Landesamt für
Gesundheit und Arbeitssicherheit
des Landes
Schleswig-Holstein

Human milk biomonitoring

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> PPTOX 2007 Abstr. 56 <

Transfer of xenobiotics into breast milk

- **Diffusion processes**
- MW
- Lipophilicity
- Plasma Protein binding
- Ionisation (pKa)
- **weakly acidic : plasma > < milk : weakly alkaline**
- **Carrier mediated**
- Cation transporter (Cimetidine)
- Anion transporter (Benzylpenicillin)

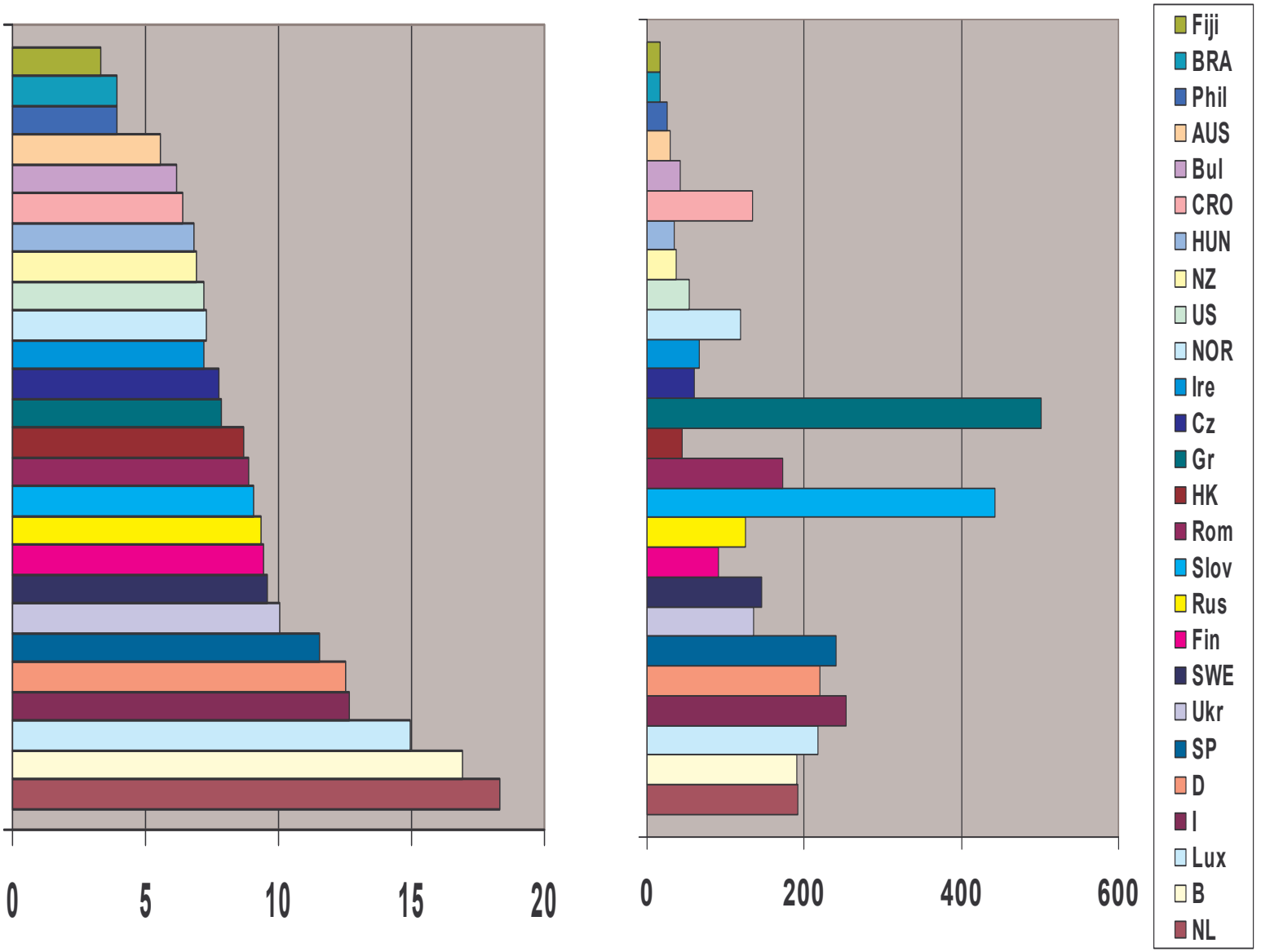
- **In favour**
- Low (< 200)
- High
- Low
- Cationic

- **??????**

Hypothesis of the molecular sive of the mammary gland

- For essential compounds appearing significantly in breast milk GI absorption (bioavailability) will be adequate
- similarly:
- non-essential compounds (Xenobiotics) appearing in breast milk will most likely be bioavailable by GI adsorption in the infant

