# Environmental impacts of Veterinary Medicines

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# State of knowledge, options for improvement

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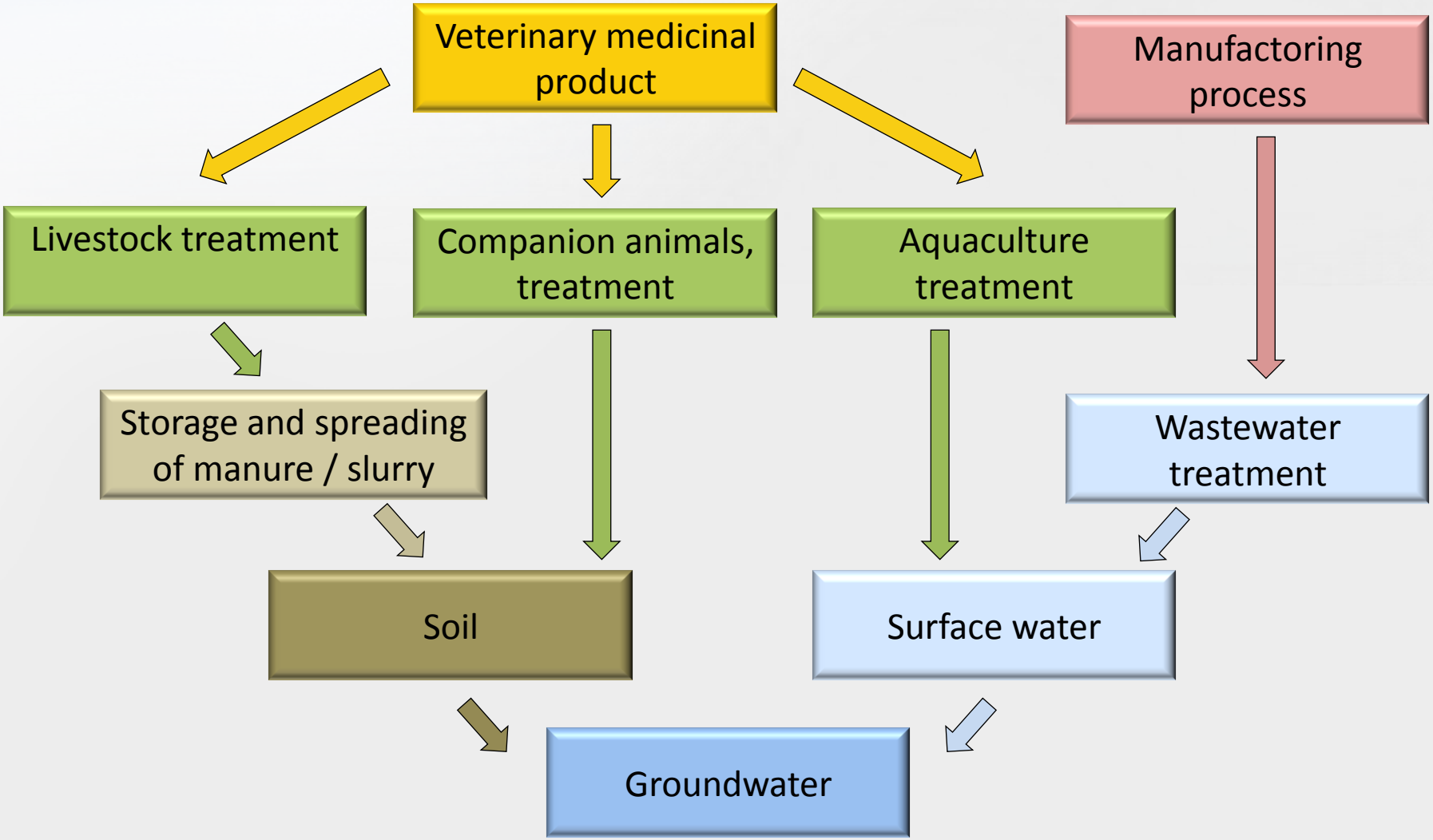
# Scope of the problem

- 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

Margalida, A., et al. "One Health approach to use of veterinary pharmaceuticals." *Science* 346.6215 (2014): 1296-1298.

