



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Antimicrobial resistance (AMR): Presentation on the joint EMA/EFSA RONAFA opinion Harmonisation of SPCs of antimicrobial veterinary medicines

EMA Veterinary Medicines Info Day 16-17 March 2017, London

Presented by Helen Jukes on 16 March 2017
Chair of the CVMP's Antimicrobials Working Party, co-chair of the RONFA group

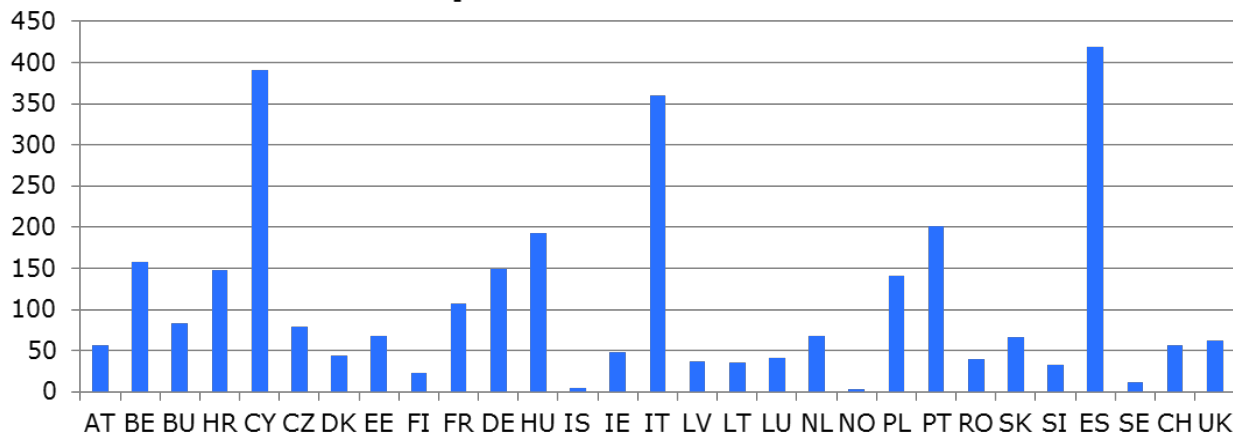
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Introduction

**Sales of antimicrobials (mg/PCU) in
29 European countries in 2014**



(ESVAC 2016)

- Lowest user: **3.1** mg/PCU
- Highest user: **418.8** mg/PCU

>100x difference!



‘RONAFA’: Reduction Of the Need for Antimicrobials in Food-producing animals and Alternatives



Terms of Reference for the opinion provided by the European Commission (2015)

- Review the **measures** that have been taken by MSs to **reduce the use** of, and **need to use**, antimicrobials in food-producing animals
- Review ‘**alternatives**’ to the use of antimicrobials
- Assess the **impacts** of the measures and alternatives on the occurrence of **AMR**
- **Recommend options** to **reduce** antimicrobial use and for **responsible use**

Working Group and Data / information

RONAFA group, collaboration between experts from EMA, EFSA

Review of information from:

- **National antimicrobial use and AMR surveillance reports**
- **EU: ESVAC sales report, ECDC/EFSA AMR surveillance reports**
- **Publications in scientific journals, literature reviews** (*Alternatives, Organics*)
- **Surveys and questionnaires** (FVE, DG SANTE/FVO, food retailers)
- **Grey literature, hearing expert**

Sales of veterinary antimicrobial agents in 29 European countries in 2014

Trends from 2011 to 2014
Sixth ESVAC report

ANTIMICROBIAL USE IN FOOD-PRODUCING ANIMALS



29-Feb-16

Replies to EFSA/EMA questions on the use of antimicrobials in food-producing animals in EU and possible measures to reduce antimicrobial use.



This presentation will focus at high level on a selection of the **eleven recommended options to reduce AMU** and for **responsible use**, and the **supporting information** from the report.

1. Development of **national strategies** and action plans
2. Harmonised integrated **systems for monitoring AMU and AMR** in animals, humans and food
3. Establishing **targets** for reduction of AMU, especially for CIAs
4. **On-farm health management** with professional input
5. Increased responsibility by **veterinarians for prescribing**
6. Increased oversight of **preventive and metaphylactic** use, especially for groups of animals
7. **Training and education**, raising public awareness
8. Availability of rapid and reliable **diagnostics**
9. Improvement of **husbandry and management** procedures for disease prevention and eradication; use of **vaccination**
10. **Re-thinking of livestock systems**
11. Development of **alternative treatments** to AMs

Option 2: Harmonised systems for monitoring **AMU** and surveillance for **AMR**, integrating data from humans, animals, food



- Monitoring impacts of policies on AMU
- Impacts of AMU on AMR
- Transfer of AMR between reservoirs – ‘One Health’

e.g.



