健康畜禽 Healthy Livestock

# Monitoring individual water consumption for optimization of antibiotic treatments in herds

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*INTHERES*
*Therapeutic Innovations & Résistances*

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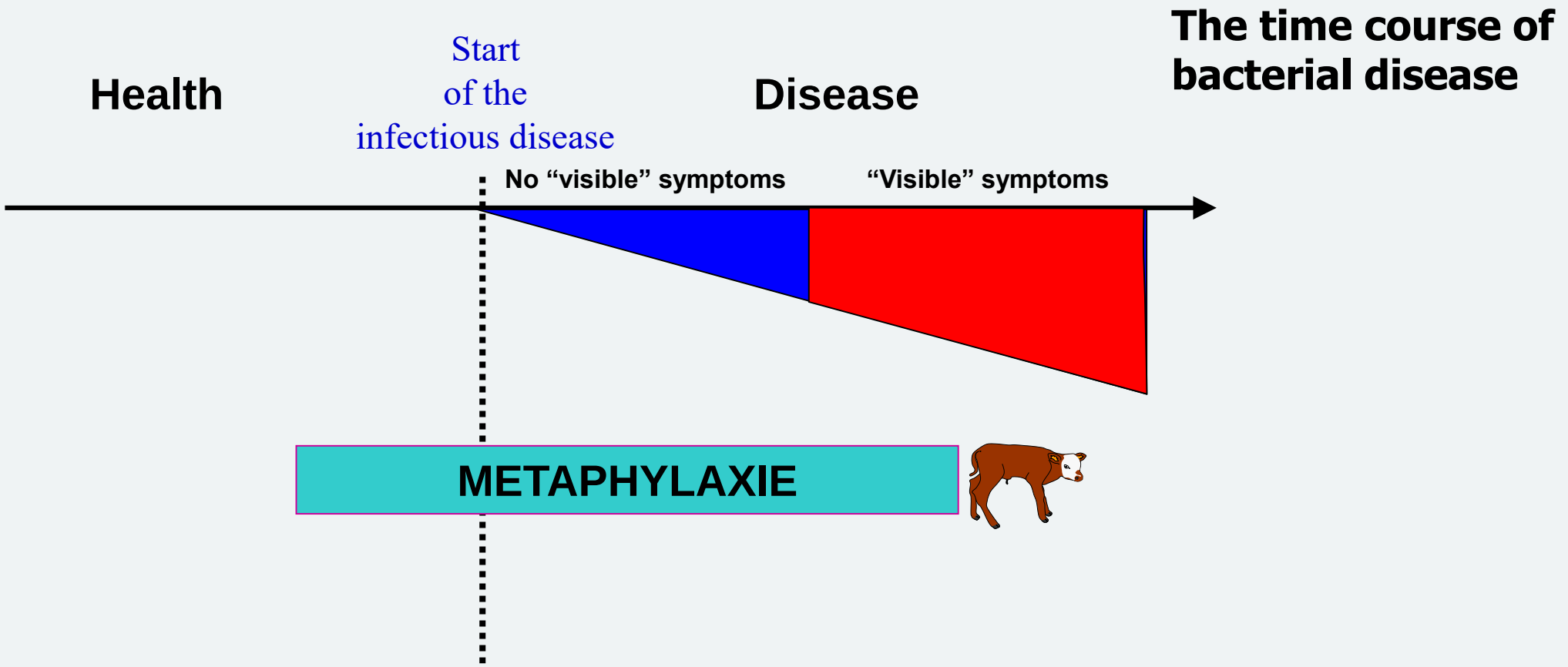
Horizon2020

