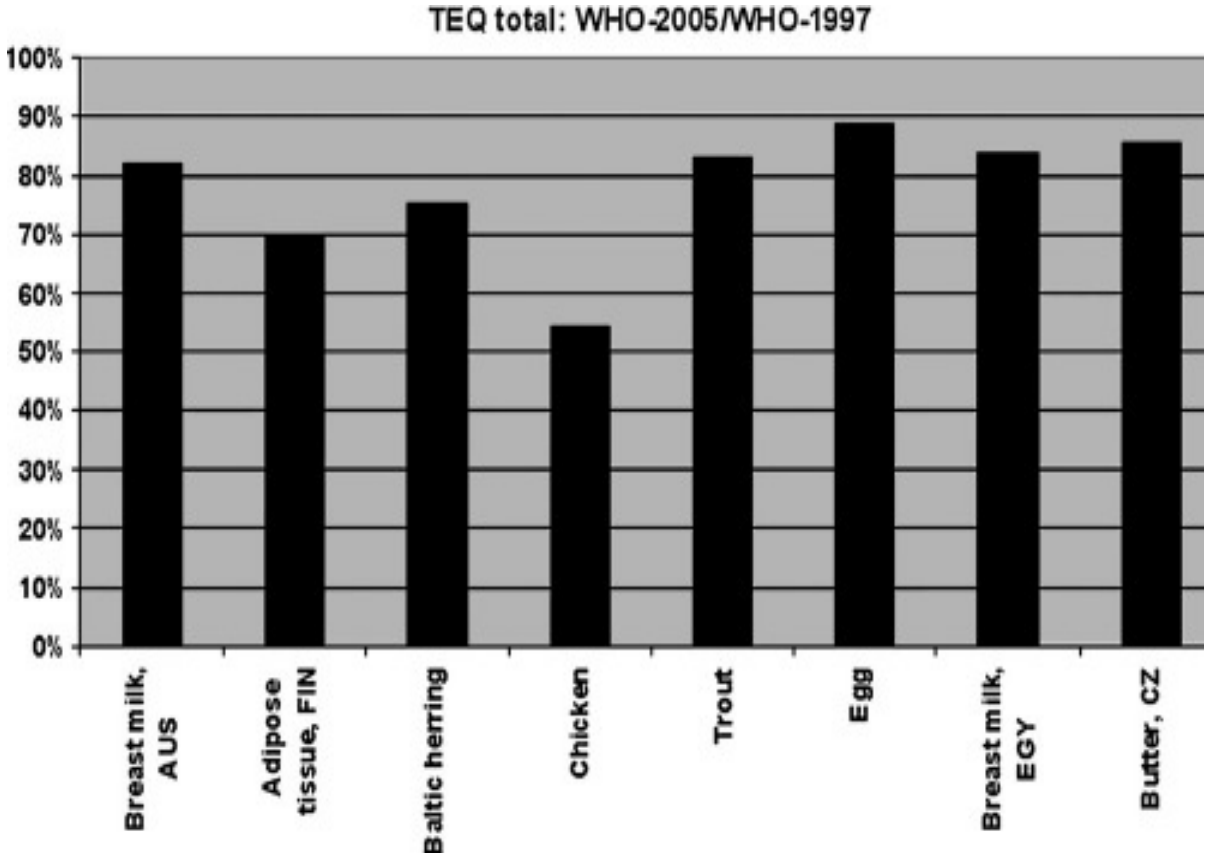
TCDD	1
PeCDD	1
HxCDDs	0.1
HpCDD	0.01
OCDD	0.0003
TCDF	0.1
12378-PeCDF	0.03
23478-PeCDF	0.3
HxCDFs	0.1
HpCDFs	0.01
OCDF	0.0003

