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.


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

**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
2. Monitoring of substances - SCALE-
Legislative action - Overall chemicals policy


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

By the nature of their effects most of the Endocrine disrupters 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.
Drinking water policy
Dir 98/83/CEE

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.

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).
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 vinylic 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.

**ADI**

- Long-term studies in rats methyl, ethyl and propyl
- Inadequacies and uncertainties
- Teratogenicity study
- Cell proliferation study in the rat
• 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.
CONTAM Panel

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
Organotins in foodstuffs

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 µg/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
TDI: 0.25 µg/kg bw

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

- TBT: 7.0 µg/kg of fresh weight
- DBT: 2.5 µg/kg of fresh weight
- TPT: 4.0 µg/kg of fresh weight

OTC seafood >>> fish

Fish consumption

- EU mean 24.5 kg/head/year
- Norway 50.8 kg/head/year

Intake calculations

- Combined intake estimated TBT, DBT & TPT -Median- 0.018 µg/kg bw/day
  7% of the TDI
- Mean 0.083 µg/kg bw/day
  33% of the TDI
TDI: 0.25 µg/kg bw

High consumers -Median- 0.037 µg/kg bw
15% of the TDI

Mean 0.17 µg/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

EAC's
Cascade Spring School