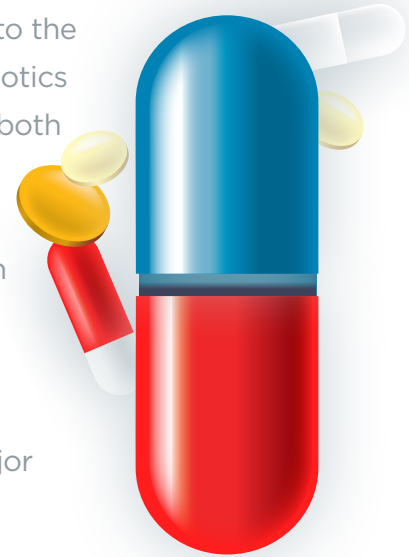




FDA'S EFFORTS FAIL TO END **MISUSE OF LIVESTOCK ANTIBIOTICS**

Antibiotic resistance is one of the top five threats to public health, according to the Centers for Disease Control and Prevention.¹ The overuse and misuse of antibiotics that are important for human medicine (“medically important antibiotics”) in both hospitals and livestock production is contributing to the spread of antibiotic-resistant bacteria that put public health at risk.² Critically, though, **70%** of medically important antibiotics in the US are sold for livestock use, not human use.³ FDA has launched Guidance #213, an initiative for pharmaceutical companies to voluntarily end sales of medically important antibiotics for certain purposes in the meat and poultry industry. But Guidance 213 fails to curb the risky, routine use of antibiotics in meat and poultry production, a major contributor to the development of antibiotic resistance.⁴

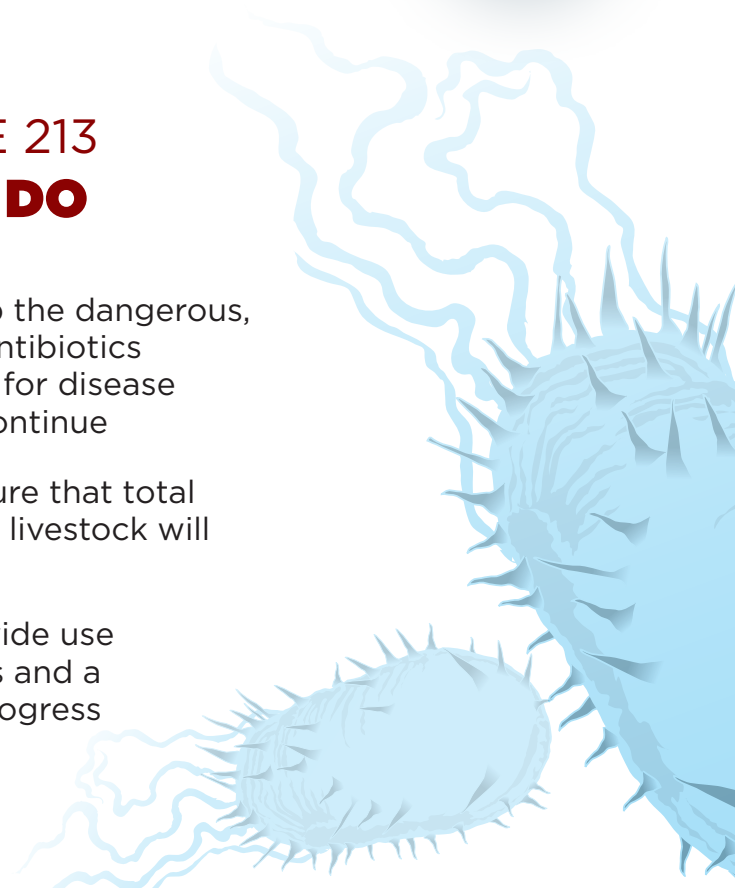


WHAT GUIDANCE 213 **DOES**

- 1** Encourages animal drug companies to stop selling medically important antibiotics for “growth promotion” purposes, i.e. for speeding up animal growth
- 2** Encourages companies to switch to selling antibiotics for use in livestock with veterinary oversight.