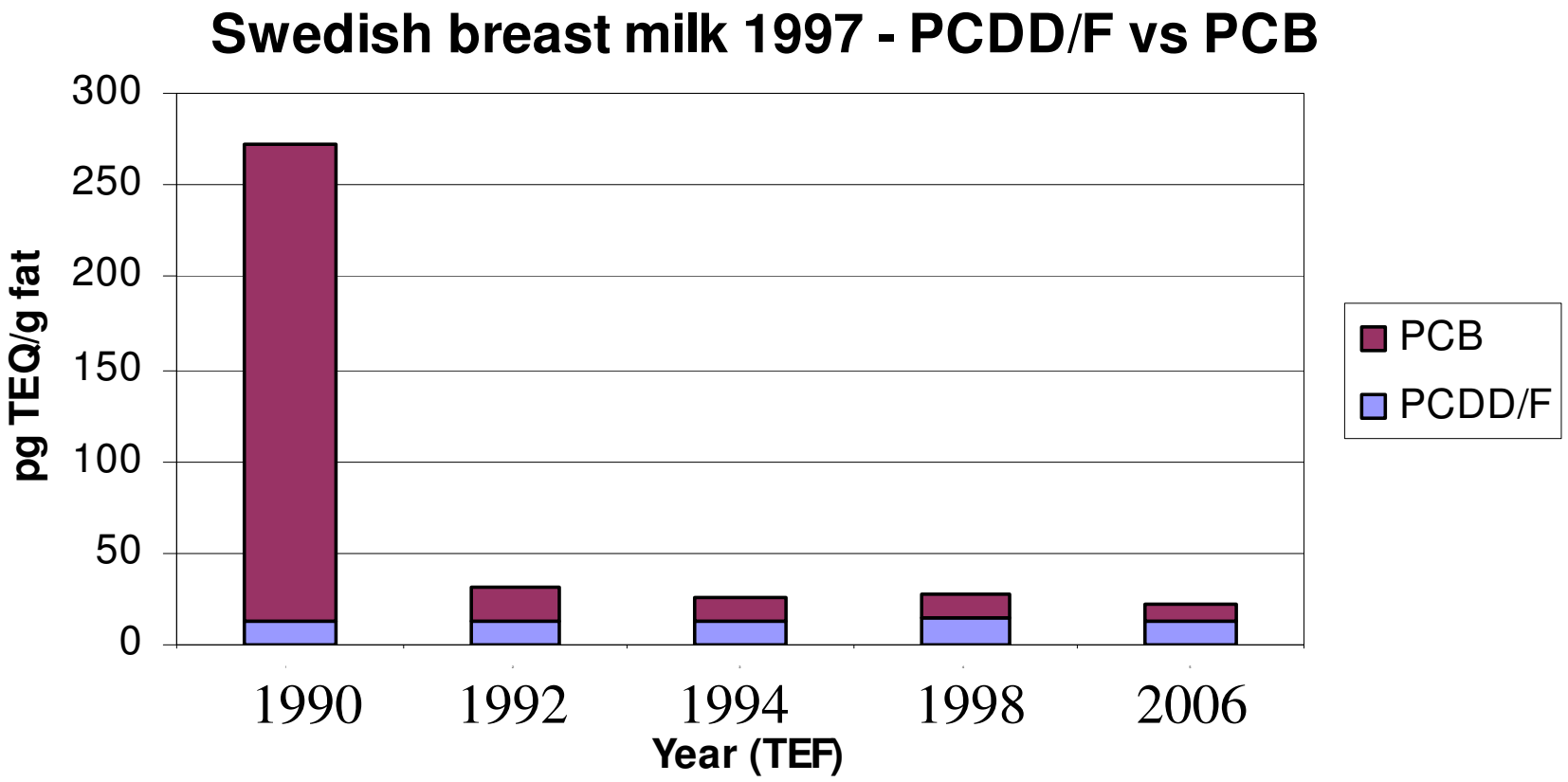
PCB 81	0.0003
PCB 77	0.0001
PCB 126	0.1
PCB 169	0.03
PCB 105	0.00003
PCB 114	0.00003
PCB 118	0.00003
PCB 123	0.00003
PCB 156	0.00003
PCB 157	0.00003
PCB 167	0.00003
PCB 189	0.00003

