Reduction in Antimicrobial Use in Animals –
Do We See Effects on Antimicrobial Resistance?

Dik Mevius
Antibiotic usage in humans and animals in Europe
Antibiotic use in animals in NL (Source FIDIN)

90% oral administration by group/flock mediation
Animal versus human use in kg

van Geijlswijk, et al, TvD, 2009
What does this mean

Dutch food-producing animals are an ideal environment for multidrug resistant organisms

- Risk??
  - Animal health?
    - Yes, if they cause infections
  - Public health?
    - Yes if:
      » Food-borne pathogens
      » Zoonotic organisms
      » Transferable genes

MRSA, ESBLs
EARSS-net 2012 report (ECDC)

MRSA

ESBLs
Live Stock associated MRSA (ST398)

- Many pigs and veal calves carry LA-MRSA in their noses (poultry, horses, companion animals…)

- Increased risk for carriersonhip of farmers and vets
  - Contact infection, no human to human spread,
  - Food products not considered to be an important source

- Global problem

- In NL, measurable effects in human health care
  - Infections
  - Increased costs
ESBL-Prevalences in the Netherlands

> 50% in (herds) animals

- Broilers (100%)
- Layers
- Veal calves
- Fattening pigs
- Turkeys
- Dogs
- Cattle 41%

Environment

- Soil
- Surface water

13% birds (waders) ESBL-positive

Is poultry the source or part of the problem??

Knapp, Dolfing et al. 2009

Characteristics of Cefotaxime-Resistant Escherichia coli from Wild Birds in The Netherlands
“Convenants” (MoA) signed by “all” stakeholders in livestock production in December 3, 2008

- Control of antimicrobial resistance by
  - One-in-One relation between farmer and vet
    - Better options to control responsible, prudent use of antibiotics
    - Responsibilities for prescription and administration better defined
  - Full transparency in antibiotic use
    - All antibiotic use registered
Reduction targets defined in 2010

- **2010 KNMvD**
  - Proposed 20% reduction
- **Debate in parliament about ESBLs in poultry**
  - Mandatory targets defined (20% in 2011 and 50% in 2013) in addition to the MoA’s
  - (70% 2015)
Reduction targets were based on sales data

- 20% reduction indicated a target of 400 tons in 2011
- 50% indicated a target of 250 tons in 2013
- 70% in 2015 (app. 150 tons) was defined as target for livestock production as a whole
Independent control institute essential
Netherlands Veterinary Medicines Authority (SDa)

Spring 2011

Tasks
- Define and specify reduction targets by animal species based on DDDA/Y
- Analyse data
- Report publically

Table 2. Quantitative benchmark indicators for antibiotics usage (ADD/DY) in broilers, sowspiglets, fattening pigs, cattle and veal calves for 2013. Green means 'no immediate action required'; orange means 'high usage, requires additional attention'; and red means 'immediate action required'.

<table>
<thead>
<tr>
<th>Animal Type</th>
<th>Target Level 2012-2015</th>
<th>Signaling Level 2013</th>
<th>Action Level 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Dairy cattle</td>
<td>0 - 3 (4#)</td>
<td>&gt; 3 - 6 (&gt; 4 - 7#)</td>
<td>&gt; 6 (7#)</td>
</tr>
<tr>
<td>- Suckler cows</td>
<td>0 - 1</td>
<td>&gt; 1 - 2</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>- Beef bulls</td>
<td>0 - 15</td>
<td>&gt; 1 - 25</td>
<td>&gt; 25</td>
</tr>
<tr>
<td>- Rearing cattle</td>
<td>0 - 15</td>
<td>&gt; 1 - 25</td>
<td>&gt; 25</td>
</tr>
<tr>
<td>Veal calves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- White veal calves</td>
<td>0 - 23</td>
<td>&gt; 23 - 39</td>
<td>&gt; 39</td>
</tr>
<tr>
<td>- Rose starter</td>
<td>0 - 67</td>
<td>&gt; 67 - 110</td>
<td>&gt; 110</td>
</tr>
<tr>
<td>- Rose fattening</td>
<td>0 - 1</td>
<td>&gt; 1 - 6</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>- Rose combination</td>
<td>0 - 12</td>
<td>&gt; 12 - 22</td>
<td>&gt; 22</td>
</tr>
<tr>
<td>Pigs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Sows and piglets</td>
<td>0 - 10</td>
<td>&gt; 10 - 22</td>
<td>&gt; 22</td>
</tr>
<tr>
<td>- Fattening pigs</td>
<td>0 - 10</td>
<td>&gt; 10 - 13</td>
<td>&gt; 13</td>
</tr>
<tr>
<td>Broilers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ADD/DY</td>
<td>0 - 15</td>
<td>&gt; 15 - 30</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>- Treatment days*</td>
<td>0 - 17*</td>
<td>&gt; 17 - 34*</td>
<td>&gt; 34*</td>
</tr>
</tbody>
</table>

* The figure between parentheses is the value determined on the basis of the LEI methodology.
* Expressed as the number of treatment days per year.
$ Indicative values; will be adjusted in the autumn of 2013 or 2014 as necessary.