# Context - Metaphylactic use of antibiotics

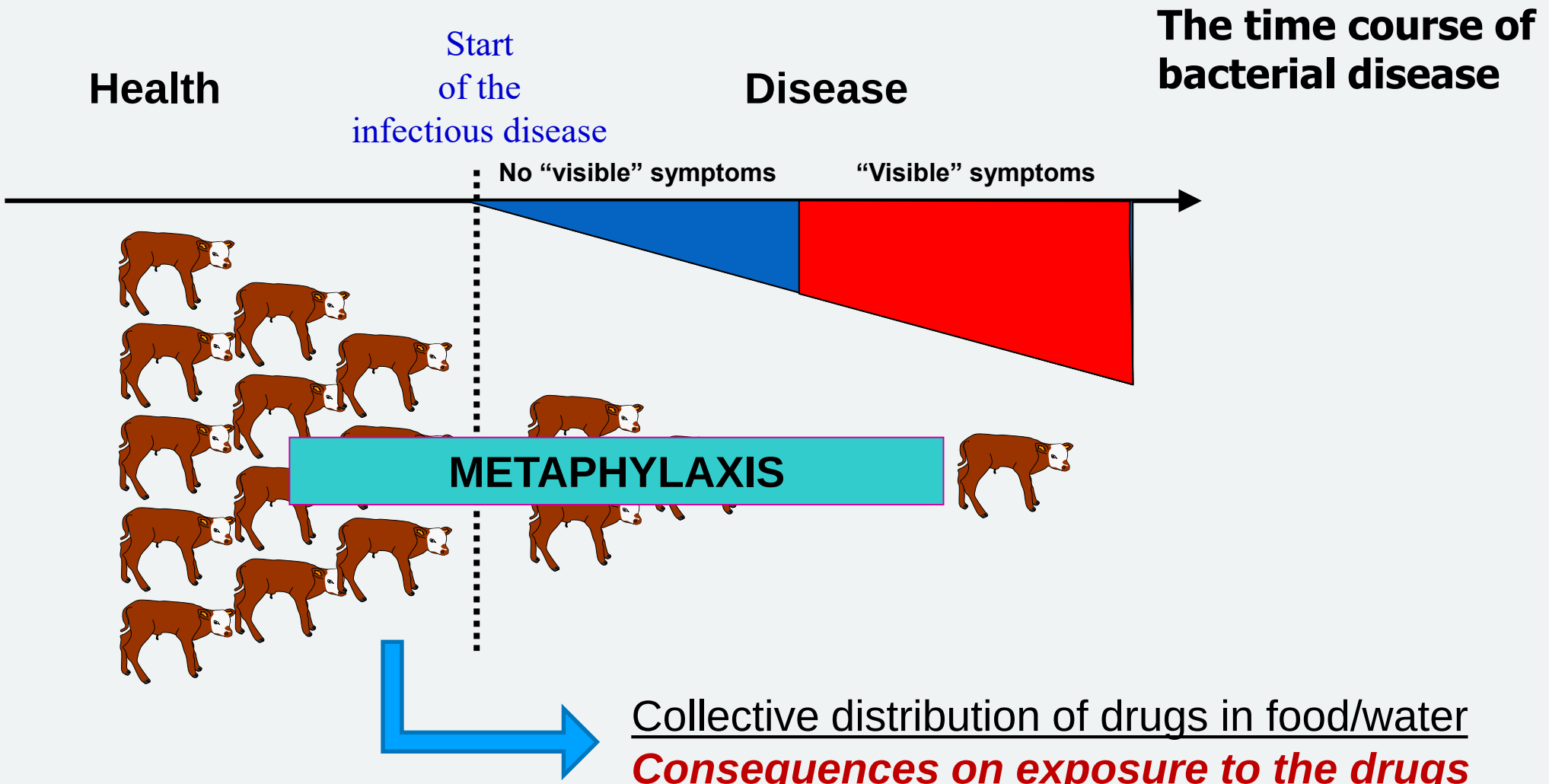





Bacterial contamination / Host defenses
Growth of the initial inoculum

# Context - Metaphylactic use of antibiotics






Collective distribution of drugs in food/water

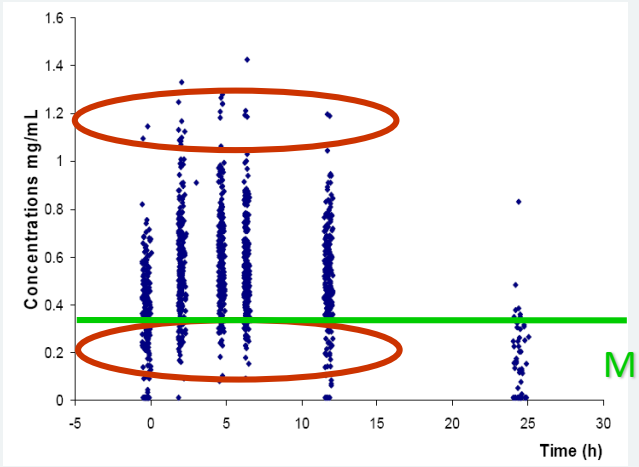
***Consequences on exposure to the drugs and efficacy ?***

# Context - Variability associated to collective drug distribution

August 29, 2019

**Doxycycline in medicated food**

**n = 215**




Exposure variability of fosfomycin administered to pigs in food or water: Impact of social rank

Alejandro L. Soraci [a,*], Fabián Amanto [b], María O. Tapia [a], Eulalia de la Torre [a], Pierre-Louis Toutain [c]

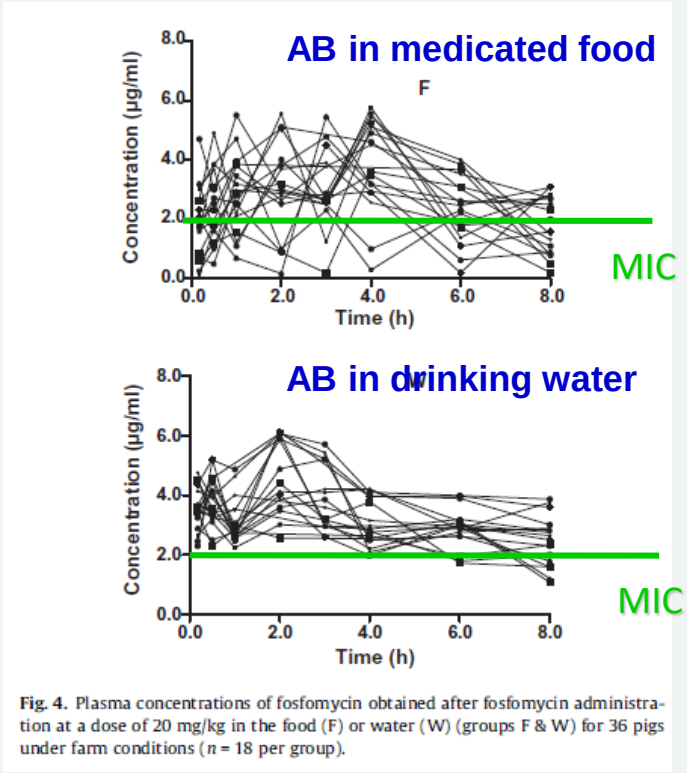



**Fig. 4.** Plasma concentrations of fosfomycin obtained after fosfomycin administration at a dose of 20 mg/kg in the food (F) or water (W) (groups F & W) for 36 pigs under farm conditions ($n$ = 18 per group).

# Context - Variability associated to collective drug distribution



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 July 2018
EMA/CVMP/849775/2017
Committee for Medicinal Products for Veterinary Use (CVMP)

Reflection paper on dose optimisation of established veterinary antibiotics in the context of SPC harmonisation

For **oral *ad libitum* administration**, plasma concentrations are related to the **feeding and water intake behaviour** (depending on e.g. the health status, the animal social rank), meaning that **it induces new individual variabilities** that the method presented here cannot take into account.

