Prioritisation of veterinary pharmaceuticals prior to a monitoring campaign: Case of Brittany, an intensive husbandry area

Lise Charuaud, School of Public Health, Rennes, France
Emilie Jardé, Géosciences Rennes, France
Anne Jaffrézic, National Institute For Agricultural Research, Rennes, France
Thierry Panaget, Regional Health Agency of Brittany, Rennes, France
Maud Billon, DREAL of Brittany, Rennes, France
Barbara Le Bot, School of Public Health, Rennes, France
Pharmaceutical residues in aquatic environments → increasing topic of interest

Veterinary residues remain largely unknown!


Brittany = 1st french region of livestock activities
- 3.3 millions inhabitants, 2 millions cows, 7.5 millions pigs, 89 millions chickens
- 27 208 km²

Vulnerability of water resources = 80% of tap water is produced with surface water

Monitoring of the contamination through sampling in water resources and tap waters
Context: EXPO-VETO study

Progress of the project:

- Selection of the veterinary drugs of interest ✓
- Sampling strategy ✓
- Sampling campaign during one year
  200 samples on 26 sites

Expected results:
- First information of contamination in water resources and tap water in Brittany

Prioritise the veterinary drugs of interest

⇒ Objective: reflect the aquatic environment contamination by veterinary drugs
Method: Selection of criteria

First list: 76 veterinary drugs

Soulier and al. (2015); Working Group PRSE2 (2016)

Three criteria following the route of the veterinary residues in the environment:

1). Potential to enter the environment

2). Potential to run off or to leach from soil to water

3). Persistence in water

+ The metabolism of the molecules into animals was considered

Parent compounds, metabolites or both?

Summary of product characteristics from ANSES
Prescribed veterinary drugs at Brittany scale
(Soulier and al. 2015)

- Veterinarians specialised in cattle, pigs and poultry
- Semi-qualitative survey

Very little prescribed
Little prescribed
Moderately prescribed
Very prescribed
The most prescribed
Animal target and route of administration

According to percentages of livestock in Brittany (DRAAF, 2011):

<table>
<thead>
<tr>
<th>Animal</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigs</td>
<td>36%</td>
</tr>
<tr>
<td>Cattle</td>
<td>23%</td>
</tr>
<tr>
<td>Poultry</td>
<td>23%</td>
</tr>
<tr>
<td>Sheep</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Horses</td>
<td>11%</td>
</tr>
<tr>
<td>Rabbits</td>
<td>34%</td>
</tr>
<tr>
<td>Goats</td>
<td>56%</td>
</tr>
</tbody>
</table>

And antibiotic sales by species in France (Chevance et al. 2015):

Goats/sheeps/horses/rabbits... only
Either cattle, either poultry, or both Pigs + cattle OR poultry
Pigs + cattle AND poultry

Topical application VS other routes

**Method: Mobility from soil to water**

\[ \text{Koc} = \text{Soil organic carbon – water partitioning coefficient} \]

= Sorption of the active compound on the organic matter of soil (mL/g)

- 4000 > Non-mobile
- 500 - 4000 = Slightly mobile
- 75 - 500 = Moderately mobile
- 15 - 75 = Mobile
- < 15 = Very mobile

**PSD Pesticide Data Requirement Handbook (2005)**
Method: Persistence in water

**Groundwater**

**Surface Water**

Half-life in water (DT 50) = Time required to degrade 50% of the compound in water

8,7 days
15 days
38 days
60 days
180 days

*PBT Profiler US EPA (estimation)*
Method: Scoring system

- For each molecule, addition of the score for each criteria:

  1 POINT
  2 POINTS
  3 POINTS
  4 POINTS
  5 POINTS

  + 1 supplementary point if aquaculture use

Objective: around **40-50 residues of interest** for the monitoring campaign

Selection of veterinary residues:
- Score ≥11 if all four criteria are available
- Score ≥ 10 if 3 criteria are available
- Score ≥ 9 if 2 criteria are available

Aquaculture

Surface waters
Method: Final priority list

43 molecules

- 25 antibiotics
- 12 antiparasitics
- 3 anticoccidians
- 3 anti-inflammatory drugs

- Parent Compounds
- Metabolites

86%

14%
Limits of the method

- Lack of information about environmental fate (and toxicity) of veterinary residues

- Some chemical families are extensively studied in the litterature while information is still scarce for others

- Necessity to use estimation/calculation softwares to COMPARE the veterinary residues
Conclusion

First approach to prioritise veterinary residues prior to a monitoring campaign, according to the veterinary prescriptions of Brittany

Methodology can be adapted and applied to other regions

WHAT’S NEXT?