# Entry routes into the environment



# Scope of the problem

- Veterinary drugs a 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

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- 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)



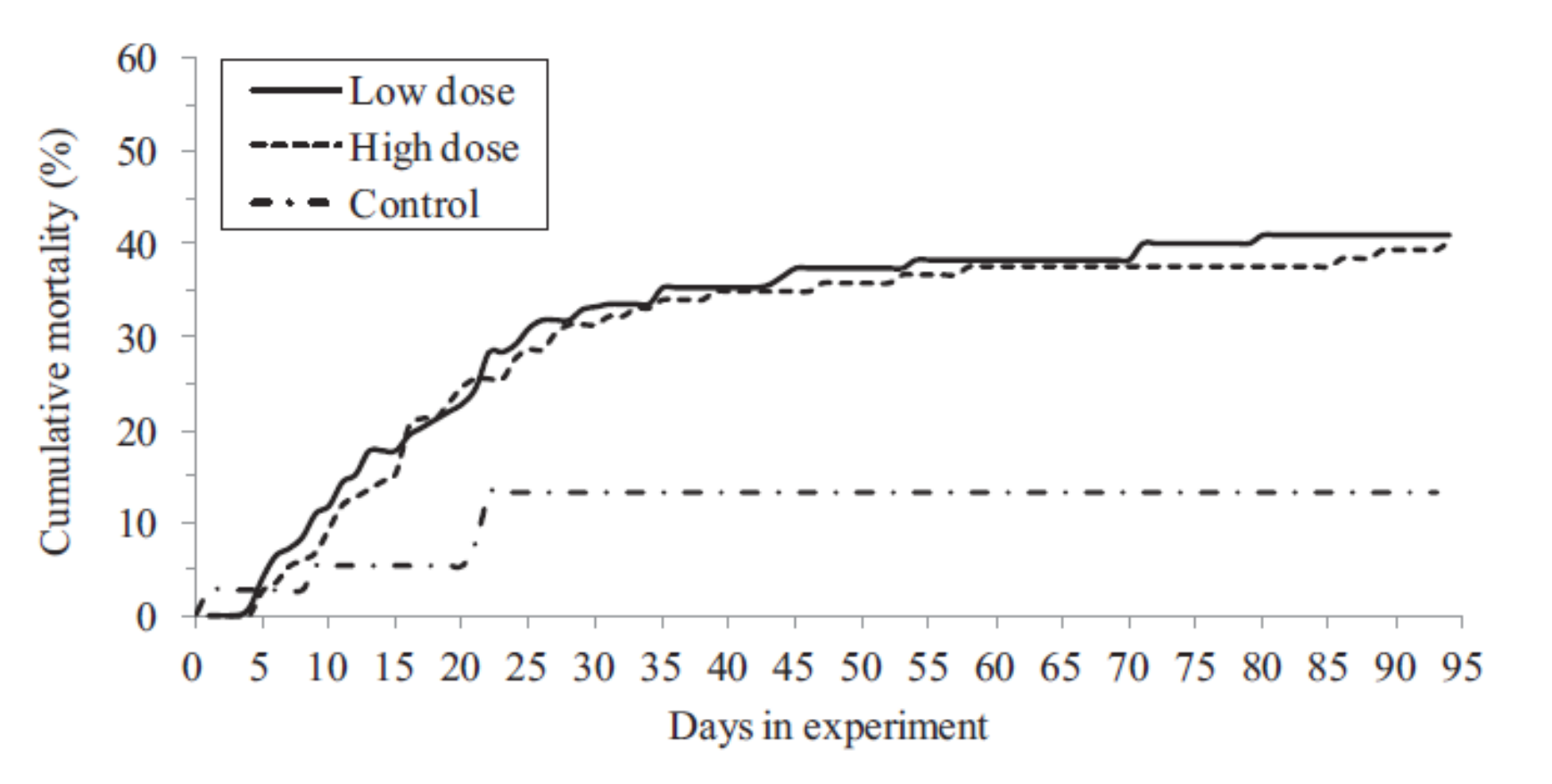
Some other guy
(**non-target** species)

# Environmental Impacts of Teflubenzuron



Samuelsen, Ole B., et al. "Mortality and deformities in European lobster (Homarus gammarus) juveniles exposed to the anti-parasitic drug teflubenzuron." *Aquatic Toxicology* 149 (2014): 8-15.