Objectives :

1. To describe variability of blood exposure associated with distribution of drugs in water
2. To build pharmacokinectic models taking into account this variability in order to
3. Propose dosage regimens optimizations

# Oviboost project
# Fattening lambs units
# Sulfadimethoxine

**Individual water consumption**

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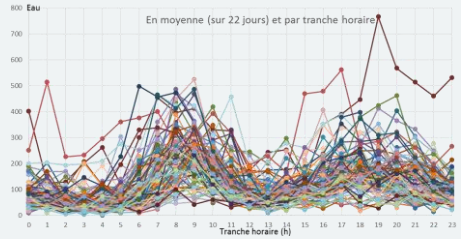
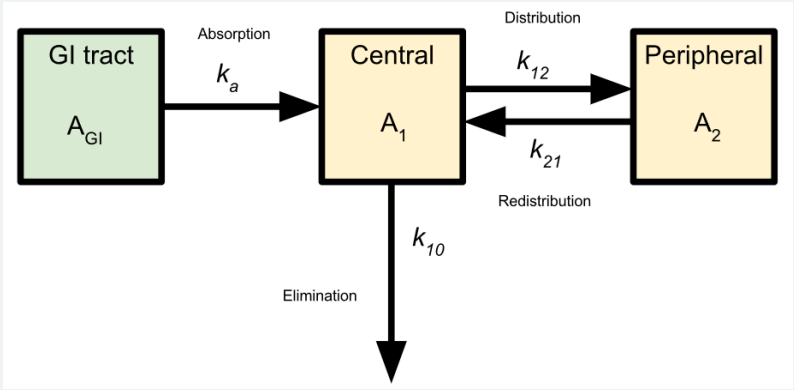



**Pharmacokinetic (population) model**

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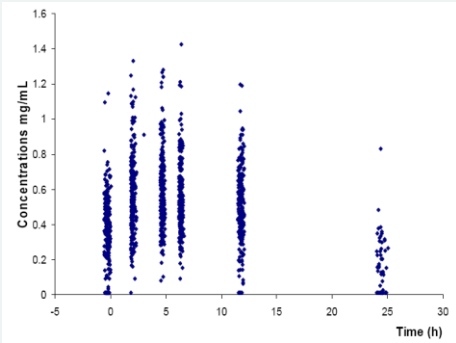

# Classical pharmacokinetic model



## 8 (males, females) Lacaune lambs

**Week 1**
Lambs just after weaning

**Week 2**

**Week 3**
Lambs ≈ 45 days

**ORAL ADMINISTRATION** | **INTRAVENOUS ADMINISTRATION** | **ORAL ADMINISTRATION**

Sulfadimethoxine (25 mg/kg) + Trimethoprim (5 mg/kg) bolus

13 blood samples | 13 blood samples | 13 blood samples

**Determination of plasma concentrations by UPLC/MS/MS**

**Determination of Pharmacokinetic parameters**

Intravenous administration

Oral administration / single drenching

# Antibiotic PK parameters: Results

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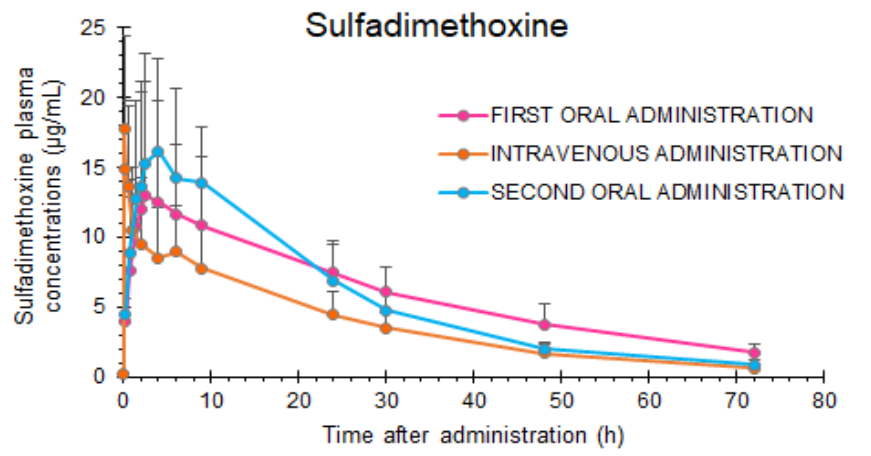
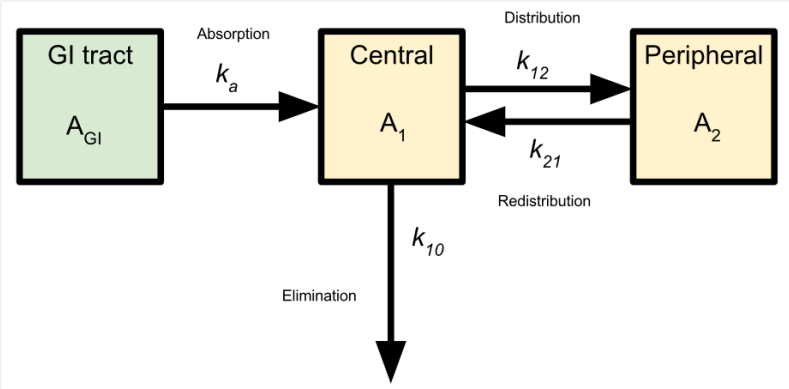



