

Food Safety and Endocrine Active Compounds: the EU policy

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1998 European Parliament: Called upon the Commission to take action

1999 SCTEE issued an opinion on human and wildlife effects of EDC: there is an association between EDC and human health disturbances; negative effects on wildlife.

1999 Commission adopted a Communication on a Community Strategy for Endocrine Disrupters COM (1999) 706

2001 Implementation of the Communication on a Community Strategy for Endocrine Disrupters COM (2001) 262

2004 Second Implementation of the Communication on a Community Strategy for Endocrine Disrupters SEC(2004)1372



Community Strategy for ED

Short-term Action

1. Establishment of a priority list of substances for further evaluation of their role in endocrine disruption.

- Candidate list of 553 subst.
- Study on 435 substances - BKH
- Study on 12 substances - WRc

2. Communication
3. Information exchange and international cooperation

- Inventory on ED activities EU, USA, Japan & international organizations.
- ED Website

Medium-term Action

1. Identification and assessment of endocrine disrupters

- OECD EDTA - Endocrine disrupter testing and assessment task force.

2. Research and development

3. Monitoring of substances -SCALE-

Long-term Action

1. Legislative actions

- Chemical policy -REACH System.
- Water policy - Dir 2000/60/EC
- Drinking water policy -Dir 98/83/EC
- PPP policy - Dir 91/414/EEC

White Paper on a Strategy for a Future Chemicals Policy, 13 February 2001

New Chemical Policy Registration, Evaluation and Authorisation of Chemicals System

- Authorisation procedure for substances of very high concern -CMR- and substances with PBTs and vPvB characteristics.
- Rigorous testing for long-term effects of substances exceeding a production volume of 100 tonnes
- Single regulatory system for new and existing chemicals.
- Obligation of manufacturers/importers and downstream users to carry out appropriate RA.

EDs under the REACH System

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By the nature of their effects most of the Endocrine disruptors would normally qualify as:

- CMR (carcinogenic, mutagenic or toxic to reproduction).
- Adverse effects on the endocrine system of wildlife species have been causally linked to certain persistent, bioaccumulative and toxic substances, which will also be subject to authorisation.
- On a case by case basis those substances of equivalent level of concern



Water Framework Directive

Dir 2000/60/EC

List of priority substances in the field of Water Policy

Measures to be proposed within 2 years aimed at ending or phasing out emissions, discharges and losses within 20 years.