TEQ - human milk from different countries - PCB

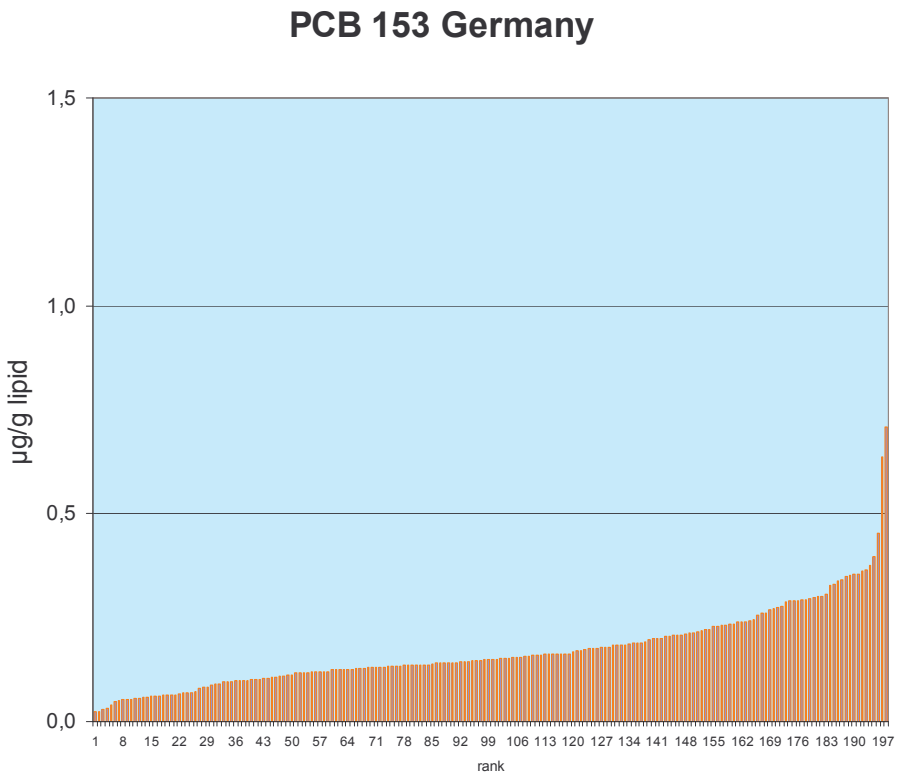


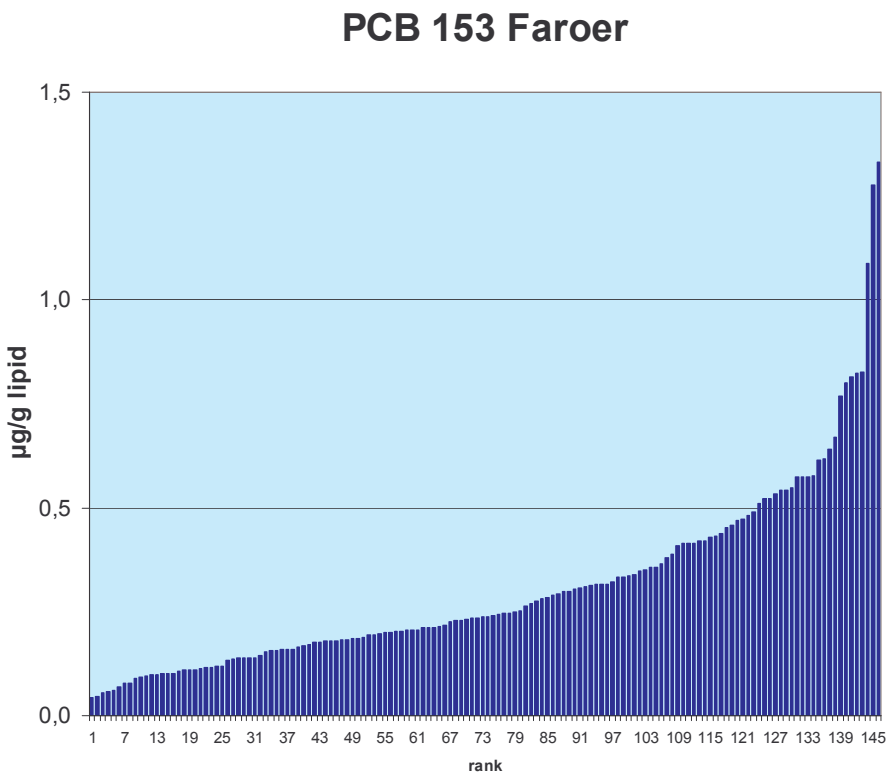
Limitations of human milk data

- Different protocols (pooled, individual)
- Incomplete reporting
- Not representative
- Different timing of sampling
- Focus on few substances (POPs)
- Limited data on partitioning , carry-over