# Environmental Impacts of Teflubenzuron



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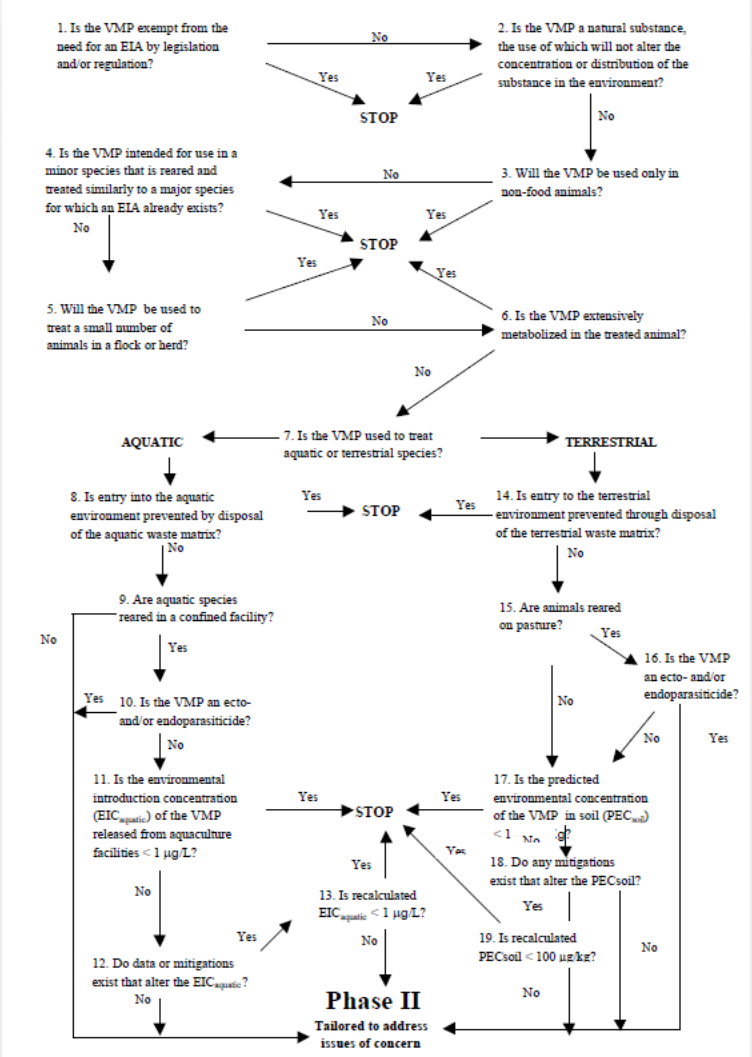
# Tiered approach for Env. Risk Assessment