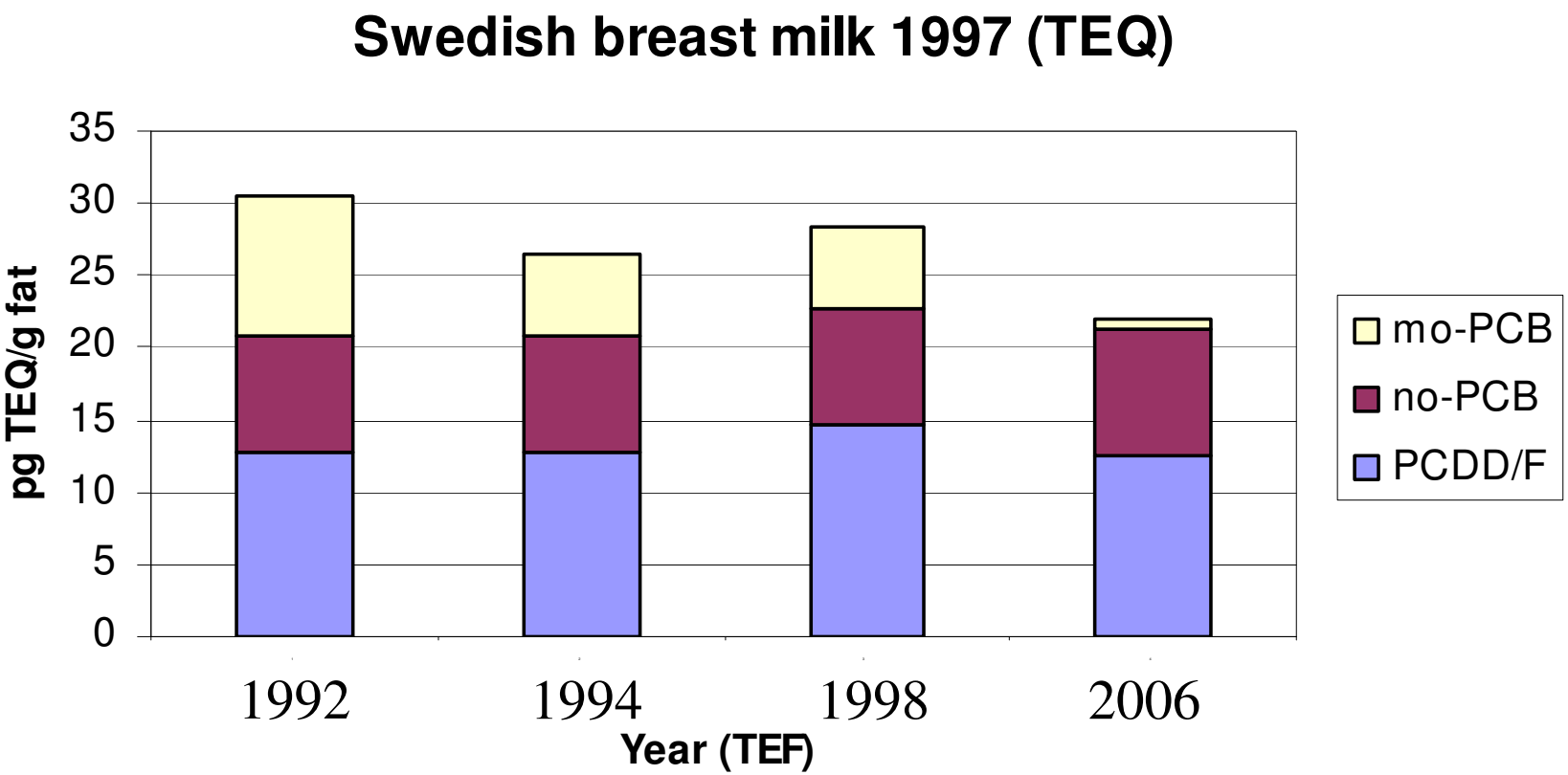
Example of TEQ-calculation: Chemical conc x TEF = TEQ (toxic conc)

Congener composition	Chemical conc (pg/g)	TEF	TEQ (pg/g)
2378-TCDD	2	1	2.0
23478-PeCDF	11	0.3	3.3
PCB 126	76	0.1	7.6
PCB 118	13 000	0.00003	0.4
Sum	**13 089**		**13.3**

2005 TEQ/1997 TEQ




Swedish breast milk 1997 - PCDD/F vs PCB
pg TEQ/g fat
300
250
200
150
100
50
0
1990
1992
1994
1998
2006
Year (TEF)
PCB
PCDD/F


Swedish breast milk 1997 (TEQ)
pg TEQ/g fat
35
30
25
20
15
10
5
0
1992
1994
1998
2006
Year (TEF)
mo-PCB
no-PCB
PCDD/F