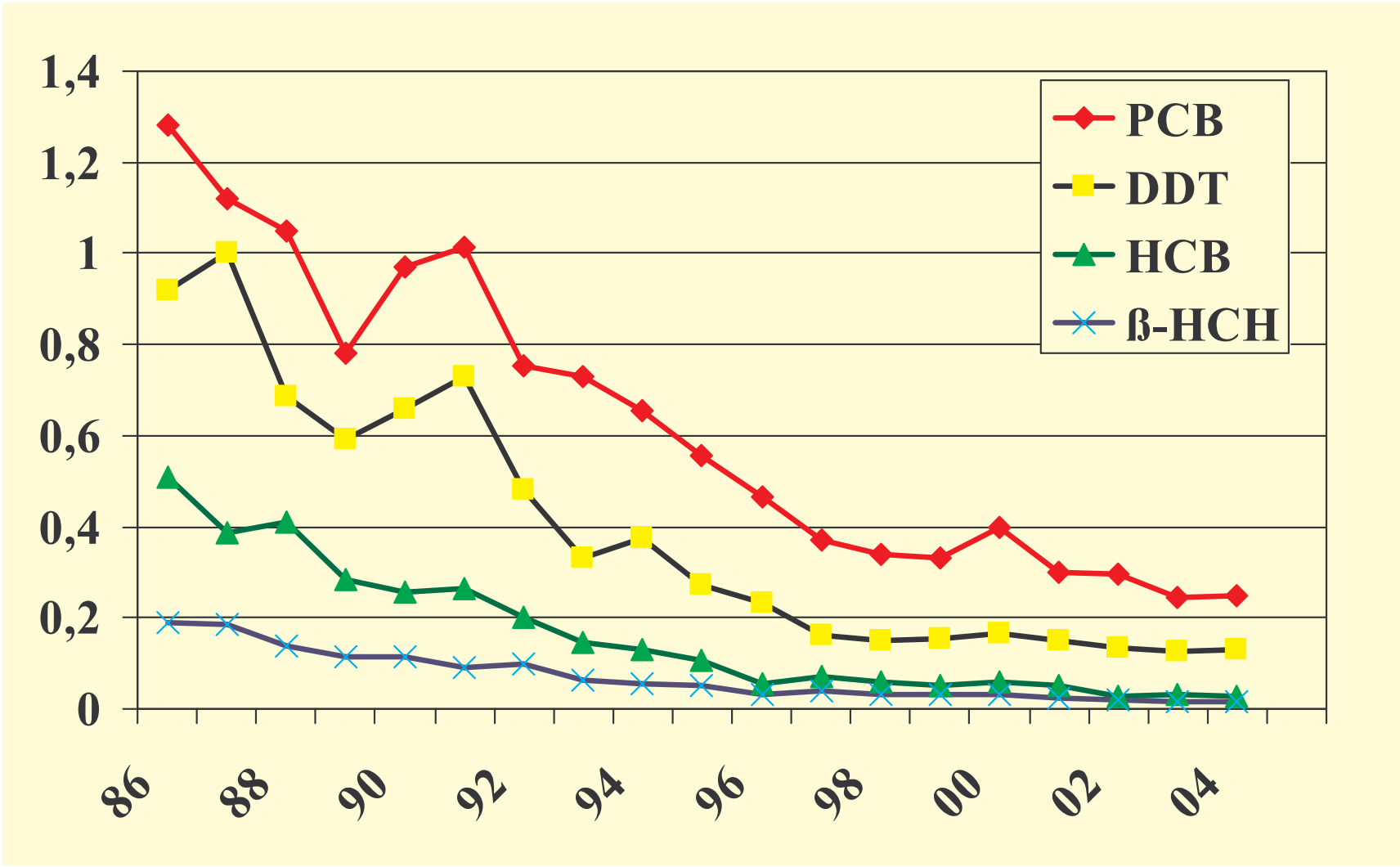
1995 cohort

PCB 153 in mothers milk [µg/g lipid]

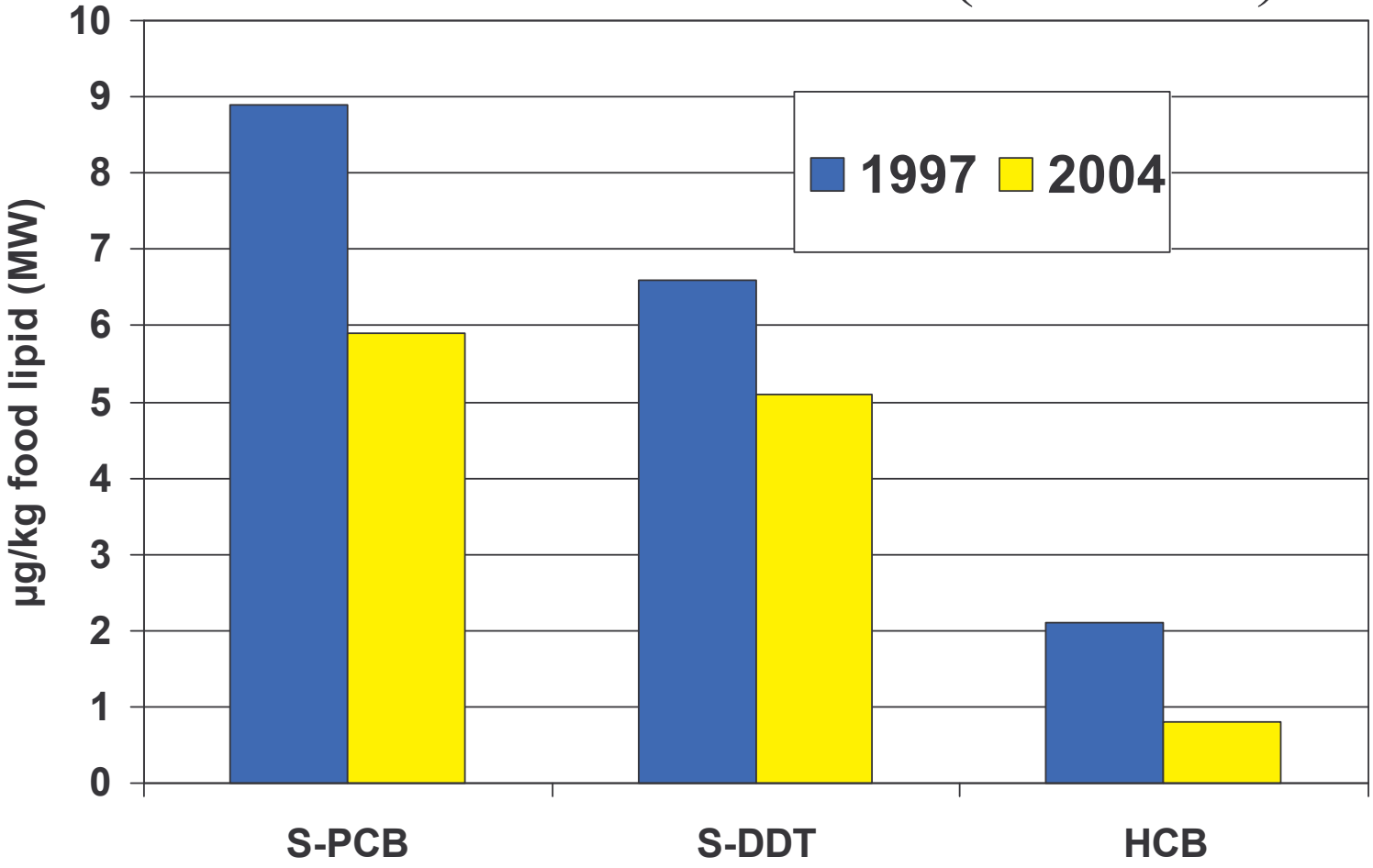




POPs in human milk in SH (µg/g lipid)