European Medicines Agency
*Veterinary Medicines and Inspections*



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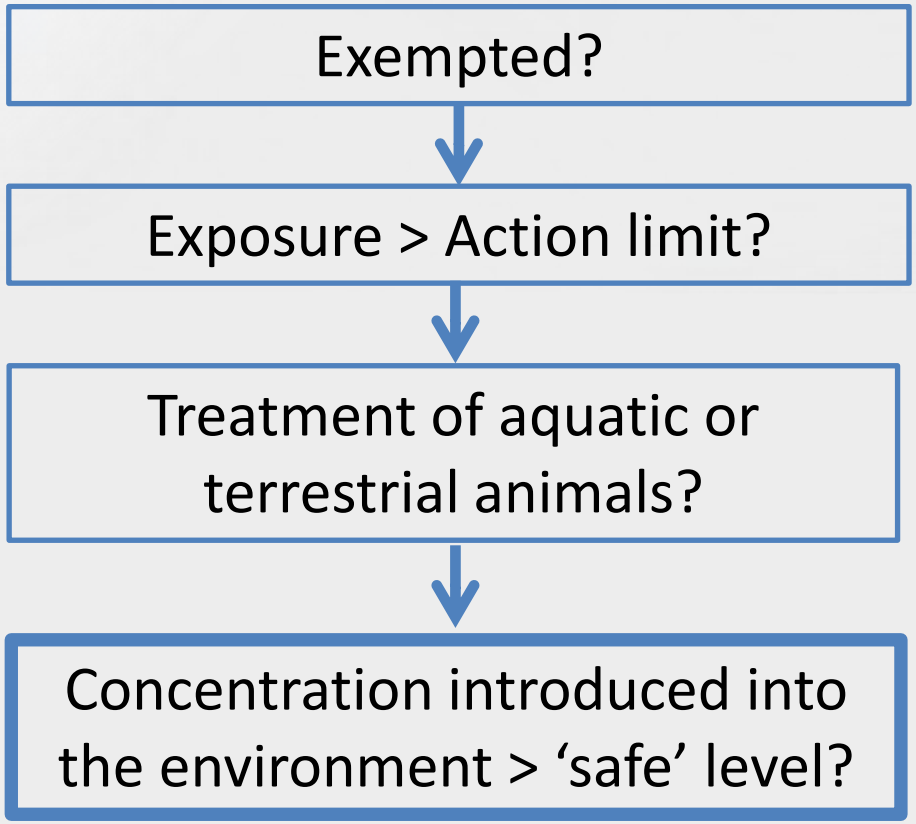
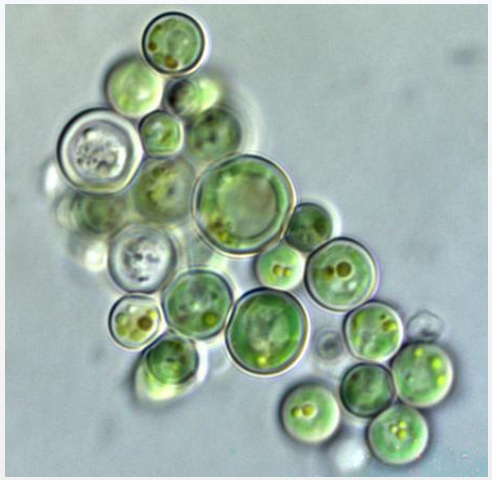


# Environmental hazard (PNEC determination)

| Medium | Studies | Toxicity endpoint | AF |
|---|---|---|---|
| Freshwater | Algal growth inhibition* | $EC_{50}$ | 100 |
| Freshwater | *Daphnia* immobilization | $EC_{50}$ | 1000 |
| Freshwater | Fish acute toxicity | $LC_{50}$ | 1000 |