SDa 2013
BENCHMARK INDICATORS

ACTION LEVEL
Direct measures necessary to reduce antibiotic usage

SIGNALING LEVEL
Please be aware

TARGET LEVEL
No direct measures necessary to reduce antibiotic usage
Antibiotica in de veeteelt en resistente bacteriën bij mensen

Om het probleem van de toenemende resistente van bacteriën tegen antibiotica te keren, moeten bepaalde soorten antibiotica gereserveerd worden voor menselijk gebruik. Deze middelen zouden uitgesloten moeten worden van gebruik in de veeteelt, om overdracht van resistente bacteriën van dier naar mens tegen te gaan. Dit schrijft de Gezondheidsraad in zijn advies Antibiotica in de veeteelt en resistente bacteriën bij mensen dat de raad vandaag aanbiedt aan de minister van VWS en de staatssecretaris van EL&I.
New targets added

**No use in animals of all new antibiotics:**
Carbapenems, tigecycline, daptomycin, oxazolidones, mupirocin etc.

**Fluoroquinolones and 3rd/4th generation Cephalosporins:**
No use in animals unless demonstrated that no alternative treatment options are available

**Colistin, beta-lactams, aminoglycosides**
All classified as second choice antibiotics
Only allowed unless appropriate diagnostics by vet
Summarizing the reduction targets

- Reduction in sales (20-50-70%)
- Quantitative targets defined by SDa in DDDA/Y
  - Specified by animal species
- Targets aimed at the quality of antibiotic use
  - Zero ADDD/Y for FQ and 3\textsuperscript{rd}/4\textsuperscript{th} gen Cephs
  - Less group treatments
  - No preventive use (EU-regulations implemented)
  - More selective use of dry cow treatments
Measures initiated by the Royal Veterinary Association (KNMvD)

- Re-definition of 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} choice ABs
- Update formularies
  - Mandatory basis for custom made treatment plan for each farm
  - Health control plan for each farm
  - Implemented in the law (UDD-rule 2013)

Empiric use, allowed to be present on farms

No unless:
- Diagnosis and argumentation by vet (yellow)
- No alternatives demonstrated (orange)
Effect on reduction in sales

Index year

(FIDIN/LEI 2012)
www.maran.wur.nl
Sales of antibiotics for (mg) per kg biomass produced (PCU) in Europe

2007  2010
ESVAC 2011

2013 less than 100 mg/PCU ??
2013 NL = 69 mg/PCU (ESVAC 2013)

Figure 21. Spatial distribution of overall sales of all antimicrobials for food-producing animals, in mg/PCU, for 26 countries, for 2013.
Use in DDDA/Y in veal calves

- Use data by livestock sector DDDA/y
- Translation of sales to usage data
DDDA/Y Pigs

Production farms (sows and piglets) (n = 2526)
# Pigs/farm range: 2 - 4400, median: 285

Slaughter pig farms (n = 5531)
# Pigs/farm range: 2 - 13000, median: 650
Broilers treatment days/Y
Trends in DDDA/Ynat by livestock species

Veal farming sector (blue), poultry farming sector (orange), sow/piglet farms (dark green), pig fattening farms (light green).
Trends in use of third-choice antibiotics: fluoroquinolones and 3\textsuperscript{rd}/4\textsuperscript{th} generation cephalosporins from 2011 to 2014
Bechmarking of veterinarians

- Based on population of farms it can be identified if vets prescribe systematically more than others
- VBI = veterinary benchmarkindicator
Effect of reductions of antibiotic use in animals on the occurrence of antimicrobial resistance in commensal E. coli

Figure Eco01: Trends in resistance (%) of E. coli isolated from broilers, slaughter pigs, veal calves and dairy calves in the Netherlands from 1998 - 2014.
Effect of reductions of antibiotic use in animals on the occurrence of antimicrobial resistance in commensal E. coli

Figure Eco01: Trends in resistance (%) of E. coli isolated from broilers, slaughter pigs, veal calves and dairy cattle in the Netherlands from 1998 - 2014.
Trends in resistance in *E. coli* isolated from meat
Reduction of resistance in human isolates of FB-pathogens

Salmonella Typhimurium  Campylobacter

[Graph showing the reduction of resistance over years for both pathogens, with specific data points for each year from 1999 to 2014.]
Effect of reduction of 3<sup>e</sup>-gen cephalosporins

Cefotaxime resistance in *E. coli*

- Ceftiofur use in hatcheries stopped
Reduction of ESBLs

- Animals
  - Poultry
    - Faeces 100% - 66%
    - Meat 100% - 67%

W. Dohmen UU-IRAS
Have we realized our reduction-ambitions?

- Yes,
  - **Quantity of use**
    - in reduction of sales
    - In reduction of prescriptions by vets and usage on farms
  - **Quality of use**
    - Substantial less use of $3^{rd}$ choice drugs
    - Less group treatments (pigs, calves)
    - More selective dry cow treatment
  - **Surprising fast and substantial effect on the occurrence of resistance in food-animals**
    - Limited or no effect in Campylobacter and Salmonella
Critical success factors were

- Clear targets defined by the authorities
- Measures initiated by private animal production sectors icw veterinary association aimed at prudent use and transparency
- Independent control institute (SDa)
  - Benchmarking of farms and vets
Is it sustainable?

- Yes, but it needs an active ongoing policy to more sustainable animal husbandry systems and awareness in all stakeholders involved.
Future actions

- Evaluate the implementation of the Health Council Report recommendations in 2016?
  - Policy on 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} choice drugs and the professional guidelines developed by the KNMvD
  - Reduction targets (quantity, quality)
  - Reduction of AMR (ESBLs, MRSA)

- Evaluate the effect of reduced use on animals health and welfare

- Measures implemented in companion animals