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

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Introduction

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

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

>100x difference!

(ESVAC 2016)

1 Joint EMA/EFSA Ronafa Opinion, EMA IFAH Info Day
‘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
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
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)

- 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

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

e.g. Denmark, use of 3/4G Cephs in pigs
- Treatment guidelines for pigs (2010)
- (Yellow card initiative 2010)
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.
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 in 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.
  - organic acids
  - probiotics
  - bacteriophages
  - immunomodulators
  - zinc oxide
  - 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**
  - Consider alternatives to antimicrobials
  - Research new alternatives
  - Develop an EU legal framework for alternatives

- **Increase responsibility of veterinarians**

- **Preventive use should be phased out**

- **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


RONAFA Opinion (EMA website):


DANMAP (Danish Integrated Antimicrobial Resistance Monitoring and Research Programme), 2016. DANMAP 2015 - use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark.
