New POPs
- Candidate Chemicals for Stockholm Convention -

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National Institute for Environmental Studies
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Topics

1) Outline of the management of chemicals

2) Brief introduction of POPs candidate chemicals

3) Analysis of PFOS and other fluorosurfactants

4) Effectiveness Evaluation of Stockholm Convention
Outline of Chemical Management in Japan

New Chemicals

Chemicals Manage. Law

OECD Test Guideline

Existing Chemicals

Toxicity evaluation

Banned/restricted Chemicals

Environmental Criteria

Emission Criteria

Risk assessment

Regular Monitoring

Initial Survey

Information on toxicity, health effects, production volume, etc.

PBT
Priority on Persistent, Bioaccumulative Toxicants
PBT, or POPs (Persistent Organic Pollutants)

**Stockholm Convention**
“to protect human health and environment from POPs”

- May 2001: Stockholm Convention adopted
- May 2004: entry into force
- May 2005: First Conference of Parties (COP-1)
- May 2006: COP-2
- May 2007: COP-3
  - POPRC on new POPs
- May 2009: COP-4
  - Effectiveness Evaluation & GMP
POPs (Persistent Organic Pollutants)

Annex A: prohibited 8 OCPs and PCB
Annex B: restricted DDT
Annex C: unintentional production PCDDs, PCDFs, HCB, PCB
Article 8: Listing of chemicals in Annexes A, B and C

1. A Party may submit a proposal to the Secretariat for listing a chemical in Annexes A, B and/or C. …

2. The Secretariat shall verify whether the proposal contains the information specified in Annex D. … it shall forward the proposal to the Persistent Organic Pollutants Review Committee (POPRC).

3. The Committee shall examine the proposal and apply the screening criteria specified in Annex D in a flexible and transparent way, taking all information provided into account in an integrative and balanced manner.

Review steps of POPRC

(1) To check whether a proposed chemical passes POPs Criteria or not
(2) To evaluate according to Risk Profile of the chemical
(3) To evaluate according to socio-economic consideration
Candidate new POPs under review by POPRC

2005
PBDE (Pentabromodiphenylether)
HBB (Hexabromobiphenyl)
Chlordecone
γ-HCH (Lindane)
PFOS (+ their derivatives)

2006
OBDE (Octabromodiphenylether)
PeCB (Pentachlorobenzene)
short-chained chlorinated paraffin
α-HCH
β-HCH

2007
Endosulfan
Category of proposed POPs

1) **OC Pesticides**  
   *long-used chemicals with established analytical methods; many monitoring*  
   - α-, β-, γ-HCH  
   - chlordecone  
   - endosulfan

2) **Flame retardants**  
   *include organobromine chemicals*  
   - PBDEs (PeBDE, OBDE) *many isomers/congeners (except HxBB)*  
   - HxBB  
   - short-chained chloroparaffins

3) **Others**  
   - PFOS (fluorinated surfactants)  
   - PeCB
Broad-spectrum Insecticide for:
seed, soil treatment
wood and timber protection
pharmaceutical use

Production estimate:
720,000 t (Voldner & Li, 1995)
<table>
<thead>
<tr>
<th>Properties</th>
<th>Criteria</th>
<th>Data (or estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>&gt;2 months</td>
<td>30~300 d</td>
</tr>
<tr>
<td>Soil</td>
<td>&gt;6 months</td>
<td></td>
</tr>
<tr>
<td>Sediments</td>
<td>&gt;6 months</td>
<td></td>
</tr>
<tr>
<td>*Bioacumulative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAF/BCF</td>
<td>&gt;5,000</td>
<td>log BCF=2.26~3.85</td>
</tr>
<tr>
<td>Log $K_{o/w}$</td>
<td>&gt;5</td>
<td>3.5</td>
</tr>
<tr>
<td>*Long Range Transport</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Toxicity/Ecotoxicity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( \gamma \)-HCH
Chlordecone

Insecticide, and material for production of other insecticide (Kelevan)

Production:

USA 1966~1975 total 1,600 t
12~70 t used domestically
90~99.2% => export for
Kelevan production
Africa, Europe, Latin Am.
**Chlordecone**

**Properties**

*Persistent*
- Water: >2 months
- Soil: >6 months 1~2 years
- Sediments: >6 months

*Bioaccumulative*
- $\text{BAF/BCF} > 5,000$  
- $\text{Log } K_{o/w} > 5$  
- $\text{t}_{1/2\text{air}} > 2 \text{ d}$  

*Long Range Transport*
- $\text{t}_{1/2\text{air}} > 2 \text{ d}$  
- *Toxicity/Ecotoxicity*  
- □ / □

**Criteria**

Data (or estimates)
- >60,000
- 4.5~6.0
$\alpha$-,$\beta$-,$\gamma$-HCHs

Fig. 9. Global lindane usage distribution accounted for in the search. The total usage was estimated at 720,000 metric tonnes.