Drinking water policy
Dir 98/83/CEE

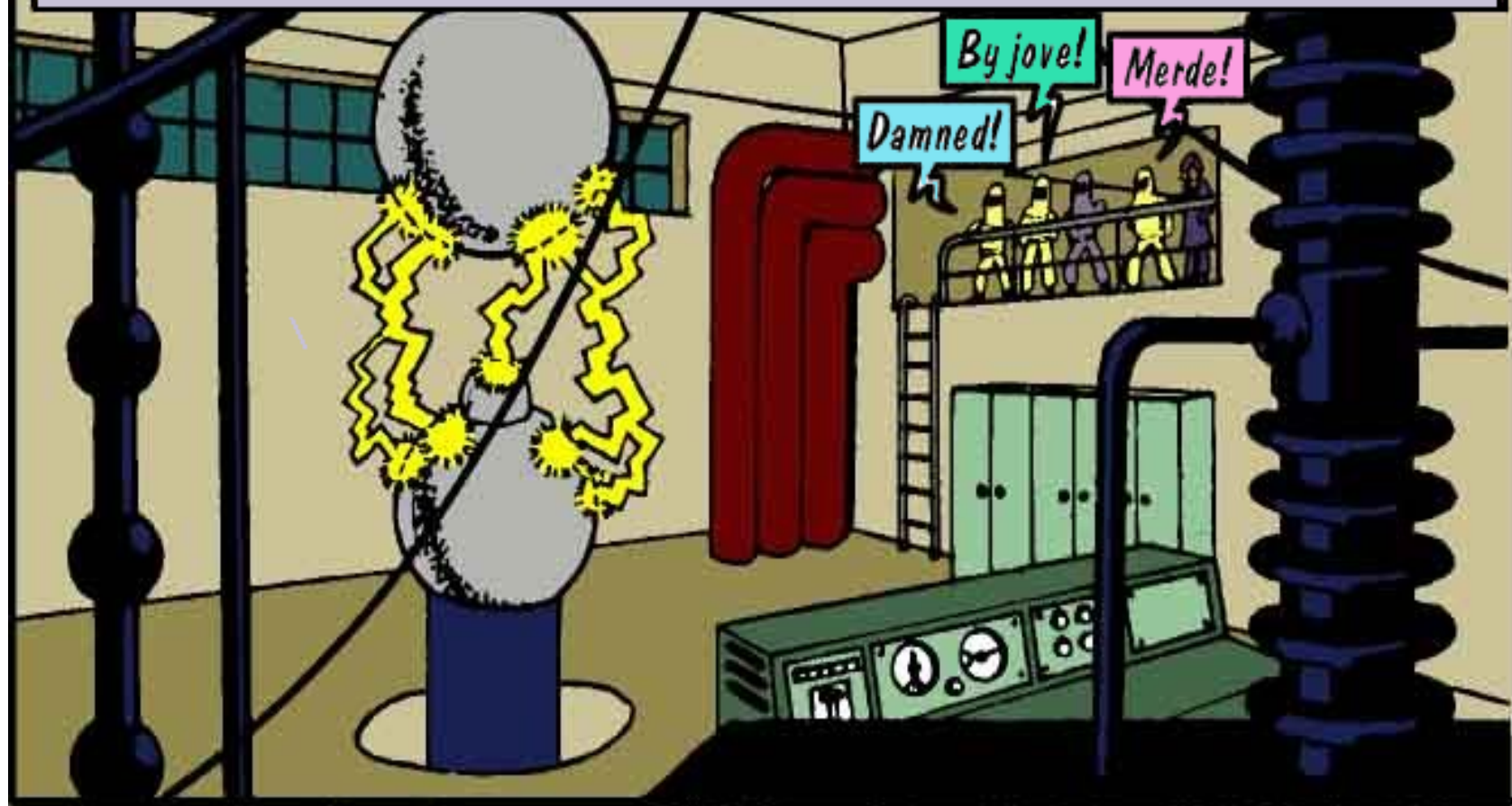
Every 5 years, the Commission shall review the different Annexes in the light of scientific and technical progress and make proposals for amendments (Monitoring of new substances - EDs)

Dir 91/414/CEE

Within the last few years many EDCs have been managed under Dir 91/414/EEC. However the assessment of ED properties is still not sufficient, as expressed by the SCP.

A systematic test strategy is still not defined, although a priority setting for substances is actually under development.

Endocrine Active Compounds



Scientific Panels which will be dealing with EACs

- Food additives, flavourings, processing aids, materials in contact with food (AFC)
- Additives and products in animal feed (FEEDAP)
- Plant health, Plant Protection Products (PPR)
- Contaminants in the food chain (CONTAM)
- SES – Pesticide Risk Assessment (PRaPER)

EAC's related opinions

AFC Panel

• Implications for human health of the use of Bisphenol A diglycidyl ether (**BADGE**) in epoxy resins and vinyllic organosols used in internal can coating.

Provide an opinion on the safety of **paraben** usage in foods.