**Pharmacokinetic model**



# Fattening unit – Individual real-time water intake

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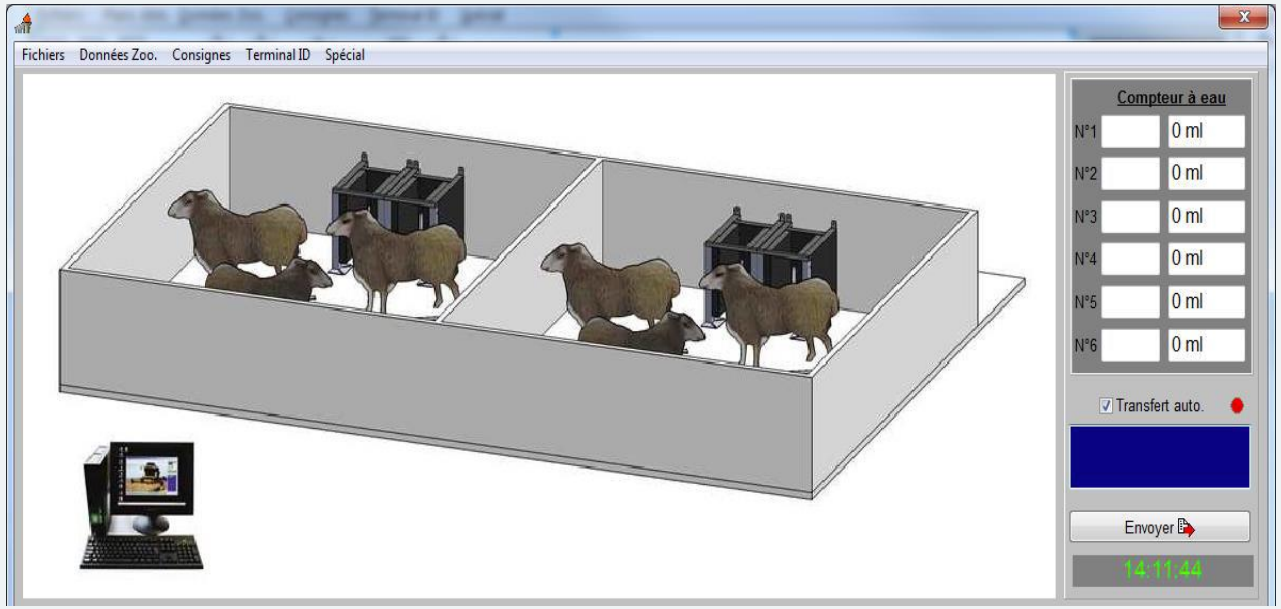