WHAT GUIDANCE 213 **FAILS TO DO**

- 1** Fails to stop the dangerous, routine use of antibiotics by allowing use for disease prevention to continue
- 2** Fails to ensure that total antibiotic use in livestock will decrease
- 3** Fails to provide use reduction goals and a way to track progress



WHY AND HOW ANTIBIOTICS ARE USED IN MEAT & POULTRY PRODUCTION

Antibiotic resistance refers to the phenomenon of antibiotics becoming less effective against

bacteria. As shown on the right, use of lower antibiotic doses for long periods of time is risky because these practices allow antibiotic-resistant bacteria to survive and thrive.⁵ Antibiotic use on larger numbers of animals creates more incubators for resistant bacteria.⁶ Such routine use in the absence of disease creates unnecessary risk that could be avoided with better management practices.⁷ Low-dose and herd-wide or flock-wide use appears to be the norm both for FDA-approved “growth promotion”⁸ and “disease prevention” purposes.⁹

HIGHER RISK OF RESISTANCE

Occurs when antibiotics are given:

- in low doses
- regularly or continually
- for long periods of time
- to large numbers of animals
- in the absence of disease



GROWTH PROMOTION:
to speed up growth

DISEASE PREVENTION:
to reduce risk of disease from poor conditions or inappropriate diets



DISEASE CONTROL:
to control the spread of disease in barn, pen or coop

DISEASE TREATMENT:
to treat sick animals



No antibiotic use

LOWER RISK OF RESISTANCE

Occurs when antibiotics are given:

- in higher doses
- only when needed
- for a shorter, defined time
- to individual/few animals
- to stop a disease

1 GUIDANCE 213 FAILS TO STOP THE DANGEROUS, ROUTINE USE OF ANTIBIOTICS BY ALLOWING USE FOR DISEASE PREVENTION TO CONTINUE

The Guidance allows the ongoing, prolonged, low-dose use of antibiotics in a large number of animals, typically in feed or in water—to counter the disease pressure from animals being fed inappropriate diets or being raised in crowded, stressful and unsanitary confinement conditions. Routine and widespread low-dose use in the feed and water of large numbers of animals creates a higher risk of antibiotic resistance regardless of the justification for use, whether for growth promotion or disease prevention.

“Because antibiotics in feed or water are typically administered to herds or flocks of food producing animals, in-feed or in-water antibiotic use leads to an increased risk of selecting for resistance.”

President’s National Action Plan for Combating Antibiotic Resistant Bacteria



2 GUIDANCE 213 FAILS TO ENSURE THAT TOTAL ANTIBIOTIC USE IN LIVESTOCK WILL DECREASE

The same drugs can continue to be used in the same, risky ways as before. Under Guidance 213, even if the use of medically important antibiotics—i.e. antibiotic classes also used in human medicine—is stopped for growth promotion reasons, these same classes of antibiotics can still be used for disease prevention purposes in essentially the same ways. Drugs in every medically-important class of antibiotics used in the feed and water of livestock are approved for both growth promotion and disease prevention purposes and are used in low-dose, herd-wide or flock-wide applications for prolonged periods.¹⁰

In fact, for some drugs, farmers would not have to change their risky practices at all under Guidance 213—they could continue to use the same drugs, at the same doses and same durations that they had been using for growth promotion, but now for “disease prevention.” That’s because, in every one of these antibiotics classes, some drugs overlap in the approved dosage and duration of use for growth promotion and disease prevention. Even the animal pharmaceutical industry agrees that stopping use only for “growth promotion” would not significantly affect sales of antibiotics.

















































































As we mentioned above, FDA has recommended veterinary oversight for all antibiotic uses in feed and water. Veterinary oversight (the equivalent of prescriptions) is a step in the right direction but as we’ve seen in human medicine, requiring prescriptions is not enough on its own to curtail misuse and overuse.¹¹ Additional policy measures are needed to ensure that antibiotics are not misused and that use decreases.

