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

- Livestock treatment
  - Storage and spreading of manure / slurry
    - Soil

- Companion animals, treatment
- Aquaculture treatment
  - Wastewater treatment
    - Surface water
      - Groundwater
Scope of the problem

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

- Concentrations between µg/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

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Environmental Impacts of Teflubenzuron

Sea Louse (target species)

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

Environmental Impacts of Teflubenzuron

Tiered approach for Env. Risk Assessment

1. Is the VMP exempt from the need for an EIA by legislation and/or regulations?
   - Yes → STOP
   - No → 2.

2. Is the VMP a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment?
   - Yes → STOP
   - No → 3.

3. Will the VMP be used only in non-food animals?
   - Yes → STOP
   - No → 4.

4. Is the VMP intended for use in a minor species that is reared and treated similarly to a major species for which an EIA already exists?
   - Yes → STOP
   - No → 5.

5. Will the VMP be used to treat a small number of animals in a flock or herd?
   - Yes → STOP
   - No → 6.

6. Is the VMP consistently administered as the treated animal?
   - Yes → STOP
   - No → AQUATIC

AQUATIC

7. Is the VMP used to treat aquatic or terrestrial species?
   - Yes → STOP
   - No → 8.

8. Is entry into the aquatic environment prevented by disposal of the aquatic waste matrix?
   - Yes → STOP
   - No → 9.

9. Are aquatic species reared in a contained facility?
   - Yes → STOP
   - No → 10.

10. Is the VMP an active and/or administered medicated?
    - Yes → STOP
    - No → 11.

11. Is the environmental introduction concentration (IEC envi) of the VMP released from aquaculture facilities < 1 µg/L?
    - Yes → STOP
    - No → 12.

12. Do date or mitigation exist that alter the EIC envi?
    - Yes → STOP
    - No → 13.

13. Is recalculated EIC envi < 1 µg/L?
    - Yes → STOP
    - No → 14.

14. Is entry to the terrestrial environment prevented through disposal of the terrestrial waste matrix?
    - Yes → STOP
    - No → 15.

15. Are animals reared on pasture?
    - Yes → STOP
    - No → 16.

16. Is the VMP an oro- and/or enteric medicated?
    - Yes → STOP
    - No → 17.

17. Is the predicted environmental concentration of the VMP in soil (PECsoil) < 1 µg/L?
    - Yes → STOP
    - No → 18.

18. Do any mitigations exist that alter the PECsoil?
    - Yes → STOP
    - No → Phase II

Phase II
Targeted to address issues of concern

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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 ship hulls
- 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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