Food contamination (SH-DDS)



(2) Estimated cumulated dose
(Cssfat [ng/g fat])

- ***Cssfat = DI * t ½ [days] * (1/ln2) / Vd***

- ***DI*** = ***daily intake***
- ***t ½*** = ***half-life***
- ***Vd*** = ***Volume of distribution***

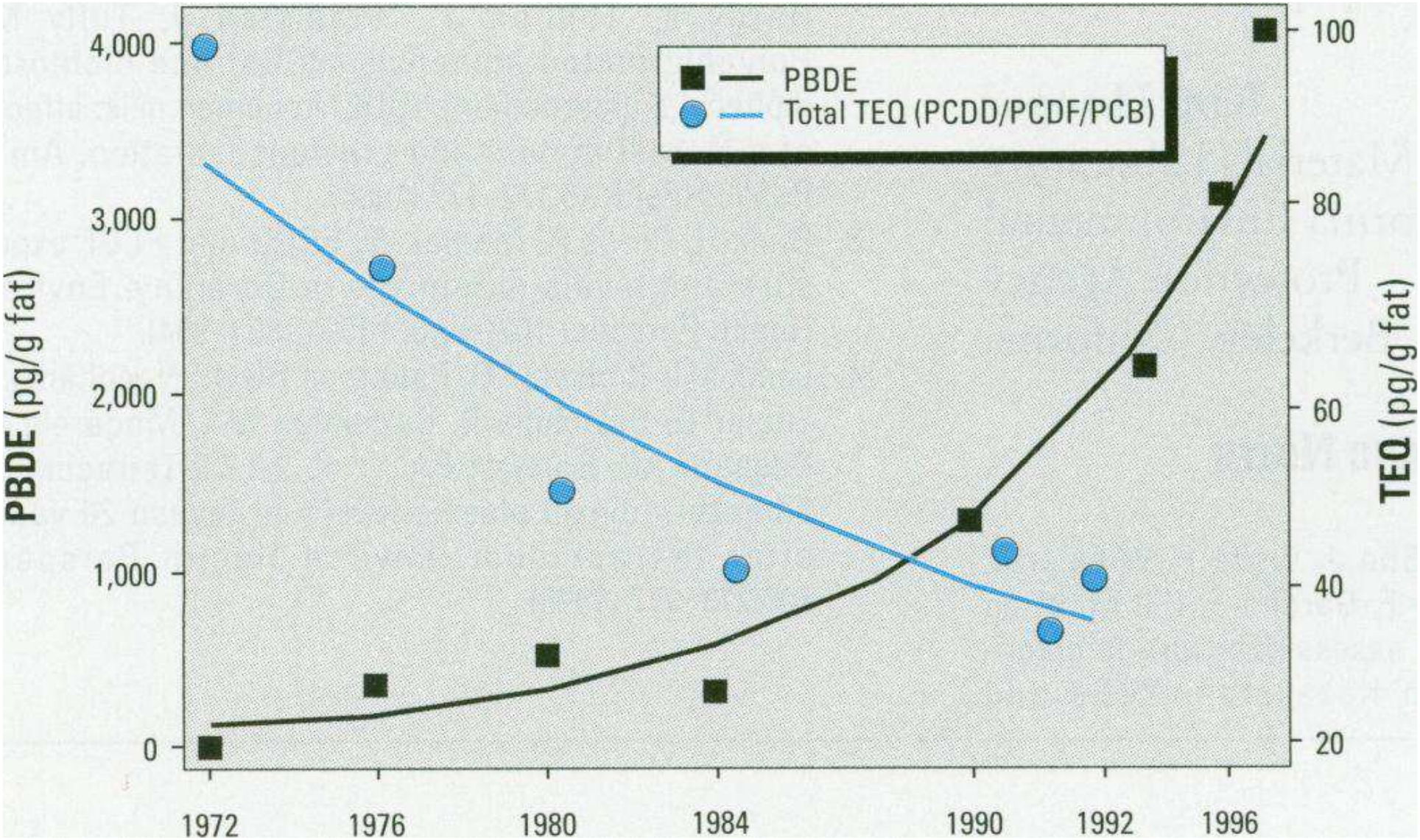
- from Rowland und Tozer (1980)

Biaccumulation and estimated t ½

	Σ-PCB	**Σ-DDT**	**HCB**	**TEQ**
Daily intake (DI) [ng/kg KG/d]	12	8	1,5	1 pg
Body burden [µg/kg milk fat]	274	164	32	26 pg
Half-life t ½ [years]	**6.9**	**6.2**	**6.5**	**7.5**

Calculated half-life of PCB

PCB-congener	t ½ (y)
28	**0,55**
52	**0.38**
101	**1.5**
118	**2.8**
138	**5.0**
153	**6.8**
180	**7.5**

