Environmental impacts of Veterinary Medicines - State of knowledge, options for improvement

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Scope of the problem

- 6051 tons active ingredients used in 2004
- 5393 tons of antibiotics, 194 tons of antiparasitics
- 2000 incompletely assessed or untested Veterinary Drugs on the European market

Entry routes into the environment

Veterinary medicinal product

- Livestock treatment
  - Storage and spreading of manure / slurry
  - Soil
- Companion animals, treatment
- Aquaculture treatment
  - Wastewater treatment
  - Groundwater

Manufacturing process
Scope of the problem

- Veterinary drugs are routinely found in surface waters, ground water, sediments and the terrestrial environment.

- Concentrations between $\mu g/L$ and $ng/L$. 
Scope of the problem

- Veterinary drugs are tailored towards being as biologically active as possible.
- Some are made to be as toxic as possible (e.g. antibiotics, antiparasitics, fungicides).
Vultures eradicated by Diclofenac

- Most abundant large raptor in the world in the 1980s
- Near extinct in 1990 due to lethal Diclofenac poisoning
- Diclofenac use banned in India, Meloxicam as a suitable alternative
Vultures eradicated by Diclofenac

- Spain authorized marketing of diclofenac for use in cattle, pigs, and horses in 2013.
- Spain holds >95% of the European population of vultures.
- EMA/CVMP (2014) confirmed risk for European vultures.
Environmental Impacts of Teflubenzuron

- Sealice infestation is a common problem in salmon aquaculture
- Treatment with anti-parasitics such as Teflubenzuron
- Acyl urea drug
- Inhibits chitin biosynthesis
Environmental Impacts of Teflubenzuron

Sea Louse (target species)

Some other guy (non-target species)
Environmental Impacts of Teflubenzuron

Tiered approach for Env. Risk Assessment

European Medicines Agency
Veterinary Medicines and Inspections
Tiered approach for Env. Risk Assessment

- Exempted?
- Exposure > Action limit?
- Treatment of aquatic or terrestrial animals?
- Concentration introduced into the environment > ‘safe’ level?
### Environmental hazard (PNEC determination)

<table>
<thead>
<tr>
<th>Medium</th>
<th>Studies</th>
<th>Toxicity endpoint</th>
<th>AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freshwater</td>
<td>Algal growth inhibition*</td>
<td>EC$_{50}$</td>
<td>100</td>
</tr>
<tr>
<td>Freshwater</td>
<td><em>Daphnia</em> immobilization</td>
<td>EC$_{50}$</td>
<td>1000</td>
</tr>
<tr>
<td>Freshwater</td>
<td>Fish acute toxicity</td>
<td>LC$_{50}$</td>
<td>1000</td>
</tr>
</tbody>
</table>
Test Organisms vs. ignored organisms
Ignored Organisms: toxicity not usually determined
Toxicity of Chlortetracycline to natural lake bacteria

Brosché, Backhaus, (2010): Toxicity of five protein synthesis inhibiting antibiotics and their mixture to limnic bacterial communities, Aquatic Toxicology, 99(4), 457-465
Medetomidine

- Sedative for mammals
- $\alpha_2$-receptor agonist, octapamine receptor agonist
- Inhibits settling of barnacles on shiphulls
- Currently evaluated as a biocide

Lennquist: Responses to fish exposed to medetomidine, Marine Env. Research, 2010
Medetomidine

- Inhibits settling of barnacles on ship hulls
- Currently evaluated as a biocide
- Also disturbs pigmentation of flatfish
- Classified as a potential candidate for substitution
Insufficient regulatory assessment for environmental hazards and risks

- ‘Old’ veterinary drugs exempted
- Insufficient documentation and availability of data
- Incomplete suite of test organisms
Insufficient regulatory assessment for environmental hazards and risks

- No consideration of PBT properties (but activities ongoing)

- No consideration of combination effects

- Insufficient consideration of metabolites
Steps forwards

- All veterinary drugs undergo the same assessment
- Data compiled, quality-checked and publically disseminated on a European level
- Substitution principle
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