- The sites of the study are selected and prioritized
- One pilot study was achieved
- Analytical development for the selected veterinary residues is ongoing
- First monitoring campaign on veterinary drugs in water resources and tap water in France (200 samples collected from 26 sites)
Thanks for your attention

Contacts:

- **Lise Charuaud**, PhD student, EHESP-LERES, IRSET Rennes, lise.charuaud@ehesp.fr
- **Emilie Jardé**, Research Fellow (CNRS) UMR 6118 Géosciences Rennes, emilie.jarde@univ-rennes1.fr
- **Barbara Le Bot**, Research Professor EHESP-LERES, IRSET, UMR 1085, Rennes, barbara.lebot@ehesp.fr


Kim and al. (2008) “Prioritizing veterinary pharmaceuticals for aquatic environment in Korea”

Kools and al. (2008) “A ranking of european veterinary medicines based on environmental risks”

Capleton and al. (2006) “Prioritising veterinary medicines according to their potential indirect human exposure and toxicity profile”

Selected molecules for EXPO VETO

43 molecules

<table>
<thead>
<tr>
<th>Metabolite</th>
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</thead>
</table>


**Antiparasitics**: Eprinomectin, Ivermectin, Amitraz, Clorsulon, Flubendazole, Fenvalerate, Levamisole, Deltamethrin, Diazinon, Triclabendazole/ **Triclabendazole sulfoxide / Triclabendazole sulfone** (12)

**Anticoccidians**: Toltrazuril/ **Toltrazuril Sulfoxide/Toltrazuril sulfone** (3)

**Anti-inflammatory drugs**: Dexamethasone, Meloxicam, Flunixin (3)
<table>
<thead>
<tr>
<th>Catégorie 1</th>
<th>Molécules non utilisées en bovin ou porcin ou volailles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mébendazole, Dicyclanil, Phenylbutazone</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Catégorie 2</th>
<th>Molécules utilisées en bovins ou volailles (pas en cutané)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phénoxympethylpénicilline, Cloxacilline, Cefalexine, Céfalonium, Albendazole, Clorsulon, Closantel, Nitroxynil, Oxycozanide, Amprolium, Decoquinate, Diclazuril,</td>
</tr>
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<thead>
<tr>
<th>Catégorie 3</th>
<th>Molécules utilisées en porcins +/- bovin ou volailles (pas en cutané)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Benzylpénicilline, Ceftiofur, Dihydrostreptomycine, Apramycine, Gentamicine, Florfénicol, Sulfaguanidine, Sulfadoxine, Trimethoprim, Marbofloxacine, Tiamuline, Fenbendazole, Flubendazole, Oxibendazole, Pipérazine, Kétoprofène, Méloxicam, Altrénogest, PMSG, Dinoprost, Cloprosténol, Oxytocine</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Catégorie 4</th>
<th>Molécules utilisées à la fois porcins et bovins et volailles (pas en cutané)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amoxicilline, Ampicilline, Doxycycline, Lincomycine, Erythromycine, Tilmicosine, Tylosine, Colistine, Spectinomycine, Sulfadiazine, Sulfaméthazine, Sulfaméthoxypyridazine, Sulfadiméthoxine, Acide oxolinique, Fluméquine, Enrofloxacine, Toltrazuril, Dexaméthasone</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Catégorie 5</th>
<th>Molécules utilisées par voie cutanée sur les troupeaux (porcins, bovins, volailles)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cefquinome, Chlortétracycline, Oxytétracycline, Spiramycine, Néomycine, Lévamisole, Ivermectine, Eprinomectine, Triclabendazole, Amitraz, Deltamethrine, Fenvalerate, Diazinon, Phoxim, Flunixin</td>
</tr>
</tbody>
</table>
Comparison with another prioritisation (AFSSA, 2008)

118 veterinary residues studied

- Three criteria:
  - Tonnages at national scale
  - Water affinity: Solubility
  - Activity: Acceptable Daily Intake

- Calculation of a risk index using those criteria

- Top ten most critical antibiotics:
  Only 3 were common: Dihydrostreptomycin, Oxytetracycline and Tylosin