Voldner & Li (1995)
Alpha-HCH Emission in 1990
From current usage in 1990
(with 1X1 lat/long resolution)

Global Chemical Transport Model –
$\alpha$-HCH Concentration at Surface Level

[Koziol and Pudykiewicz 1999]
PeBDE

Mixture of tri-heptabrominated flame retardant used for;

- High-impact polystyrene
- ABS
- Polyurethane foams
- Polyurethane elastomers
- Other plastics

Annual production/consumption;
- 8,500 t (POPRC1-INF5-b; Norway)
- 4,000 t (Env. Health Criteria 162)
- (usage in EU ~10,000t/y in 1989)
## PeBDE Properties and Criteria

<table>
<thead>
<tr>
<th>Properties</th>
<th>Criteria</th>
<th>Data (or estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>&gt;2 months</td>
<td>150 days</td>
</tr>
<tr>
<td>Soil</td>
<td>&gt;6 months</td>
<td>150 days</td>
</tr>
<tr>
<td>Sediments</td>
<td>&gt;6 months</td>
<td>600 days</td>
</tr>
<tr>
<td>*Bioaccumulative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAF/BCF</td>
<td>&gt;5,000</td>
<td>&gt;27,400</td>
</tr>
<tr>
<td>Log $K_{o/w}$</td>
<td>&gt;5</td>
<td></td>
</tr>
<tr>
<td>*Long Range Transport</td>
<td>$t_{1/2}\text{air}&gt;2$ d</td>
<td>10~20 d</td>
</tr>
<tr>
<td>*Toxicity/Ecotoxicity</td>
<td>NOAEL</td>
<td>=1mg/kg/d</td>
</tr>
</tbody>
</table>
Hexabrominated flame retardant used for:
ABS (PBB content ~10%; EHC152) coatings and lacquers
polyurethane foams

Production:
USA hexa 1970~1974 5,369 t
    octa, deca ~1979 (total 6,000 t)
Germany  poly ~1985
France    deca ~ a few hundreds t/y
UK        deca  ~1977
<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td>*Persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>&gt;2 months</td>
<td></td>
</tr>
<tr>
<td>Soil</td>
<td>&gt;6 months</td>
<td>Stable</td>
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<tr>
<td>Sediments</td>
<td>&gt;6 months</td>
<td></td>
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<tr>
<td>*Bioaccumulative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAF/BCF</td>
<td>&gt;5,000</td>
<td>&gt;10,000</td>
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<tr>
<td>Log K&lt;sub&gt;o/w&lt;/sub&gt;</td>
<td>&gt;5</td>
<td>6.39~7</td>
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<tr>
<td>*Long Range Transport</td>
<td></td>
<td></td>
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<tr>
<td>*Toxicity/Ecotoxicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOAEL</td>
<td></td>
<td>=0.15mg/kg/d</td>
</tr>
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</table>

HxBB
Flame retardants: PBDE, HBB, chlorinated paraffins

Polybrominated diethylethers:
- Pentabrominated (PeBDE)
- Octabrominated (OcBDE)
- Decabrominated (DeBDE)

PBDEs in human Breast milk (ng/g lipid)
PBDEs

- Adult mammalian toxicity
  - Hepatic enzyme induction and toxicity
    - DBDE – hepatocarcinogen (very high dose)
  - Endocrine disruption
    - Thyroid
    - Estrogen/anti-androgen

- Developmental reproductive Toxicity
  - Penta/Octa, BDE99
    - Delayed puberty both sexes, sex organ wt changes, ovarian tox, decreased sperm counts

- Developmental neurotoxicity
  - Penta/BDE47, 99, 203, 206, 209
    - Deficits in sensory, motor, and cognitive function
### PFOS Properties

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Data (or estimates)</th>
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<tbody>
<tr>
<td>*Persistent</td>
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<td>Water</td>
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<td>&gt;6 months</td>
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<tr>
<td>Sediments</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>*Bioaccumulative</td>
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</tr>
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<td>BAF/BCF</td>
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<tr>
<td>*Long Range Transport</td>
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<tr>
<td>*Toxicity/Ecotoxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2796~3100</td>
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<tr>
<td></td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>Monitoring</td>
</tr>
<tr>
<td></td>
<td>1.6mg/kg/d (rat)</td>
</tr>
</tbody>
</table>
PFOS (Perfluorooctane sulfonate)

* Produced from 1950’s
  max ~3,500 t/y (2000)
* Used for surface treatment of papers/clothes/fabrics as water/oil repellants, for semiconductor industries, for fire fighting agents, etc.
* N(L)OAEL for 2nd generation of rats 0.1(0.4) mg kg⁻¹/day