ESBL producing *Escherichia coli*
– food as a potential dissemination route to humans

**Associations between antimicrobial
use
and the prevalence of
resistant micro-organisms**

Is it possible to benchmark livestock farms
based on resistance data?

Option 3: National (high-level) reduction targets

e.g. Targets set by Dutch government, relative to 2009

2011: 20% reduction

2013: 50% reduction

2015: 70% reduction

By 2014, NL had achieved a

58 % reduction in AMU

(MARAN, 2015)

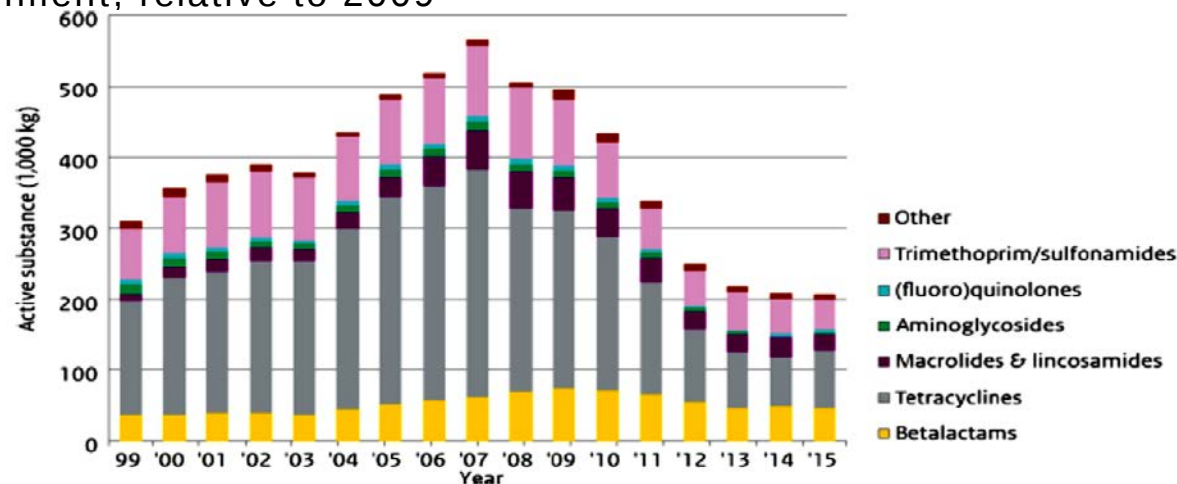


Figure 4: Antimicrobial veterinary medicinal product sales from 1999–2015 in kg (thousands) in the Netherlands (source: MARAN, 2016)

- **Set according to national circumstances**
- **With underlying supporting package of reduction measures**



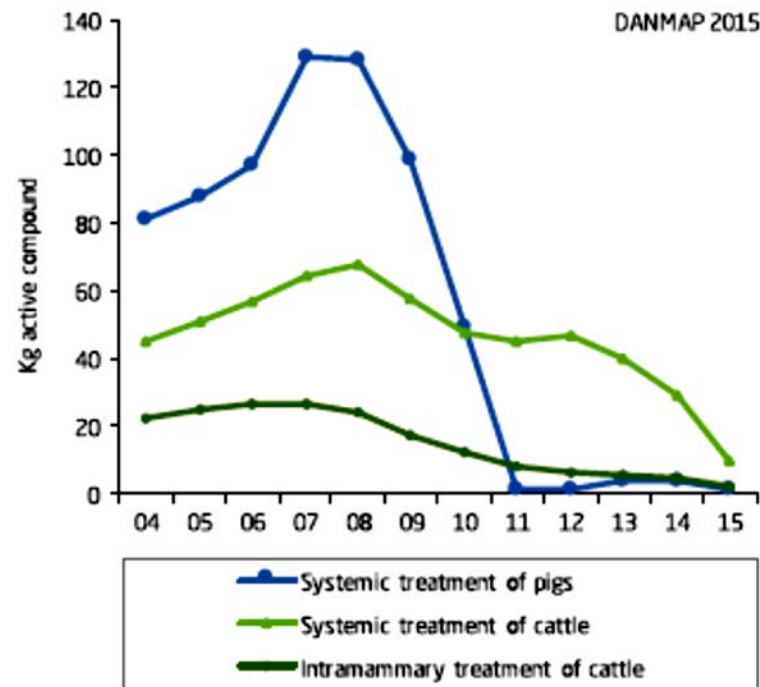
Options 3, 5 & 7: Measures on critically important antimicrobials