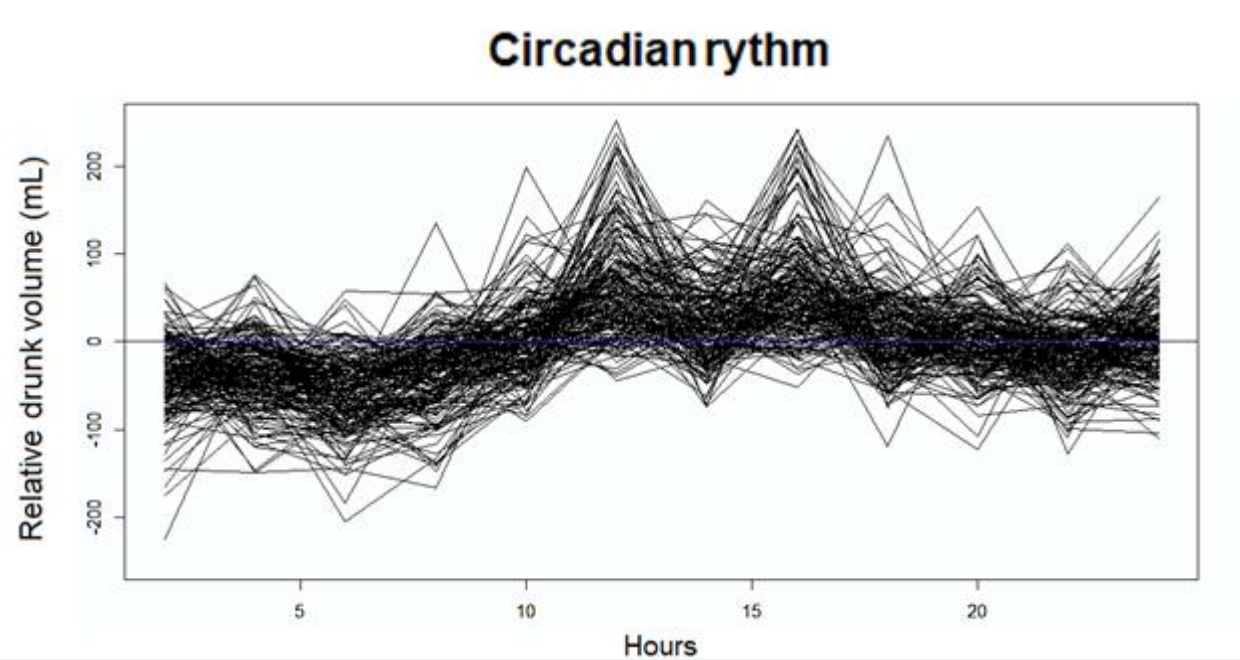

Water meters connected to troughs
Lamb detected by RFID chips in ear tag

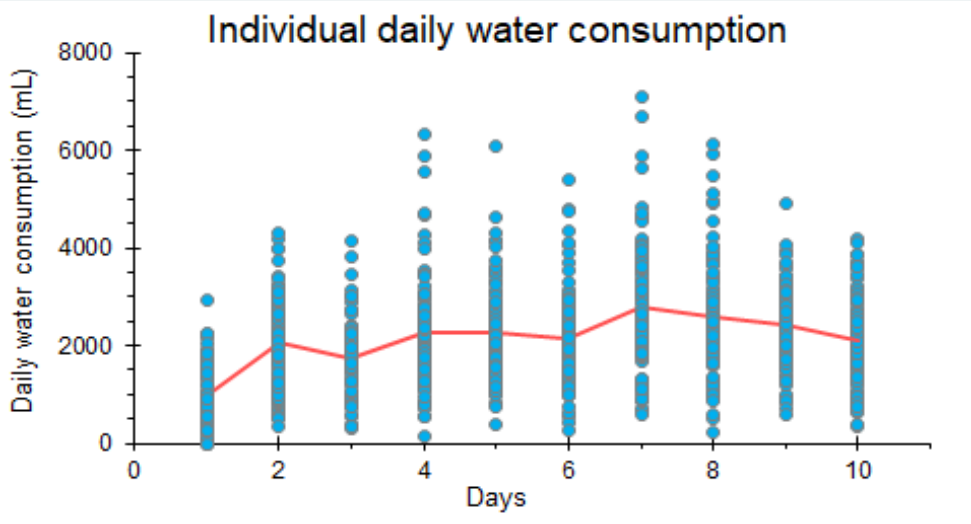
Total water consumption / day / lamb
Number of visit of each lamb to each drinking troughs
Quantity of water drunk at each visit
Time spend in the drinking trough at each visit