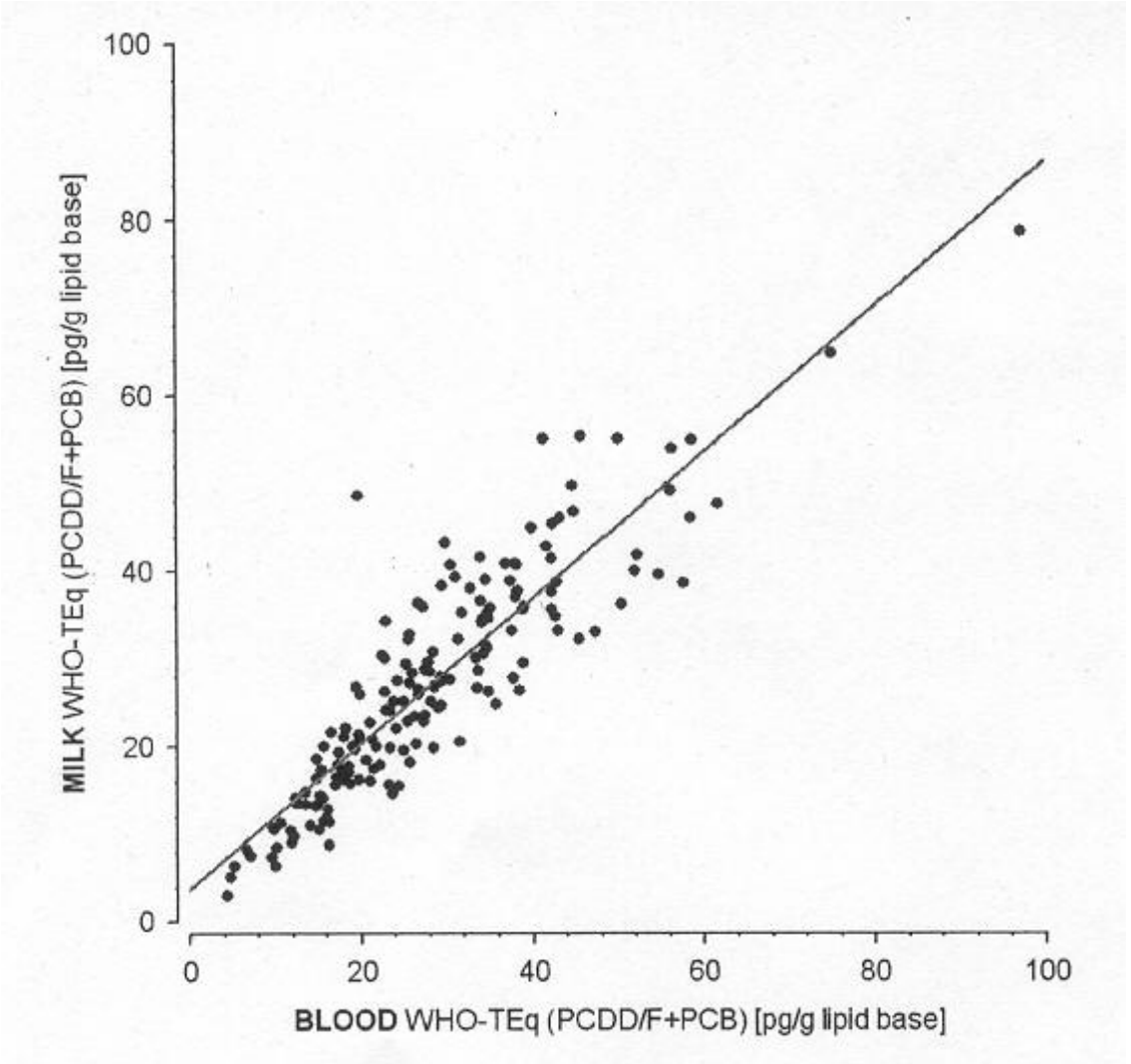


Meironyte, Noren, Bergmann: JTEH 1999

Musk fragrances in human milk (US)