[Chemical Properties of PFOS]
* Vapor pressure 3.31x10⁻⁴ Pa (20 C)
* Water sol. 519 / 25 mg/L (pure water(20 C) / seawater)
* Henry’s Law Const. 3.1x10⁻⁹ atm·m³/mole
* BCF 2,796 (Blue gill)
**Major application of PFOS-related chemicals**

**POSF** [C₈F₁₇SO₂F] **Low MW**
- Amphoteric
- Amines
- Quarternary Ammonium Salts

**FOSA** [C₈F₁₇SO₂NH(CₙH₂n+₁)]
- Oxazolidinones
- Carboxylates
- Amides
- Alkoxyaltes
- Silanes

**FOSE** [C₈F₁₇SO₂N(CₙH₂n+₁)C₂H₅OH] **High MW**
- Adipates
- Phosphate Esters
- Fatty Acid Esters
- Alcohols
- Phosphates

**PFOS**
- High MW

**Performance Chemicals**
- Fire Extinguishing Forms
- Mining & Oil Surfactants
- ElectroPlating/Etching Bath
- Household Additives
- Chemical Intermediates
- Coatings/Coating Additives
- Carpet Spot Cleaners
- Insecticides Raw Materials

**Surface Treatments**
- Carpet Protector
- Fabric/Upholstery Protector
- Apparel & Leather Protector
- Other Protective Products

**Paper & Packaging Protectors**
- Food Packaging
- Paper Products

**US Production (World)**
- **POSF** 660 t/y (830 t/y)
- **FOSA** <92 t/y (151 t/y>
- **FOSE** 1,070 t/y (2,160 t/y)
- **PFOS** 1,210 t/y (1,490 t/y)
Perfluorosurfactants

**PFOS Amides**

\[
\text{CF}_3(\text{CF}_2)_7\text{SO}_2\text{N} \quad \text{CH}_2\text{CH}_2\text{COOH} \\
\text{CF}_3(\text{CF}_2)_7\text{SO}_2\text{N} \quad \text{CH}_2\text{CH}_2\text{OH} \\
\text{CF}_3(\text{CF}_2)_7\text{SO}_2\text{N} \quad \text{H} \\
\]  

**Sulfonic acids**

[Formula]

**Alcohols**

[Formula]

**Carboxylic acids**

[Formula]

* Surfactants with oil/water repellant activity
  * not lipophilic but accumulated in the body

* PPAR\(\alpha\) (Peroxisome Proliferator Activated Receptor)
  => induce peroxisome containing fatty acid-metabolizing enzymes
Life Cycle Waste Stream Estimates of PFOS
(Battelle Memorial Institute (2000))

| Summary of estimated FC waste stream (PFOS equivalent; lbs./y) |
|-------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                   | Customers        |                  |                  |                  |                  |
|                   | Suppl. Chain     | End use          | Disposal         | BU Total         | 3M Mfg. Process |
|                   | Process          |                  |                  | 3M Mfg. Waste Str. | Release        |
| Air               | 2,600            | 3,300            | 0                | 5,900            | N/A 19,000     |
| Waste water       | 110,000          | 180,000          | 350              | 290,000          | 51,000 10,000  |
| Solid waste       | 59,000           | 200,000          | 1,300,000        | 1,500,000        | 1,037,000 -    |
| *Landfill         |                  |                  |                  |                  | 380,000 N/A    |
| *Incineration     |                  |                  |                  |                  | 657,000 N/A    |

: Conservative, worst case assumption based on 1997 sales data
PFOS: Peroxisome proliferators

- β-oxidation
- $\text{H}_2\text{O}_2$ respiration
- Cholesterol metabolism

* Inhibit lipid/sugar metabolism
* Produce active oxygen species

1) Carcinogenic (promoter)
2) Diabetes, Arteriosclerosis
3) Modulation of immune/inflammation reaction

Strong sub-acute/chronic toxicity; Species-specificity

Fatty acid-binding protein

9-cis retinoic acid

PPARα

Peroxisome enzymes

Promoter
Table 1. PFOS concentrations in serum (ng/ml) and in various tissues (ng/g) on a wet weight basis.