- **Livestock sector targets for CIAs, voluntary sector bans**
- **Susceptibility testing**
- **Treatment guidelines**

e.g. Denmark, use of 3/4G Ceph in pigs

- **Treatment guidelines** for pigs (2010)
- **Voluntary ban on use of 3 / 4G cephs** in pig sector (2010)
- (Yellow card initiative 2010)

Consumption of 3/4G Cephalosporins in pigs & cattle in DK





Option 6: Increased oversight of preventive and metaphylactic AMU

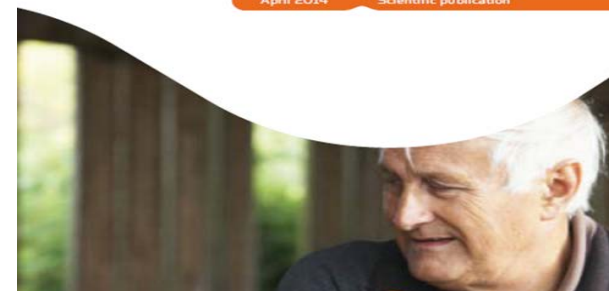
- **Preventive use to be phased out** except in exceptional cases.
- **Phase-out based on review by livestock sector professionals** of endemic diseases, risk factors, local husbandry.
- **Metaphylactic use to be refined:** Principles to be developed at national level.



Assessment of the risks of emergence of antimicrobial resistance associated with modes of antibiotic use in the field of animal health

ANSES Opinion
Extracts from the Working Group's report:
Chapters 4 and 5 and maps

April 2014 Scientific publication





Option 9: Improvement of husbandry for disease prevention, control and eradication

- **Preventing spread of infections between farms**: external biosecurity, compartmentalisation according to health status (e.g. SPF), eradication e.g.
 - PRRS* from pigs in Sweden (Carlsson, 2009)
 - BVD† from Scandinavian countries (Stahl, 2012)
- **Preventing spread of disease on the farm**: internal biosecurity, housing, production groupings 'all-in, all-out'
- **Increasing disease resilience**: nutrition, genetics, vaccination, stress reduction

*PRRS Porcine Reproductive and Respiratory syndrome

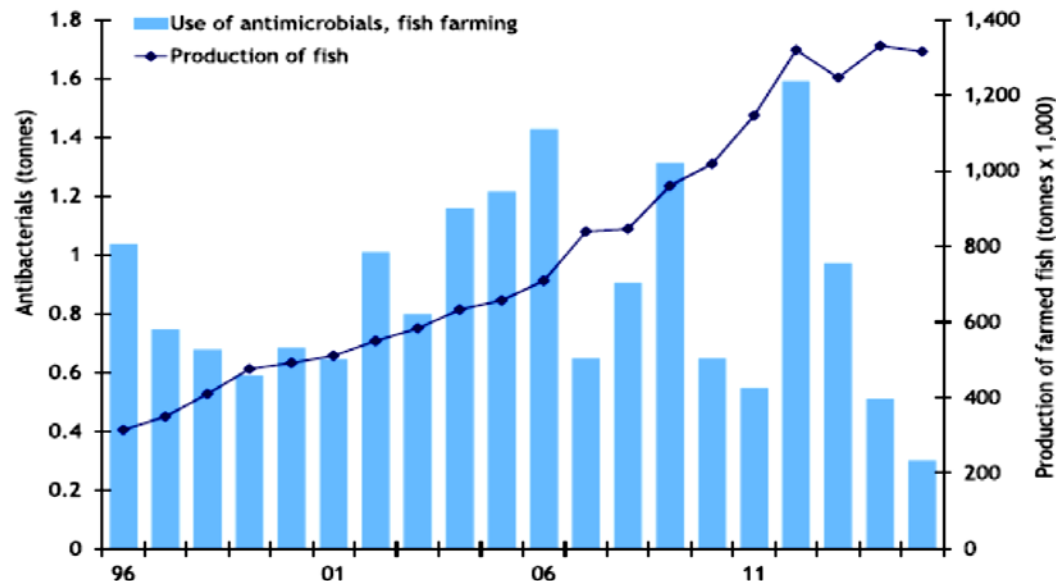
†BVD Bovine viral diarrhoea

Example: Norway - Use of vaccines in fish production

- Fish production increased >3x from 1996 to 2015 (1.3M tonnes)
- AMU remains c. 1 tonne/year
- Government/industry investment in vaccine development (vibriosis, furunculosis)
- Mandatory use of vaccines