*On Guidance 213:
“Growth uses of medically important antibiotics represent only a small percentage of overall use, so even if all other factors are static it’s unlikely overall use would be greatly affected.”*

Animal Health Institute, drug company trade association

ANTIBIOTICS STILL APPROVED FOR ROUTINE USE

All Classes of Medically Important Antibiotics Used in Livestock Are Approved for Both Growth Promotion and Disease Prevention, Including at Overlapping Dosages and Durations

ANTIBIOTIC CLASS AND IMPORTANCE IN HUMAN MEDICINE ¹²	HUMAN DISEASES TREATED	SPECIES Approved for use in: Chickens, Pigs, Cows	APPROVED FOR GROWTH PROMOTION [■]	APPROVED FOR DISEASE PREVENTION [◆]	APPROVED AT OVERLAPPING DOSAGES AND DURATIONS ^{▲13}
MACROLIDES (critical)	 <ul style="list-style-type: none"> •Treatment for severe Campylobacter infections¹⁴ •Respiratory infections, including whooping cough¹⁵ 	  	  	  	  
LINCOSAMIDES (high)	 <ul style="list-style-type: none"> •MRSA infections common to diabetic patients¹⁶ •Methicillin Resistant Staphylococcus Aureus (MRSA) infections in children¹⁷ 	  	 	 	 
PENICILLINS (high)	 <ul style="list-style-type: none"> •Strep throat¹⁸ •(Group B) Strep infections¹⁹ 	  	 	 	
STREPTOGRAMINS (high)	 <ul style="list-style-type: none"> •Resistant Enterococcal infections after surgery²⁰ 	  	  	  	  
TETRACYCLINES (high)	 <ul style="list-style-type: none"> •MRSA infections in children²¹ •Chlamydia²² 	  	  	  	  
AMINOGLYCOSIDES (high)	 <ul style="list-style-type: none"> •Infections in newborns due to Listeria, E. coli, etc.²³ •Enterococcal infection of the heart²⁴ 	  	  	  	  
SULFONAMIDES (critical*)	 <ul style="list-style-type: none"> •Urinary tract infections²⁵ •Foodborne illness²⁶ 	  		  	

* indicates that Sulfonamide is one of two antibiotic classes which comprise the drug, and that the combination drug is identified as critical for human health by FDA²⁷

■ This risky routine use would be discontinued under FDA's recommendations ◆ This risky routine use would still remain in place. ▲ For some drugs in these classes, not only is the drug approved for both uses, the approved use for the two purposes even overlaps. As of April 1, 2015, there is overlap in approved dosage and durations for at least one antibiotic drug in the class and for one or more of the following species: chicken, cattle, and swine.