asserva
AUTOMATISMES EN ÉLEVAGE

# Fattening unit – Individual real-time water intake

August 29, 2019



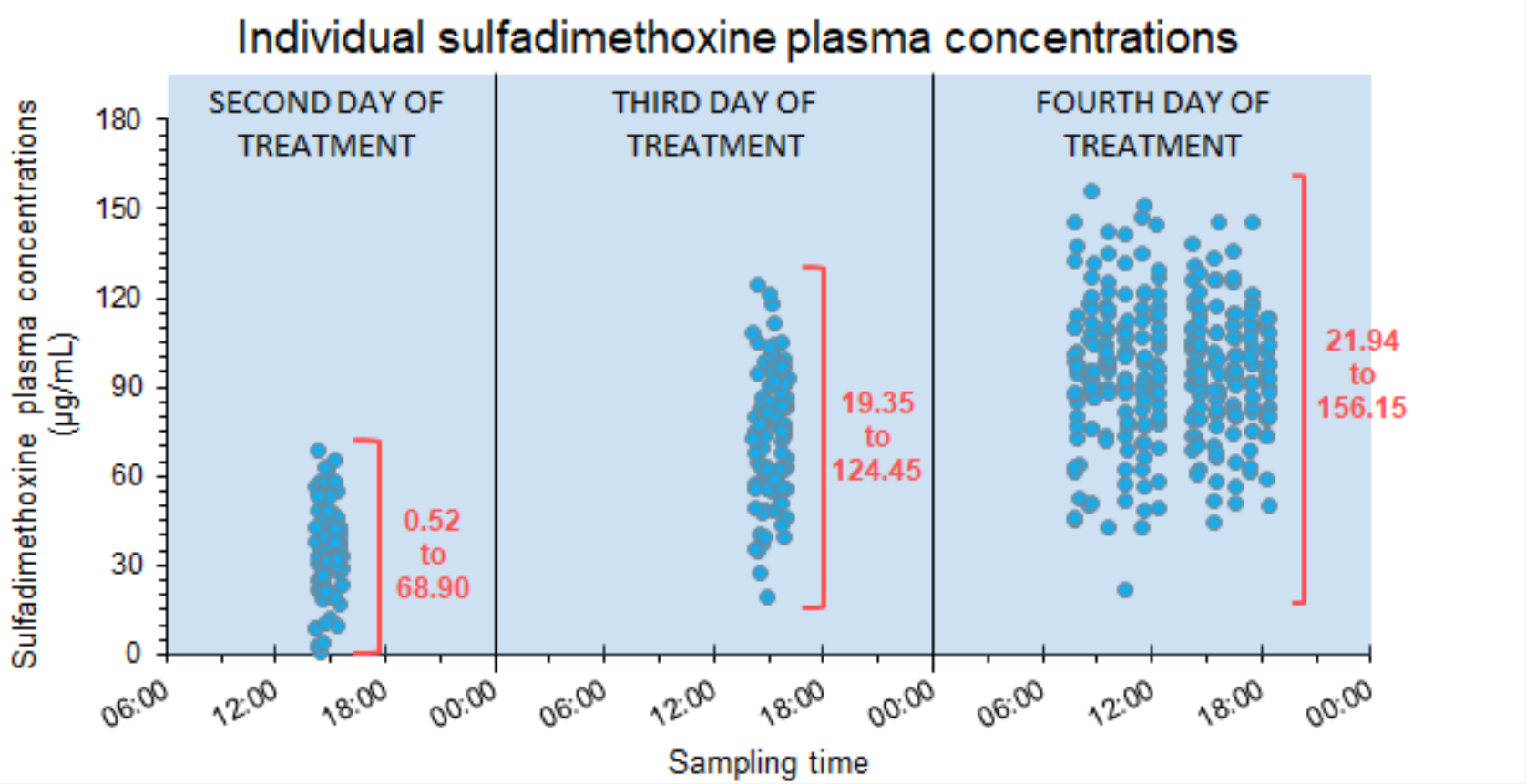




- **Daily water intake highly variable:**
  - Between lambs
  - Day-by-day for the same lamb
- Average daily water intake lower than expected (2.5 L/day)
- No difference with antibiotic in water