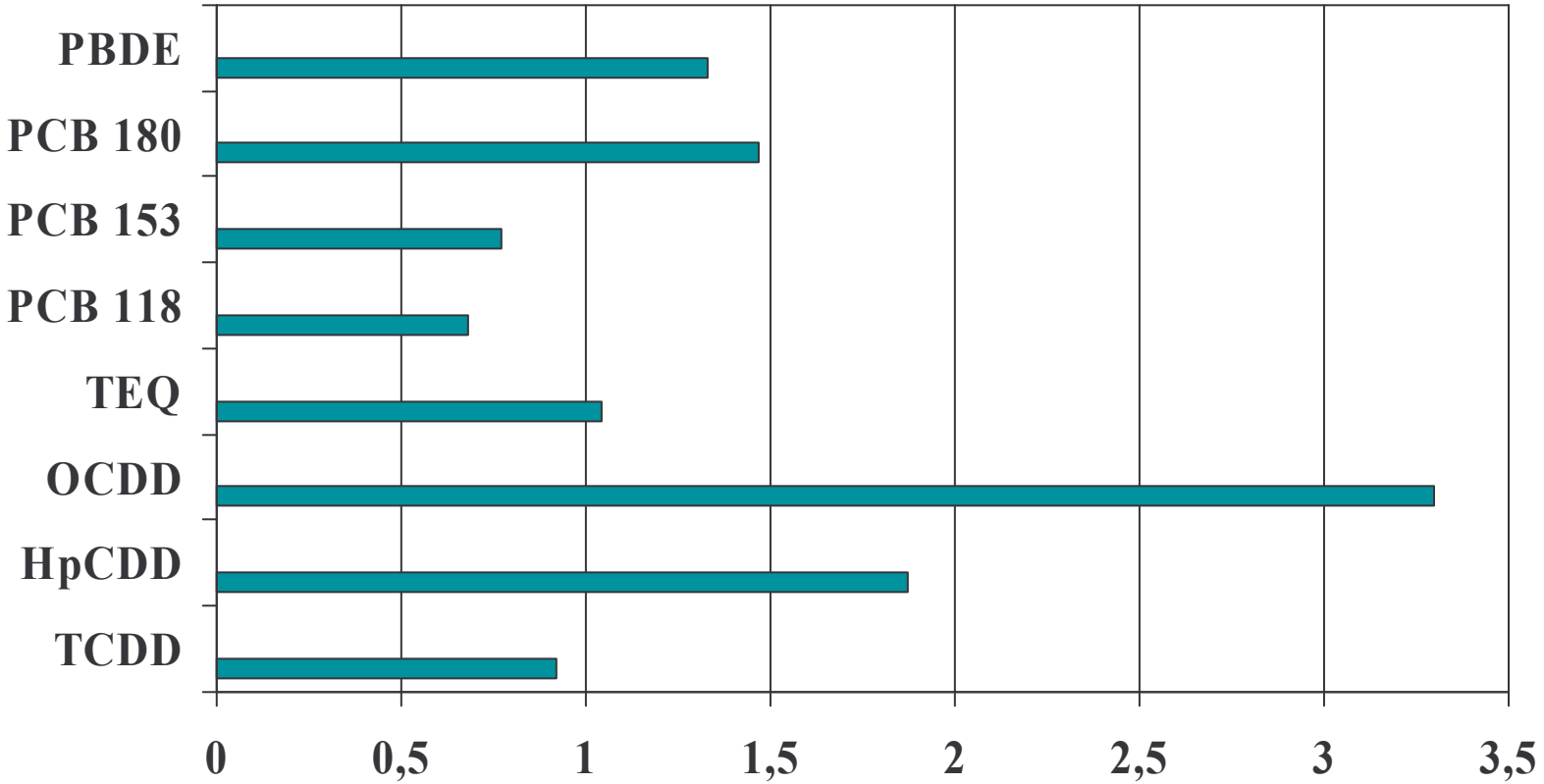
• Musk xylene	• 2 – 150 [ng/g lipid]
• Musk ketone	• 2- 238
• **HHCB (Galaxolide)**	• **5 – 917 (220 mean)**
• AHTN (Tonalide)	• 4 -144
• HHCB-lactone	• 10 -88
• PhIP	• 23 pg/ml