3 GUIDANCE 213 FAILS TO PROVIDE USE REDUCTION GOALS AND A WAY TO TRACK PROGRESS

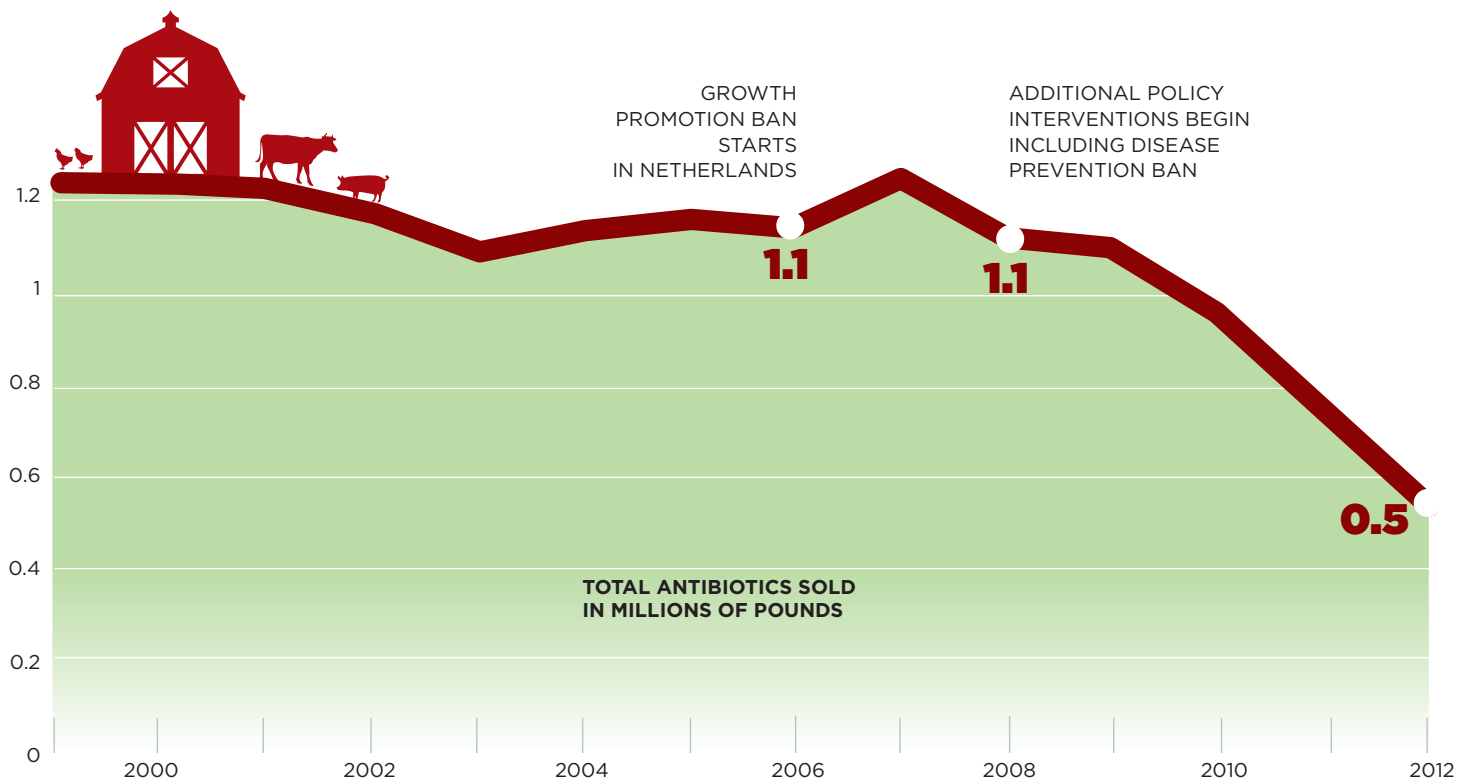
Guidance 213 does not set antibiotic-use reduction goals, will not collect the data needed to track progress, and offers no alternate plan if antibiotic use continues unchanged or increases.²⁸

To truly reduce the proliferation of antibiotic resistance from farms, policies must address routine, risky uses of medically important antibiotics in livestock for both growth promotion and “disease prevention.” Otherwise, these risky practices are likely to continue under a more benign-sounding (but equally risky) label.

STOPPING GROWTH PROMOTION ALONE IS NOT ENOUGH TO REDUCE **ANTIBIOTIC USE**

For example, the Netherlands first imposed a ban on growth promotion uses of antibiotics in livestock, but total livestock use of antibiotics did not decline.²⁹

It was only after Netherlands initiated a series of other policy changes, including better reporting of use and a mandatory phase out of use for disease prevention,³⁰ that use declined, and dramatically—by **50%** over four years.³¹