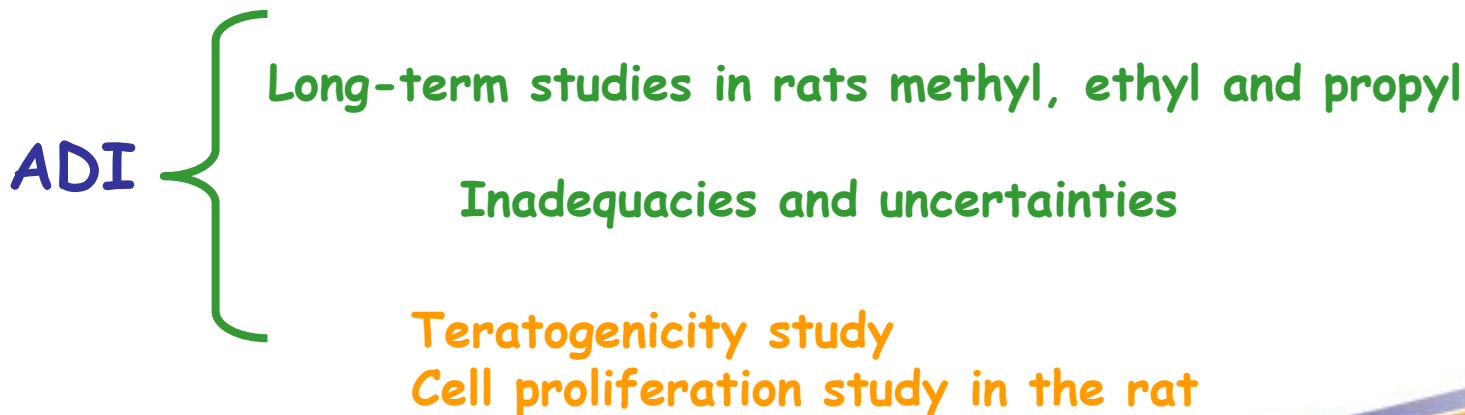
Risk assessment of **flavouring compounds**

Re-evaluation of **phthalates**

Provide an opinion on the safety of paraben usage in foods.

SCF (1994) evaluated the parabens

ADI - temporary- of 0-10 mg/kg bw as a sum of methyl, ethyl and propyl p-hydrobenzoid acid esters and their sodium salts.



- No evidence of developmental toxicity up to:



300 (rabbits) mg/kg bw/day
550 (rodents)

- Cell proliferation study on the forestomach cells in rat

Effect will be seen above a certain threshold but without concern for human exposure, when using parabens as preservatives in food.

Oestrogenic activity

In vitro: several parabens shown oestrogenic activity.



In vivo: No oestrogenic activity for methyl, ethyl and propyl parabens in uterotrophic assay
 P-hydroxybenzoic acid; common metabolite of paraben was considered to be non-oestrogenic.

Dietary administration



Propyl paraben to juvenile male rats -4 weeks-

Reduced daily sperm production in the testis in all dose groups, including the lowest level 10 mg/kg/bw/day.

LOAEL

>>> dose levels: Decrease number of sperm cells, impaired spermatogenesis and reduced testosterone levels

Dietary administration



Methyl and Ethyl paraben to juvenile male rats -4 weeks-

No effect on sex hormones and the male reproductive organs in juvenile rats at dose levels up to 1000 mg/kg/bw/day.

NOAEL

Acceptable Daily Intake -ADI-



A full group **ADI 0-10 mg/kg bw**

for the sum of methyl and ethyl paraben and their sodium salts.

Propyl paraben: should not be included in this group ADI due to its effects on sex hormones and the male reproductive organs.

Due to uncertainties for establishing a NOAEL, no ADI was recommended by the Panel.

EAC's related opinions

CONTAM Panel

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Health risks to consumers associated with exposure to **organotins** in foodstuffs

Requests related to **Camphechlor** as undesirable substance in animal feed

Requests related to **Zearalenone** as undesirable substance in animal feed

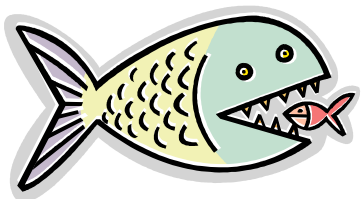
Health risks to consumers associated with exposure to **organotins** in foodstuffs

TBT, DBT, TPT

TBT, TPT: cause masculinisation in female snails and in fish at low concentrations (**1 ng/ml in water**)

Reproductive and developmental toxicity in rodents at relatively low doses (**1 mg/kg bw/day**)

Critical toxicological endpoint considered: immunotoxicity (NOAEL: 0.025 mg/kg bw/day)



TBT oxide in chronic studies

TBT, DBT, TPT

Exert their immunotoxic effects by similar mode of action and potency, the Panel considered it reasonable to establish a group tolerable daily intake (TDI) for these organotin compounds.

