

Pharmaceuticals in the Environment: Sweden and the EU

Ted Schettler MD, MPH

Science and Environmental Health
Network

Health Care Without Harm

European efforts

- European Medicines Agency (EMA) 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 (EMA) 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>

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

- Swedish Medical Products Agency report August, 2004.

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 ecotoxicologic 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.

ENVIRONMENTALLY
CLASSIFIED
PHARMACEUTICALS
2005

	PBT index	* Data gap	DDD
M Musculoskeletal system			
Anti-inflammatory and anti-rheumatic agents			
Diclofenac	7		6 484 198
Tenoxicam	4		192 680
Ibuprofen	5		9 555 847
Naproxen	7		3 666 094
Ketoprofen	7*		1 973 231
Valdecoxib	9*		167 740

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=7242 SCC Brochure
- http://www.janusinfo.se/imcms/servlet/GetDoc?meta_id=7236 SCC home page on pharmaceuticals and environment
- <http://www.emea.eu.int/pdfs/human/swp/444700en.pdf> EMEA draft guideline for risk assessment of pharmaceuticals for human use