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

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Context: Veterinary residues in tap water in Brittany?

- Pharmaceutical residues in aquatic environments → **increasing topic of interest**
- **Veterinary residues** remain largely unkown!

Scopus: 28 articles « human » vs 6 articles « veterinary » (2006-2016)

- **Brittany** = 1st french region of **livestock activities**

-3.3 millions inhabitants, 2 millions cows, 7.5 millions pigs, 89 millions chickens

-27 208 km^2 **(AGRESTE, 2015)**

- **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

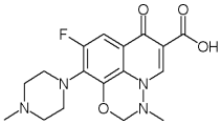
Progress of the project:

- Selection of the veterinary drugs of interest ✓
- Sampling strategy ✓
- Sampling campaign during one year

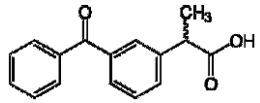
  200 samples on 26 sites

Expected results:

- First information of contamination in water ressources 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

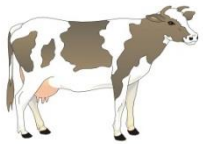
+ The metabolism of the molecules into animals was considered

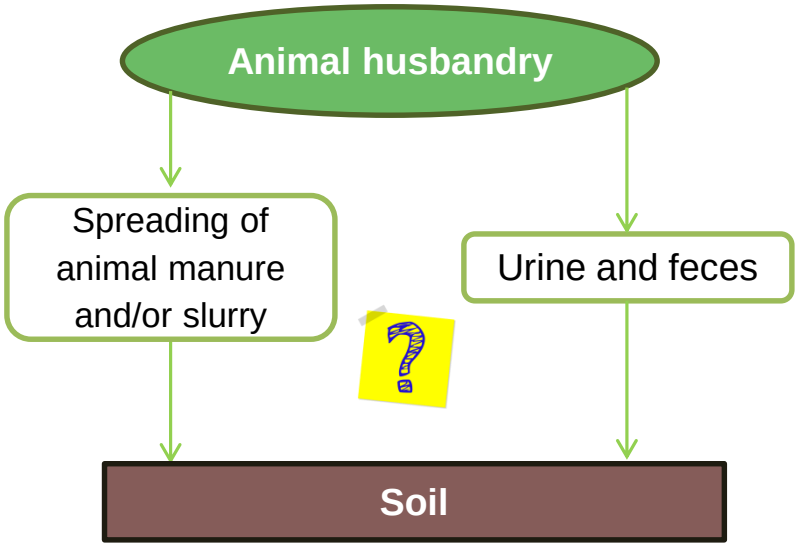
Parent compounds, metabolites or both?

Summary of product characteristics from ANSES

Method: Potential to enter the environment (1)

❖ Prescribed veterinary drugs at Brittany scale
(Soulier and al. 2015)





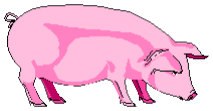
- Veterinarians specialised in cattle, pigs and poultry
- Semi-qualitative survey

Very little prescribed
Little prescribed
Moderately prescribed
Very prescribed
The most prescribed

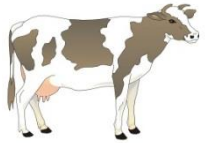
Method: Potential to enter the environment (2)

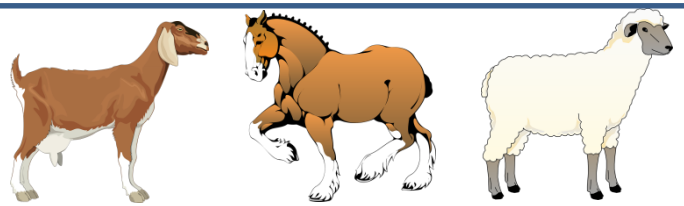
❖ Animal target and route of administration