Background exposure in EU (2000)

- Adults: 1.2-3.0 pg TEQ/kg/d
- Children: 2-4 times higher
- Breastfed infants: ca 160 pg TEQ/kg/d

- **Tolerable Daily Intake (TDI): 2 pg/kg**

- Via food (fish, dairy, meat, mother´s milk

Need of regular revision process

- Compilation, evaluation and integration of new data
- Identification of data gaps and efforts to cover those
- Refine/revisit TEF-scheme inclusion criteria
- Refine/revisit TEQ-concept criteria

Breast feeding in high exposure groups: concern and recommendations

Artic Monitoring and Assessment Programme report 2002.

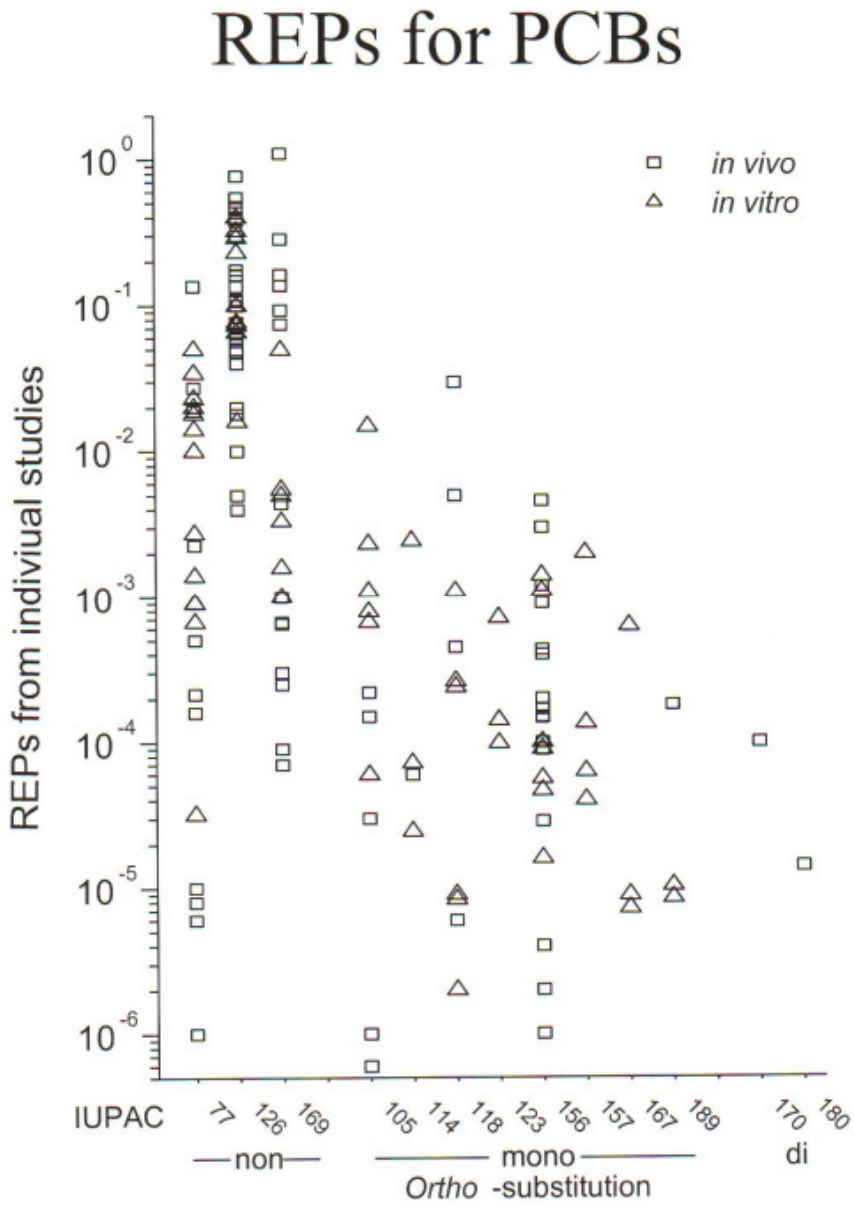
"Breast-feeding continue to be recognized as a practice that benefits both mother and child. Nonetheless, if contaminant levels increase or more information indicates risk, the potential need for restrictions should continue to be evaluated"

Artic Monitoring and Assessment Programme report 2009.