- Reiner et al, EST 2007

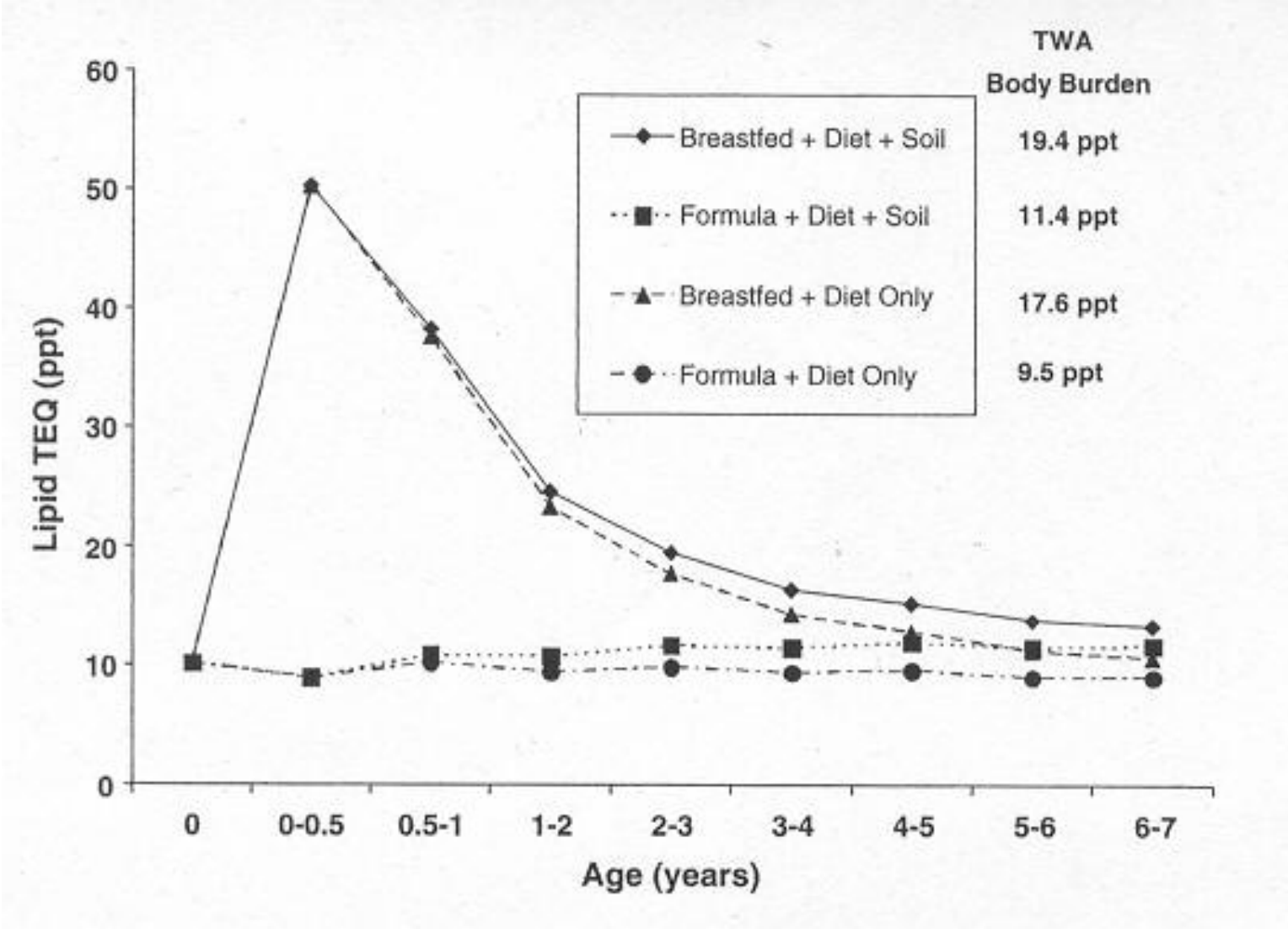


Wittsiepe et al.; Chemosphere 2007

B/M ratio (lipid base)