Fish production and use of antimicrobials
fish farming in Norway (1996-2005)

Ronafa, Appendix C





Option 11: Development of treatments which are alternatives to antimicrobials

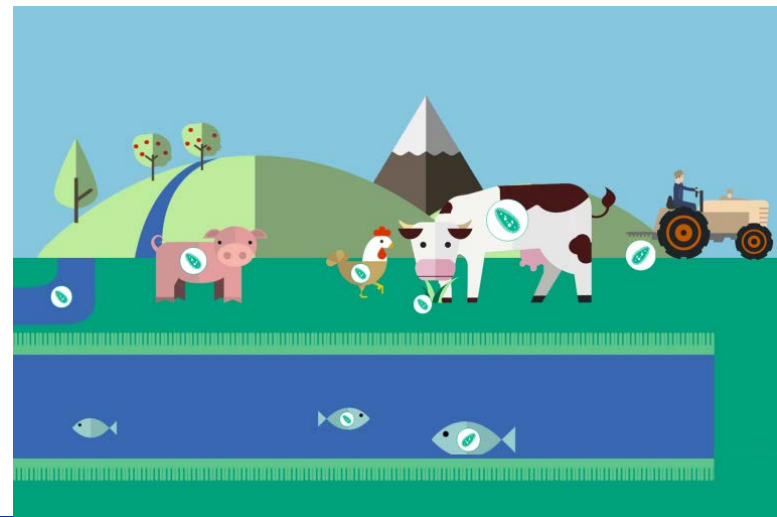
- Limited robust scientific evidence of **impacts on health parameters**
- Studies may show reduction of disease risk; **rarely in line with veterinary 'medicinal' claims**
- Some authorised as zootechnical feed additives
- **Positive impacts** on health parameters shown for e.g.
 - o **organic acids**
 - o **probiotics**
 - o **bacteriophages**
 - o **immunomodulators**
 - o **zinc oxide**
 - o **teat sealants**

Options

- **an EU regulatory framework for 'alternatives'**
- **Additional research – controlled & meaningful clinical trials**

Features of successful strategies to reduce AMU

- **Integrated, multifaceted approach** (reflecting multiplicity of factors that underlie AMU)
- **Take account of local livestock production systems**
- **Involve all relevant stakeholders**



In conclusion



Setting targets

Increase responsibility of veterinarians

Preventive use should be phased out

Consider alternatives to antimicrobials

Research new alternatives

Develop an EU legal framework for alternatives

Improve disease prevention and control

Consider alternative farming systems

Education and awareness



Harmonisation of SPCs of antimicrobial veterinary medicines

1. **Revision to the Guideline on the SPC for Antimicrobial VMPs – public consultation Q3 2017**
2. **CVMP / MAHs Pilot Project on dose optimisation for the harmonisation of SPCs of established antibiotics**



CVMP/MAHs Pilot project on **dose optimisation** in the context of **SPC harmonisation** of established veterinary antibiotics

Background

- Absence of new antimicrobials for the veterinary market
- Need to limit the use of CIAs
- Need to **maintain a range of safe and effective established antibiotics for the veterinary market** – EU Medicine Agencies Network Strategy and CVMP's Strategy on Antimicrobials
- Proposed Veterinary Medicines Regulation requires the harmonisation of the SPCs for 'similar products' authorised before 2004
- Acknowledged that **dosing regimens vary between similar products and may not be in line with modern and responsible use principles**



- **Joint regulatory / industry initiative**: EMA sec, CVMP, AWP, IFAH-EU, EGGVP
- Inaugural meeting: 20 January, 2017; chair – Johan Schefferlie (CVMP)
 - Objective: In the absence of new studies, **explore (modelling) approaches** to improve **dose**, and to address subsequent impacts on **withdrawal periods, target animal safety, risk to the environment**

Agreed principles

- Data to be gathered from all sources (including MA dossiers) to derive **API characteristics**
- Harmonisation at **product level**
- Regulatory and procedural aspects of implementation for later discussion



- First two examples for the pilot
 - Amoxicillin for oral use in pigs, water soluble, respiratory diseases (easy)
 - Oxytetracycline injection for beef and dairy cattle, respiratory disease (difficult)

Target date for completion: end 2017





Thank you for your attention

Further information

See next slide

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References for RONAFA

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