NOAEL: 0.025 mg/kg bw/day

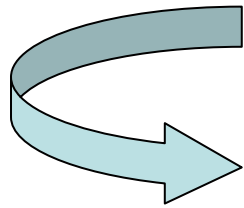
TDI: 0.25 $\mu\text{g}/\text{kg}$ bw



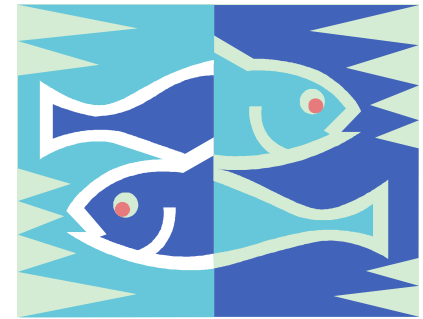
SCOOP data

Scientific cooperation on questions related to food

OTC concentrations distributions span over several order of magnitude and are severely skewed



Large variety of organisms
Farmed and wild fish, molluscs, crustaceans, cephalopodes and equinoderms



8 MS

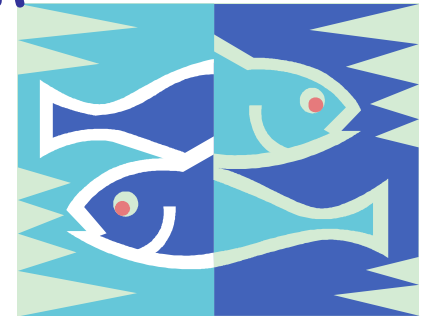
TDI: 0.25 $\mu\text{g}/\text{kg}$ bw

Based on fully aggregated data for fish and fishery products the estimated concentration medians

TBT 7.0

DBT 2.5 $\mu\text{g}/\text{kg}$ of fresh weight

TPT 4.0



OTC seafood >>> fish

Fish consumption

Intake calculations

EU mean 24.5 kg/head/year

Norway 50.8 kg/head/year

Combined intake estimated
TBT, DBT & TPT -Median-

0.018 $\mu\text{g}/\text{kg}$ bw/day
7% of the TDI

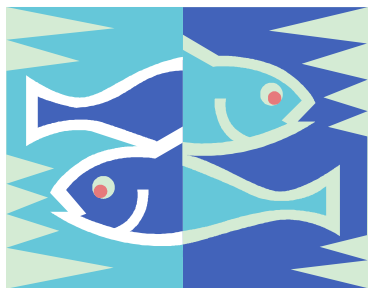
Mean

0.083 $\mu\text{g}/\text{kg}$ bw/day
33% of the TDI

TDI: 0.25 $\mu\text{g}/\text{kg}$ bw

High consumers -Median-

0.037 $\mu\text{g}/\text{kg}$ bw
15% of the TDI



Mean

0.17 $\mu\text{g}/\text{kg}$ bw
70% of the TDI

The Panel concluded that the consumption of fish, mussels and other marine animals from highly contaminated areas, such as the vicinity of harbors and heavily used shipping routes may lead to OTC intake that exceed the group TDI.