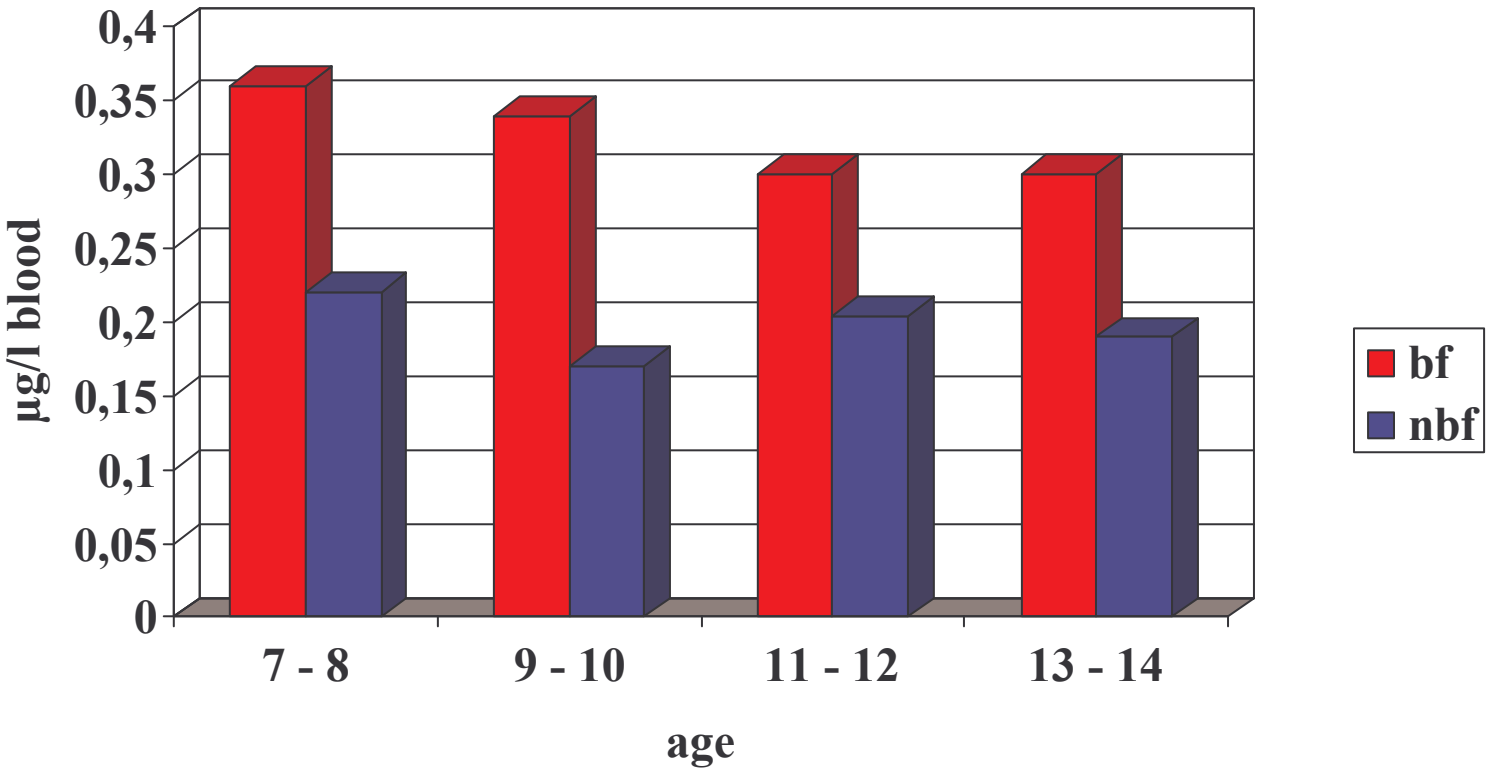
Body burden (model) and breastfeeding



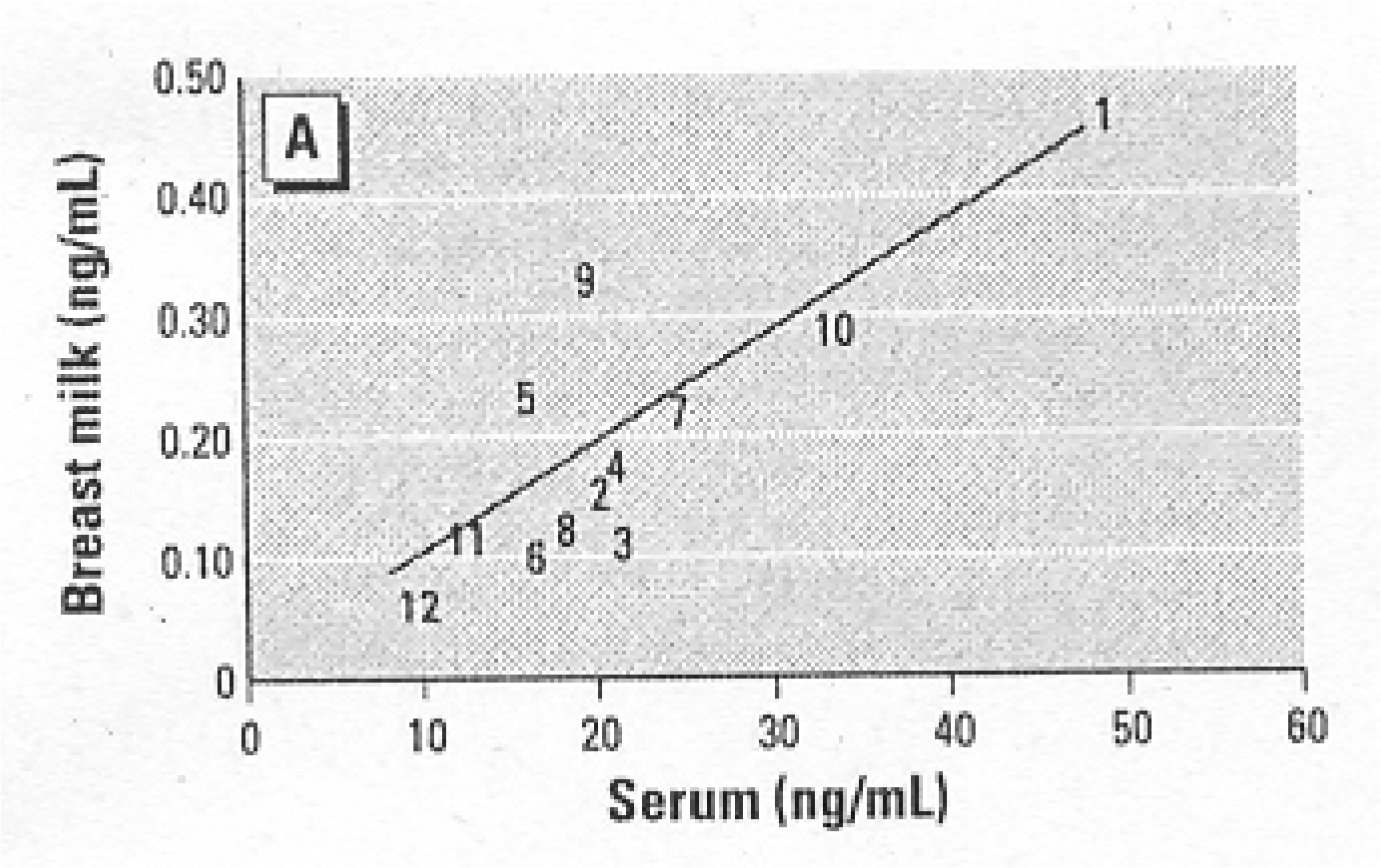
Kerger et al.,Chemosphere 2007

PCB-B and history of breastfeeding

(German KIGGS, n= 1060)



PFOS S/M partition



from Kärrman et al., EHP 2006

PFOS

- Serum : 10 – 50 ng/ml
- Milk : 0.1 – 0.5 ng/ml
- M/S ratio: 0.01
- Dose:

PFC Exposure ~ 200 ng/day

~ 40 ng/kg b.w.

TDI ~ 100 ng/ kg b.w.

Kärrman et al., EHP 2006

Biomonitoring of Phthalates

Phthalate [ng/ml]	Serum (US) Kato et al 2003	Urine Kato 2003	Milk (DK,FIN) Main et al 2005
MEHP	**4**	**-**	**9.5 - 13**
MEHHP	**-**	**17**	**?**
MEOHP	**-**	**16**	**?**

Phthalate-metabolites and toxicity

- **Metabolite IX** (MEHHP), > I >> **VI** (MEOHP) ≈ V > DEHP ≈ MEHP = 2-EH >> 2-EHA

- Secondary metabolites:
- IX = mono-(2-ethyl-5-hydroxyhexyl) phthalate

- VI = mono-(2-ethyl-5-oxohexyl) phthalate

» Regnier J, et al (2004)

Bisphenol A

- Human milk = 0.1 - 0.7 [ng/g]
- Colostrum = 3.4 (mean)
- Serum = 0 - 2.2 [ng/ml]

» from: Otaka; Ikesuki; Kuroto-Niwa; Sajiki

Study proposal

- Development of breast cancer?
- Sensitization with Bisphenol A
- Induction by carcinogen PhIP

Risk- assessment for postnatal contaminants

- Dose concept (% TDI, MOS)
- Single compounds? Tox. End-points ?
- PBPK and AUC concept (bioavailability)
- Biomonitoring infant (RfC)
- Benefits of BM!: masking negative effects?
- Cohort ? : breast fed – bottle fed
- Vulnerable group ? : preterm babies !!

American Academy of Pediatrics (AAP)

- Exclusive breastfeeding for approximately the first six months
- and support for breastfeeding as long as mutually desired by mother and child.

» Pediatrics 2005

Conclusions

- Sentinel: constant vigilance to monitor trends and to detect new xenobiotics!
- Harmonize study protocols
- Investigate partition (develop model)
- Integrated risk-assessment
- „Breastfeeding or not ?“ is not the question !
- Goal: low pre- & postnatal exposures