ENDNOTES

- 1 Centers for Disease Control and Prevention, Top, December 17, 2013, (accessed June 12, 2015), <http://blogs.cdc.gov/cdcworksforyou/24-7/2013/12/cdc%E2%80%99s-top-ten-5-health-achievements-in-2013-and-5-health-threats-in-2014/>
- 2 Centers for Disease Control and Prevention, Antibiotic Resistance Threats in the United States, 2013, p. 31, www.cdc.gov/drugresistance/threat-report-2013/
- 3 The Pew Charitable Trusts, "Did you Know? Get the Facts on Antibiotic Resistance," May 8, 2011, (accessed September 3, 2015), <http://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2011/05/08/did-you-know-get-the-facts-on-antibiotic-resistance>
- 4 Food and Drug Administration, Guidance for Industry No. 213 , New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209 (December 2013), <http://www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm299624.pdf>
- 5 Andersson, D. and D. Hughes, "Microbiological effects of sublethal levels of antibiotics," *Nature Reviews Microbiology*, 12(2014):465-478; Gullberg et al., "Selection of Resistant Bacteria at Very Low Antibiotic Concentrations," *PLoS Pathogens*, 7(2011):1-24
- 6 Alexander T. et al., "Effect of subtherapeutic administration of antibiotics on the prevalence of antibiotic resistant *Escherichia coli* bacteria in feedlot cattle, Applied and Environmental Microbiology, 14(2008):4405-4416; Holman, D. et al., "Impact of subtherapeutic administration of tylosin and chlortetracycline on antimicrobial resistance in farrow-to-finish swine, FEMS Microbiology Ecology, 85(2013):1-13; Brewer et al., "Effects of subtherapeutic concentrations of antimicrobials on gene acquisition events in *Yersinia*, *Proteus*, *Shigella*, and *Salmonella* recipient organisms in isolated ligated intestinal loops of swine," *American Journal of Veterinary Research*, 74(2013):1078-1083; Zaheer, R. et al., "Effect of subtherapeutic vs. therapeutic administration of macrolides on antimicrobial resistance in Mannheimia haemolytica and enterococci isolated from beef cattle, *Frontiers in Microbiology*, 4(2013):1-5
- 7 See section "Alternatives to antibiotic use in broiler facilities exist and are scalable." Natural Resources Defense Council, Pharming Chickens, April 2014, <http://www.nrdc.org/food/saving-antibiotics/files/poultry-industry-antibiotic-stewardship-1B.pdf>, (accessed May 18, 2015). USDA, "Strategies that work - Alternatives to Antibiotics in Animal Health," May/June 2012, <http://agresearchmag.ars.usda.gov/AR/archive/2012/May/animal0512.pdf#page=4&zoom=auto,-31,342>, (accessed May 18, 2015).
- 8 Food and Drug Administration, "FDA Initiatives Regarding the Judicious Use of Antibiotics in Food-Producing Animals," October 27, 2011, <http://www.animalagriculture.org/Resources/Documents/Conf%20-%20Symp/Symposiums/2011%20Antibiotics%20Symposium/Flynn,%20William.pdf>, (accessed May 18, 2015).
- 9 Disease prevention typically involves a lower dose of an antibiotic, which is administered to a herd or flock and has at times been referred to as "subtherapeutic," even by the livestock industry. American Meat Institute, "Antibiotic use in livestock production: Ensuring Meat Safety," February 2010, <https://www.meatinstitute.org/index.php?ht=a/GetDocumentAction/i/56994>, (accessed May 18, 2015); AVMA, "Antimicrobial use and antimicrobial resistance FAQ," 2015, <https://www.avma.org/KB/Resources/FAQs/Pages/Antimicrobial-Use-and-Antimicrobial-Resistance-FAQs.aspx>, (accessed May 18, 2015).
- 10 Food and Drug Administration, Guidance for Industry No. 213 , New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing dosage and duration of use for growth promotion and disease prevention. Even the animal pharmaceutical industry agrees that stopping use only for "growth promotion" would not significantly affect sales of antibiotics. Animals:Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209 (December 2013), <http://www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm299624.pdf>
- 11 Centers for Disease Control and Prevention, Antibiotic Resistance Threats in the United States, 2013, p.34, www.cdc.gov/drugresistance/threatreport-2013/ (accessed May 15, 2015).
- 12 FDA, Guidance for Industry #152 Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern, Appendix A, October 23, 2003, <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf>, (accessed May 18, 2015).