# Test Organisms vs. ignored organisms





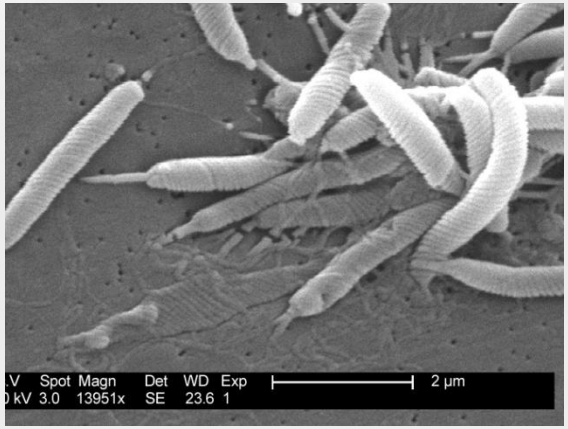






# Ignored Organisms: toxicity not usually determined

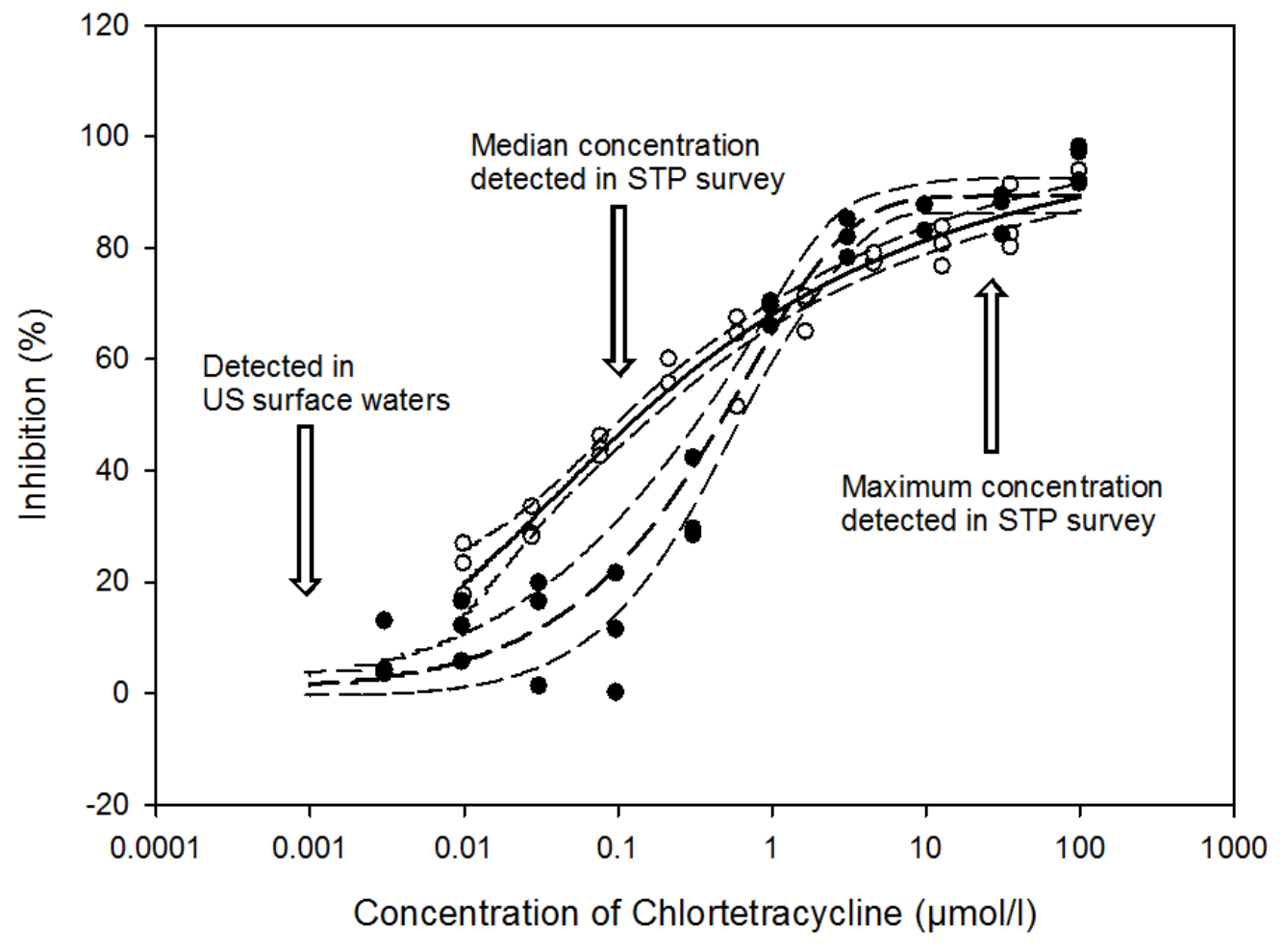






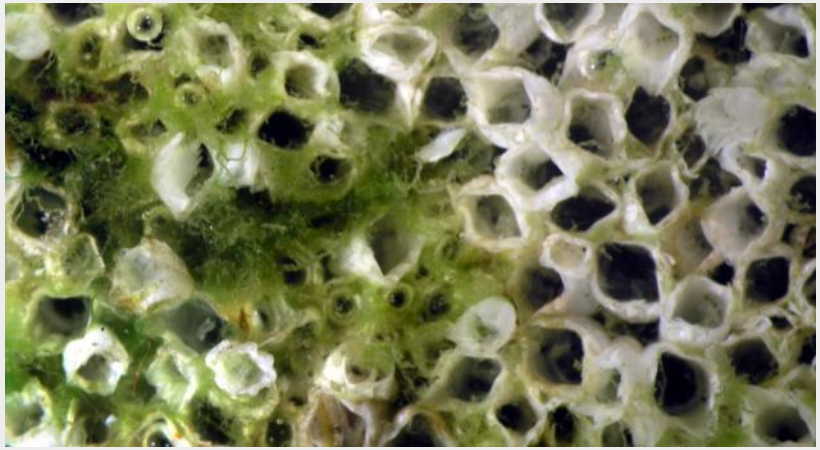



# Toxicity of Chlortetracycline to natural lake bacteria




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

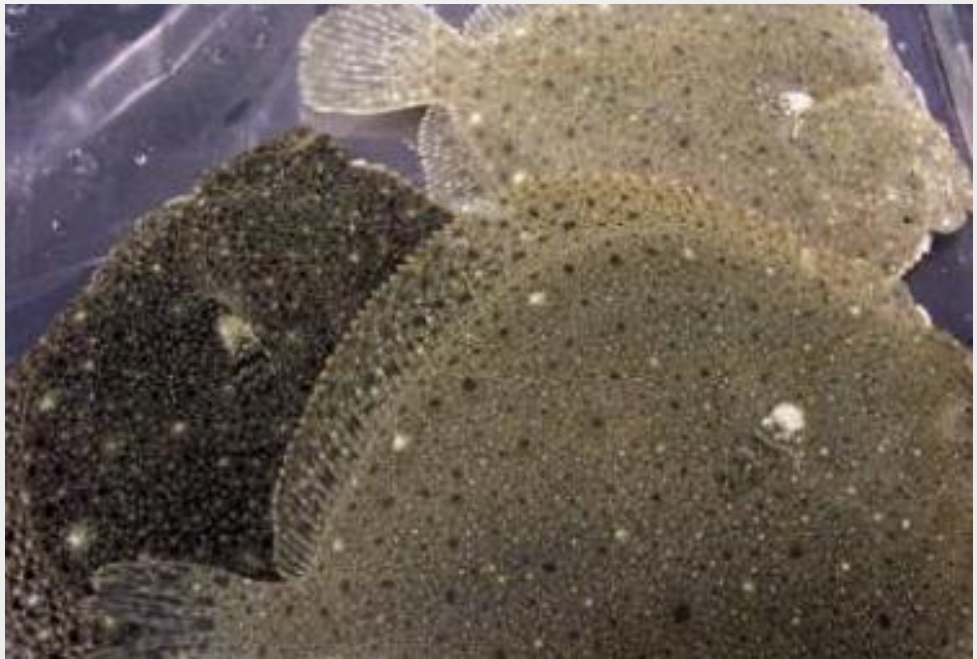
# Medetomidine



- Sedative for mammals
- α2-receptor agonist, octapamine receptor agonist
- Inhibits settling of barnacles on shiphulls
- Currently evaluated as a biocide

Dahlström et al. (2005) Evidence for different pharmacological targets for imidazoline compounds inhibiting settlement of the barnacle *Balanus improvisus*. Journal of Experimental Zoology. Part A – Comparative Experimental Biology: 303:551
Lennquist: Responses to fish exposed to medetomidine, Marine Env. Research, 2010

# Medetomidine



- Inhibits settling of barnacles on shiphulls
- 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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