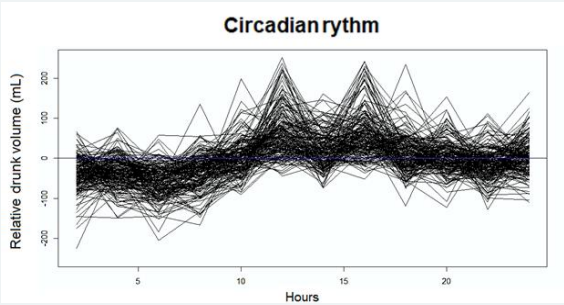
# Fattening unit – Antibiotic plasma concentrations

August 29, 2019

## 100 (males, females) Lacaune lambs



# Oviboost project
# Fattening lambs units
# Sulfadimethoxine

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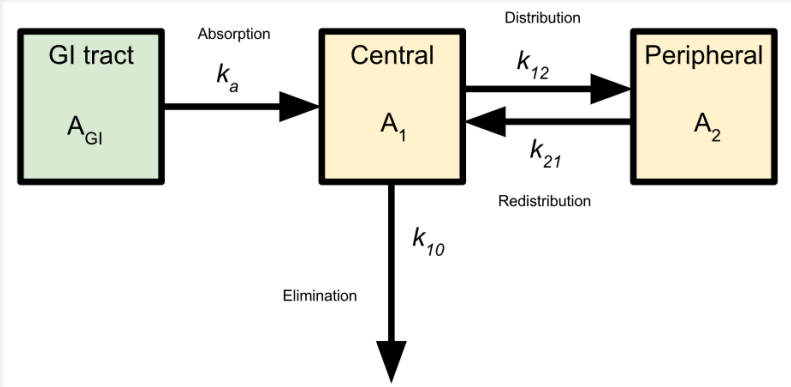
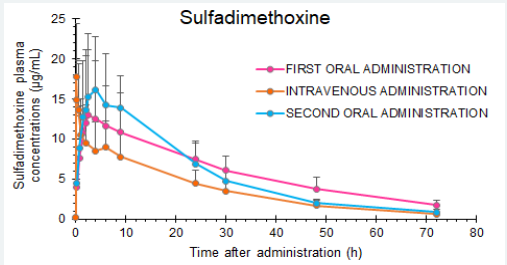
**Pharmacokinetic (population) model**

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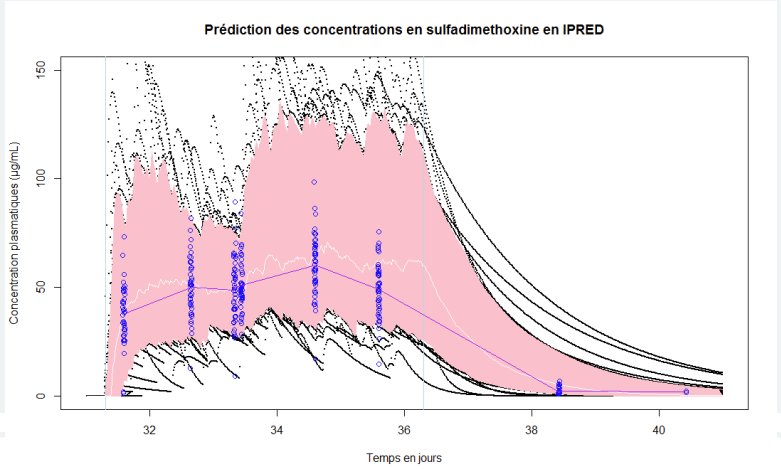

# Conclusion / perspectives



- Building generic models to predict impact of individual drinking behaviour on drug exposure
  - To identify appropriate dosage regimens
  - If not appropriate :
    - To simulate possible modifications/optimization
    - If not possible: recommendations to avoid using these formulations

**Regulatory Authorities**

- Experimental methodology applied to other farm systems : **HL WP4**

Thank you!