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

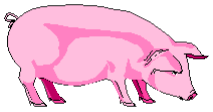

56%


34%

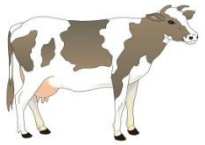

11%


<10%

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

36% → 

23% → 

23% → 

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

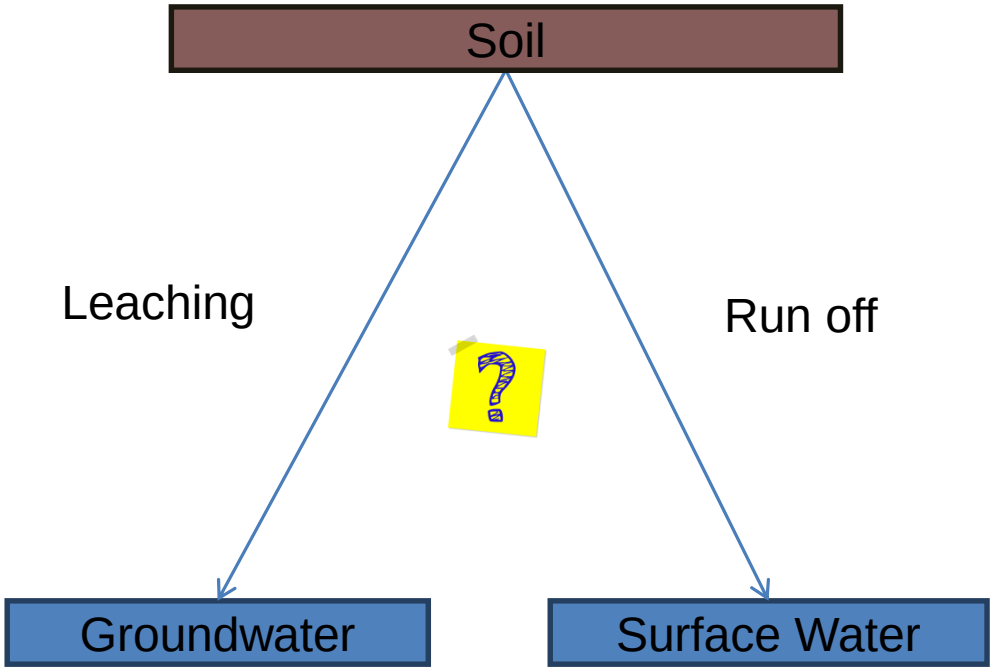
\+ **Topical application VS other routes**

Adapted from Boxall and al (2003), Capleton and al (2006) and Kim and al (2008)

Method: Mobility from soil to water

Koc = 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

Aquaculture

Surface waters

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

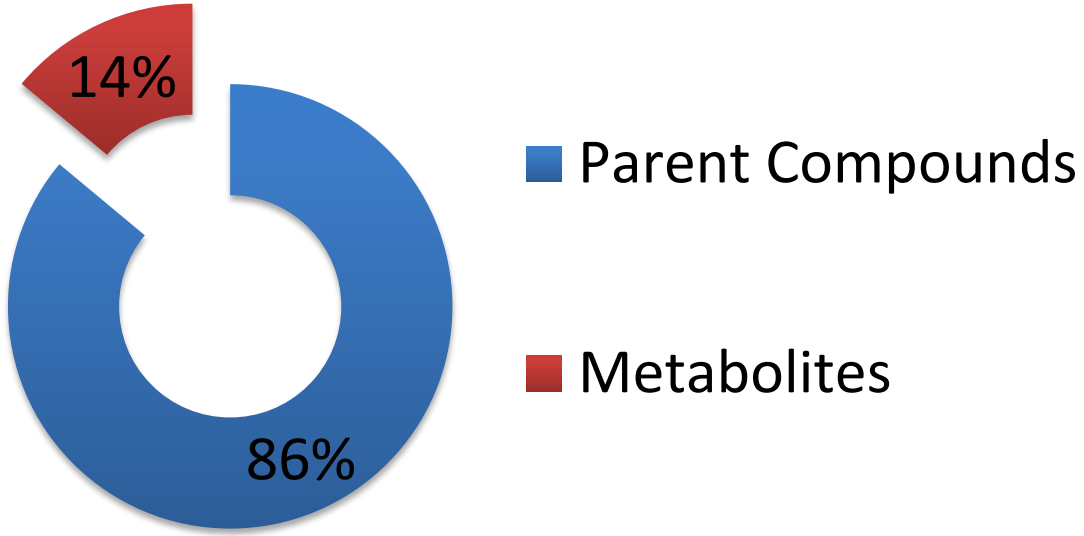
Selection of veterinary residues:

- Score ≥11 if all four criteria are available
- Score ≥ 10 if 3 criteria are available
- Score ≥ 9 if 2 criteria are available

Method: Final priority list

43 molecules

25 antibiotics
12 antiparasitics
3 anticoccidians
3 anti-inflammatory drugs



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

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Litterature (2006-2016)

- Menz and al (2015) “Usage pattern-based exposure screening as a simple tool for the regional priority-setting in environmental risk assessment of veterinary antibiotics: A case study of north-western Germany”

- Di Nica and al (2015) “RANKVET: A new ranking method for comparing and prioritizing the environmental risk of veterinary pharmaceuticals”

- 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”

- Boxall and al (2005) “Targeted monitoring study for veterinary medicines in the environment”

Selected molecules for EXPO VETO

43 molecules

Metabolite

Antibiotics: Tylosin, Florfenicol, Sulfadiazine, Sulfadimethoxin, Amoxicillin, Oxytetracycline, Lincomycin, Dihydrostreptomycin, Trimethoprim, Enrofloxacin, Ampicillin, Tilmicosin, Flumequine, Benzylpenicillin, **Desfuroylceftiofur**, Sulfamethazine, Spiramycin/ **Neospiramycin**, Chlortetracycline, Marbofloxacin, Doxycycline, Cefquinom, Erythromycin, Neomycin, Colistin (25)

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)

Catégorie 1 : Molécules non utilisées en bovin ou porcin ou volailles

Mébendazole, Dicyclanil, Phenylbutazone

Catégorie 2 : Molécules utilisées en bovins ou volailles (pas en cutané)

Phénoxymethylpénicilline, Cloxacilline, Cefalexine, Céfalonium, Albendazole, Clorsulon, Closantel, Nitroxynil, Oxyclozanide, Amprolium, Decoquinate, Diclazuril,

Catégorie 3 : Molécules utilisées en porcins + /- bovin ou volailles (pas en cutané)

Benzylpénicilline, Ceftiofur, Dihydrostreptomycine, Apramycine, Gentamicine, Florfénicol, Sulfaguanidine, Sulfadoxine, Trimethoprime, Marbofloxacine, Tiamuline, Fenbendazole, Flubendazole, Oxibendazole, Pipérazine, Kétoprofène, Méloxicam, Altrénogest, PMSG, Dinoprost, Cloprosténol, Oxytocine

Catégorie 4 : Molécules utilisées à la fois porcins et bovins et volailles (pas en cutané)

Amoxicilline, Ampicilline, Doxycycline, Lincomycine, Erythromycine, Tilmicosine, Tylosine, Colistine, Spectinomycine, Sulfadiazine, Sulfaméthazine, Sulfaméthoxypyridazine, Sulfadiméthoxine, Acide oxolinique, Fluméquine, Enrofloxacine, Toltrazuril, Dexaméthasone

Catégorie 5 : Molécules utilisées par voie cutanée sur les troupeaux (porcins, bovins, volailles)

Cefquinome, Chlortétracycline, Oxytétracycline, Spiramycine, Néomycine, Lévamisole, Ivermectine, Eprinomectine, Triclabendazole, Amitraz, Deltamethrine, Fenvalerate, Diazinon, Phoxim, Flunixine

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