"Breast-feeding.. a healthy practice, which optimizes infant growth and development. However, there is a need to reduce contaminant levels …. and to provide food advice to women of childbearing age"

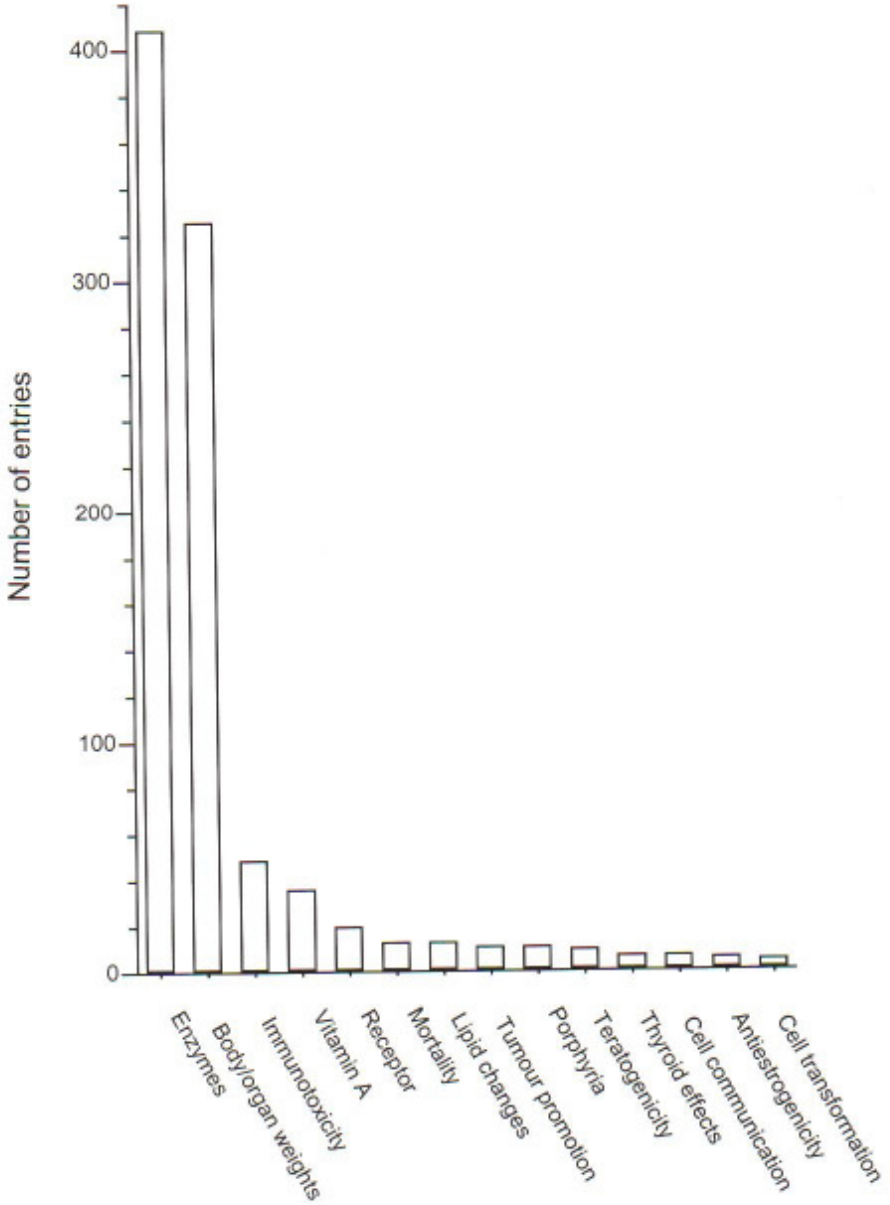
Thank you for your attention!

Toxicological effect database



- **REP:** relative potency in separate studies
- **TEF:** toxic equivalency factor, integrated overall assessment

TEF data base (PCB)



- **"Simple responses":** many entries
- **Complex endpoints:** few entries
- **Profile from 1993**: still the same. NB few entries from fetal exposure