Future work

SCs - FEEDAP Panel:
plant/herbal products

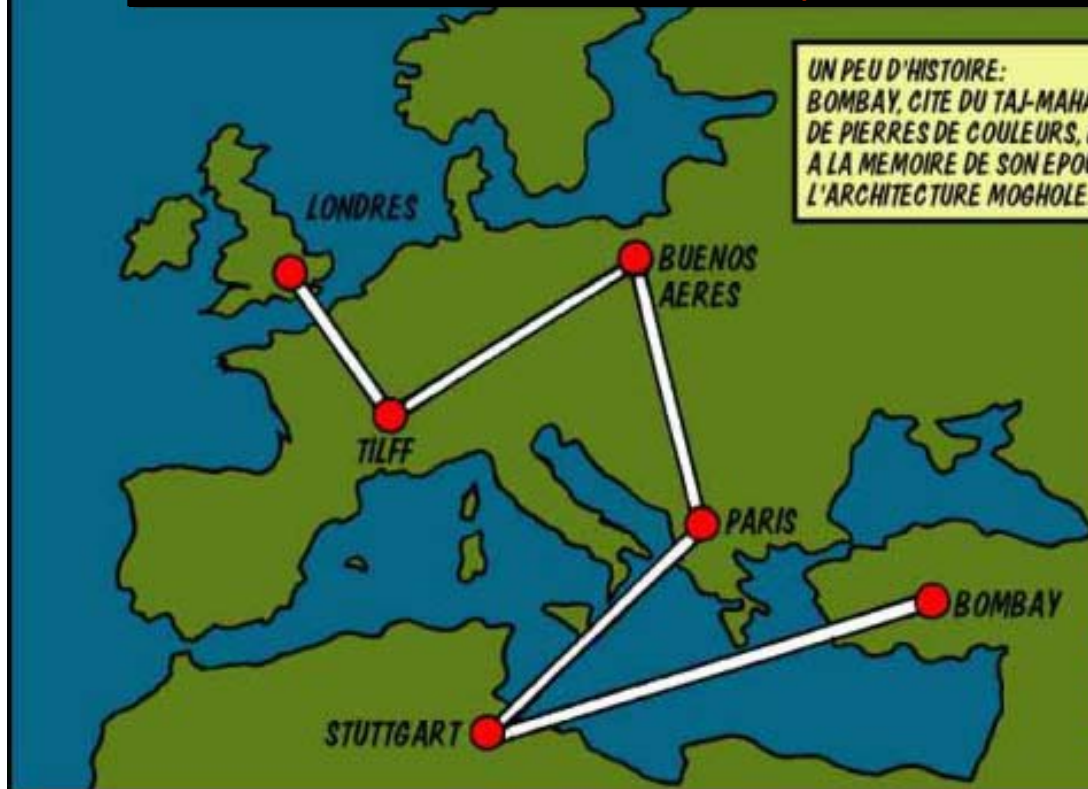
PPR

PRaPER

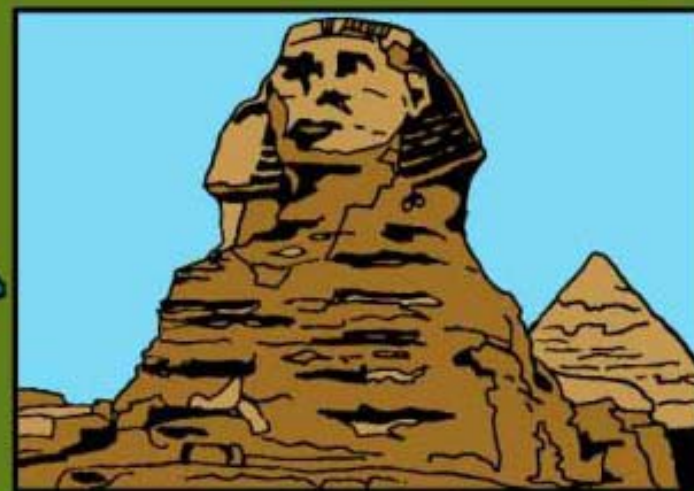
} pesticides



Cascade Spring School



UN PEU D'HISTOIRE:
 BOMBAY, CITE DU TAJ-MAHALL, OU TADJ-MAHALL. MAUSOLEE DE MARBRE BLANC INCRUSTE DE PIERRES DE COULEURS, ELEVE AU XVII^e s. PRES D'AGRA PAR L'EMPEREUR CHAH DJAHAN A LA MEMOIRE DE SON EPOUSE MUNTAZ MAHALL. L'UNE DES PLUS BELLES REUSSITES DE L'ARCHITECTURE MOGHOLE.



BOMBAY, LE TAJ-MAHALL.