Pharmaceuticals in the Environment: Sweden and the EU

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European efforts

- European Medicines Agency (EMEA) has issued draft guidelines
- Sweden has prioritized pharmaceuticals in the environment as a national environmental concern
- Stockholm County Council has taken a leadership role

Proposals from the European Commission

- Proposed new role for European Medicines Agency (EMEA) addressing environmental concerns
- New directives for human and veterinary pharmaceuticals

European Parliament proposals

- Include “risk to the environment” in the risk/benefit assessment of new drugs
- Develop an environmental classification system for new drugs
- Require eco-toxicological data on new drugs
- Require “return to pharmacy” label on all drugs

ERAPharm

- ERAPharm is a research project funded within the priority ‘Global change and ecosystems’ of the 6th framework programme of the European Commission.
- Started in October 2004; the project duration is three years.

  - [http://www.erapharm.org/summary.html](http://www.erapharm.org/summary.html)

EU proposed approach for estimating risk

- Predicted environmental concentration (PEC) in recipient; depends on:
  - Amount sold/year
  - Recipient volume
  - Requires assumptions about metabolism, degradation in STP
- Compare PEC to predicted no effect conc. (PNEC);
- **Proposed:** PEC > 0.01 microgm/L; > PNEC/1000 triggers more detailed testing and ecological RA
  (? How these numbers derived)
Stockholm County

- 1.8 million inhabitants
- 180 km from north to south
- 26 municipalities

Stockholm County Council

- Pollution of ground, water, and air with residues of pharmaceutical drugs is among the top five environmental priorities

Stockholm County Council

- **Vision**: County Council activities should not add any persisting drug residues to the ground, water, or atmosphere
- **Periodic goal**: In 2006, all County Council health care services will have adopted action plans for diminishing pollution of ground, water, and air with residues of pharmaceutical drugs.

Possible levels of intervention

- Research and production
- EU directives
- Public purchasing
- Prescriptions to patients
- Use and excretion

Research and production

- Established, together with the national pharmacy organization (Apoteket AB), a dialogue with domestic producers of pharmaceuticals
- Consensus:
  - Drugs pose an environmental problem
  - Future drugs should not be persistent
  - Preferential purchasing may be an effective tool

Public purchasing

- Method: compulsory questions on eco-toxicologic data in all public purchasing
- Environmental questions should yield:
  - Increased awareness among producers
  - Data received may be used for environmental classification of pharmaceuticals
Patient prescriptions

• Develop a classification system for drugs based on risk assessment
• Provide generic names, recommended products
• Use an easy to understand labeling system (an icon) for products that meet certain criteria
• Convince providers to consider eco-tox data in addition to all other criteria for drug selection

Use and excretion

• In 2003, a joint campaign started among Apoteket AB, drug producers, drug distributors, health care providers
• Purpose: To inform consumers that unused drugs should be returned to the pharmacy

Summary of conclusions

• Management of pharmaceutical residues requires:
  – Specific activities on several different levels
  – Collaboration among stakeholders
  – Eco-toxicological expert knowledge
  – Information and campaigning
  – Patience and sustainability

Factors to consider

• Amount sold annually
• Ecological half-life
• Recipient volume (e.g. water body)
• Eco-toxicity
• Bioavailability
• Bioaccumulation
• Constituents
• Inappropriate packaging

Stockholm County Council model

• Collaboration among SCC, Apoteket AB, and ecotoxicological experts
• Considers: persistence, bioaccumulation, toxicity to aquatic organisms.
• Each property assigned a value on a scale from 0-3. The sum of these values is the PBT index.

SCC model

• Biodegradability based on OECD test 301 or other equivalent test.
• Bioaccumulation based on OECD 107 or 117 (o/w partition coefficient) or on actual test data.
• Toxicity at three trophic levels: fish, daphnia, algae (OECD 203, 202, 201)
• Worst case assumption when no data
### Toxicity classification

- LC/EC/IC50 < 1 mg/l; very high toxicity
- LC/EC/IC50 1-10 mg/l; high toxicity
- LC/EC/IC50 10-100 mg/l; moderate toxicity
- LC/EC/IC50 >100 mg/l; low toxicity

### SCC model

- Defined daily dose (DDD): estimated average administered dose per day when used for the drug’s main indication
- Note that the number of DDDs does not necessarily correlate with quantity of active substance in kilograms.

### Environmental Classified Pharmaceuticals 2005

#### Musculoskeletal system

<table>
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<tr>
<th>Drug</th>
<th>PBT index</th>
<th>DDD</th>
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<tbody>
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<td>Diclofenac</td>
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<td>Tenoxicam</td>
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<td>Ketoprofen</td>
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<tr>
<td>Valdecoxib</td>
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</tbody>
</table>

* Data gap

### SCC recommendations

- Follow SCC’s “wise list” of recommended drugs for common diseases
- When medical efficacy, safety, and price are comparable, use the drug posing the lowest environmental risk
- Prescribe starter packs.
- Encourage patients to return unused drugs to pharmacy

### SCC recommendations

- Inform patients that even used estrogen patches contain estrogen that should not be discarded to water
- Do not prescribe more than can be used
- Review patients’ total use of medications
- Read the Swedish Medical Products Agency study “Environmental Impacts from medications, cosmetics, and hygienic products”
Recent status

- Swedish Pharmaceutical Company’s branch organization (LIF), the MPA, the Pharmacy Association and the Federation of the County Councils finalizing a common classification system for pharmaceuticals
- A combined risk and hazard assessment.
- Large pharmaceutical manufacturers involved
- The system may become a European standard for classification of the environmental effects of drugs.

Resources

- [http://www.janusinfo.se/imcms/servlet/GetDoc?meta_id=7236](http://www.janusinfo.se/imcms/servlet/GetDoc?meta_id=7236) SCC home page on pharmaceuticals and environment