- 13 FDA, Approved Animal Drug Products Online (Green Book), FDA, updated January 2015, <http://www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/default.htm> (accessed May 20, 2015). Partial list of drugs that are approved at overlapping doses for disease prevention and growth promotion (NADA): 013-388, 048-761, 094-973, 098-431, 133-334, 137-537, 138-934, 138-972, 139-473, 140-579, 140-998, 141-054, 200-424, 200-531, and 200-532.
- 14 Javid, M. et al., "Campylobacter Infections Medication," *Medscape*, August 29, 2014, June 12, 2015, <http://emedicine.medscape.com/article/213720-medication>
- 15 Centers for Disease Control and Prevention, "Pertussis (Whooping Cough)," August 28, 2013, <http://www.cdc.gov/pertussis/clinical/treatment.html>, (accessed May 20, 2015).
- 16 Bronze, M. et al., "Diabetic Foot Infections Medication," *Medscape*, February 27, 2015, <http://emedicine.medscape.com/article/237378-medication>, (accessed May 20, 2015).
- 17 Tsz-Yin, S. et al., "Community-Acquired Methicillin-Resistant *Staphylococcus aureus* infection in the Pediatric population," *Journal of Pediatric Health Care*, 22, 4(2008):211-217.
- 18 Romito, K. et al., "Antibiotics for Strep Throat," *WebMD*, August 2, 2012, <http://www.webmd.com/oral-health/antibiotics-for-strep-throat>, (accessed May 20, 2015).
- 19 Woods, C. et al., "Streptococcus Group B infections Treatment and Management," *Medscape*, August 15, 2014, <http://emedicine.medscape.com/article/229091-treatment>, (accessed May 20, 2015).
- 20 Stolberg, S. "Drug Agency Approves Antibiotic," *New York Times*, September 22, 1999, (accessed June 12, 2015), <http://www.nytimes.com/1999/09/22/us/drug-agency-approves-antibiotic.html>
- 21 Drew, R., "Emerging options for treatment of invasive, multidrug resistant *Staphylococcus aureus* infections, *Pharmacotherapy*, 27, 2(2007):227-249.
- 22 Centers for Disease Control and Prevention, "Chlamydial infections," January 28, 2011, <http://www.cdc.gov/std/treatment/2010/chlamydial-infections.htm>, (accessed May 20, 2015)
- 23 Anderson, A. et al., "Neonatal Sepsis Medication," *Medscape*, February 11, 2014, <http://emedicine.medscape.com/article/978352-medication>, (accessed May 20, 2015).
- 24 Fraser, S., et al., "Enterococcal infections - Treatment and Management," *Medscape*, August 15, 2014, (accessed June 12, 2015), <http://emedicine.medscape.com/article/216993-treatment>.
- 25 Jancel, T. and V. Dudas, "Management of uncomplicated urinary tract infections," *Western Journal of Medicine*, 176, 1(2002):51-55.
- 26 *Medscape*, "Trimethoprim/sulfamethoxazole", 2015, (accessed June 12, 2015), <http://reference.medscape.com/drug/bactrim-trimethoprim-sulfamethoxazole-342543>
- 27 FDA, Guidance for Industry #152 Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern, Appendix A, October 23, 2003, <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf>, (accessed May 18, 2015).
- 28 Food and Drug Administration, "FDA's Strategy on Antimicrobial Resistance - Question and Answers," (March 28, 2014), <http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm216939.htm#question9>, (May 20, 2015).
- 29 Bondt, N. et al., LEI Wageningen UR, "Trends in veterinary antibiotic use in the Netherlands 2004-2012," 2012, https://www.wageningenur.nl/upload_mm/8/7/f/e4deb048-6a0c-401e-9620-fab655287fbc_Trends%20in%20use%202004-2012.pdf; Government of the Netherlands, Reduced and Responsible: use of antibiotics in food-producing animals in the Netherlands, 2014, <http://www.government.nl/issues/antibiotic-resistance/documents-and-publications/leaflets/2014/02/28/reduced-and-responsible-use-of-antibiotics-in-food-producing-animals-in-the-netherlands.html>
- 30 Bondt, N. et al., LEI Wageningen UR, "Trends in veterinary antibiotic use in the Netherlands 2004-2012," 2012, https://www.wageningenur.nl/upload_mm/8/7/f/e4deb048-6a0c-401e-9620-fab655287fbc_Trends%20in%20use%202004-2012.pdf; Government of the Netherlands, Reduced and Responsible: use of antibiotics in food-producing animals in the Netherlands, 2014, <http://www.government.nl/issues/antibiotic-resistance/documents-and-publications/leaflets/2014/02/28/reduced-and-responsible-use-of-antibiotics-in-food-producing-animals-in-the-netherlands.html>
- 31 Bondt, N. et al, LEI Wageningen UR, "Trends in veterinary antibiotic use in the Netherlands 2004-2012," 2012, https://www.wageningenur.nl/upload_mm/8/7/f/e4deb048-6a0c-401e-9620-fab655287fbc_Trends%20in%20use%202004-2012.pdf; Government of the Netherlands, Reduced and Responsible: use of antibiotics in food-producing animals in the Netherlands, 2014, <http://www.government.nl/issues/antibiotic-resistance/documents-and-publications/leaflets/2014/02/28/reduced-and-responsible-use-of-antibiotics-in-food-producing-animals-in-the-netherlands.html>