<table>
<thead>
<tr>
<th>Site</th>
<th>Untreated control</th>
<th>1 mg/kg BW</th>
<th>10 mg/kg BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>BDL</td>
<td>10,490 ± 1,428</td>
<td>45,446 ± 4,120*</td>
</tr>
<tr>
<td>Tissue</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>BDL</td>
<td>26,617 ± 4,044</td>
<td>97,358 ± 25,668*</td>
</tr>
<tr>
<td>Heart</td>
<td>BDL</td>
<td>1,280 ± 697</td>
<td>23,490 ± 10,036*</td>
</tr>
<tr>
<td>Kidneys</td>
<td>BDL</td>
<td>9,381 ± 4,836</td>
<td>47,799 ± 29,512*</td>
</tr>
<tr>
<td>Spleen</td>
<td>BDL</td>
<td>76</td>
<td>15,873</td>
</tr>
<tr>
<td>Ovary</td>
<td>BDL</td>
<td>3,028</td>
<td>15,489</td>
</tr>
<tr>
<td>Adrenal</td>
<td>BDL</td>
<td>1,539</td>
<td>30,087</td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>BDL</td>
<td>&lt;50</td>
<td>15,706</td>
</tr>
<tr>
<td>Cortex</td>
<td>BDL</td>
<td>294</td>
<td>4,487</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>BDL</td>
<td>115</td>
<td>8,966</td>
</tr>
<tr>
<td>Brain stem</td>
<td>BDL</td>
<td>363</td>
<td>5,346</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>BDL</td>
<td>289</td>
<td>5,540</td>
</tr>
<tr>
<td>Rest of the brain</td>
<td>BDL</td>
<td>396</td>
<td>4,256</td>
</tr>
</tbody>
</table>

BDL, below detection limit (50 ng/g). Tissues from animals in each group were pooled for the measurement of PFOS concentrations in specific parts of the brain and in spleen, ovaries, and adrenals. n = 4–5 in each group of rats.

*p < 0.05 relative to the other groups.
BCF vs carbon chain length of PFAs in rainbow trout

Responses of the Liver to Perfluorinated Fatty Acids with Different Carbon Chain Length in Male and Female Mice: In Relation to Induction of Hepatomegaly, Peroxisomal β-Oxidation and Microsomal 1-Acylglycerophosphocholine Acyltransferase


Fig. 2. Effects of PFCAs on the Activity of Microsomal 1-Acyl-GPC Acyltransferase in the Liver of Male Mice

Fig. 5. Relationship between the Concentration of PFCAs and the Activity of Peroxisomal β-Oxidation in the Liver of Mice
Estrogen-Like Properties of Fluorotelomer Alcohols as Revealed by MCF-7 Breast Cancer Cell Proliferation

M. Maras, et al., EHP 114, 100 (2006)

Figure 3. Effect of perfluorinated chemicals on mRNA expression of estrogen-responsive genes in MCF-7 cells were treated with 0.1% DMSO, 1 nM E2, 10 μM 4-NP, 30 μM 6:2 FTOH, 10 μM 8:2 FTOH, 50 μM PFOS, 50 μM PFNA, 50 μM PFOA, or 10 nM TCDD. After exposure to the test compounds for 48 hr, mRNA levels of TFF1 (A), PGR (B), ESR1 (C), PDZK1 (D), and ERBB2 (E) were measured by real-time PCR and normalized using HPRT1 as an internal control. Results are means from three replicate measurements and are expressed as fold relative to 0.1% DMSO; error bars indicate SD. *p < 0.05, **p ≤ 0.001.
PFOS Levels in wildlife (ng/g wet)

Giesy & Kannan (2001)
Monitoring of PFOS and other fluorosurfactants
At National Institute for Environmental Studies (NIES)
Analysis of PFOS and related chemicals

Important points
1) To reduce blank levels
2) Alkaline digestion for biological samples

<table>
<thead>
<tr>
<th>Bivalve samples</th>
<th>PFOA (n=3)</th>
<th>PFOS (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recovery (%)</td>
<td>Concentration (ng/g wet)</td>
</tr>
<tr>
<td>1) <strong>Alkali + Ion pair</strong></td>
<td>101 ± 2</td>
<td>10.5 ± 0.2</td>
</tr>
<tr>
<td>2) <strong>Ion pair</strong></td>
<td>94 ± 19</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>3) <strong>PFE + Alkali + Ion pair</strong></td>
<td>86 ± 3</td>
<td>5.8 ± 0.4</td>
</tr>
<tr>
<td>4) <strong>PFE + Ion pair</strong></td>
<td>71 ± 16</td>
<td>2.6 ± 0.1</td>
</tr>
</tbody>
</table>

Yoshikane et al (Dioxin 2006)
Environmental Monitoring and Specimen Banking at NIES

Mussel sampling along Japanese coastline

Intensive Survey in Tokyo Bay
標準物質

肝臓抽出液
Effectriveness Evaluation Of Stockholm Convention

Country monitoring reports from Parties

1st Global Report
By CG

Regional Reports
By ROG

COP-4 in May 2009

Establishment of Monitoring Network needed with Specimen Banking as effective back-up

Effectiveness Evaluation: to be conducted 4 years interval