



# Weak Medicine

Why the FDA's Guidelines Are Inadequate to  
Curb Antibiotic Resistance and Protect Public Health

**TexPIRG**  
Education Fund

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# Executive Summary

Millions of Americans rely on antibiotics every year to treat infections, but unfortunately, many antibiotics are no longer working against some bacteria prevalent today. Antibiotic-resistant bacteria infect more than 2 million people per year in the United States, causing more than 23,000 deaths.

Since the discovery of penicillin, scientists have known that the overuse of antibiotics can create antibiotic-resistant bacteria, rendering important medicines unable to fight infections. That knowledge, however, has not stopped industrial agriculture from becoming the biggest consumer of antibiotics in the United States. Livestock are fed antibiotics so that they grow faster with less feed and can remain healthy in the unsanitary, disease-laden conditions common on factory farms.

The Food and Drug Administration (FDA) has asked pharmaceutical companies to voluntarily stop the sale of antibiotics to farms for animal “growth promotion.” **Unfortunately, the FDA’s action—which will change the labels used on some antibiotics—is unlikely**

**to put a serious dent in antibiotic use in factory farms.** Without a reduction in the antibiotics fed to livestock, the development and spread of antibiotic-resistant bacteria will not slow down.

**In December 2013, the FDA published recommendations in an attempt to reduce the use of antibiotics on factory farms.**

- Under *Guidance for Industry #213*, pharmaceutical companies will voluntarily remove labels from antibiotics that authorize the drugs to be fed to animals to make them grow faster with less feed. In addition, fewer antibiotics will be available over the counter and more will require a veterinarian’s approval before being added to animal feed or water.
- However, the FDA has also proposed changes to the rules regarding veterinary oversight. Under proposed revisions to rules concerning the veterinary-client-patient relationship, veterinarians may be allowed to

prescribe antibiotics without having visited the facility or examined the animal in the recent past.

**Unfortunately, the FDA recommendations are unlikely to significantly reduce the use of antibiotics on factory farms.**

- Farmers purchase the vast majority of antibiotics under FDA rules that allow them to feed drugs to their livestock to prevent diseases. According to a trade group of animal pharmaceutical companies, only 10 to 15 percent of antibiotics are currently purchased under the rules that allow farmers to feed their livestock drugs for growth promotion.
- All classes of antibiotics that can be fed to livestock to promote growth can also be used to prevent diseases for chickens, cows and pigs. Therefore, in many cases, factory farms may continue feeding these antibiotics to livestock—even if they had previously been used for growth promotion—simply by claiming that the drugs are for disease prevention purposes.

**Pharmaceutical companies do not believe the FDA's recommendations will meaningfully reduce sales of antibiotics.**

- In a presentation to shareholders, the CEO of Zoetis, the largest animal health company in the country, claimed, “Zoetis supports the U.S. FDA's efforts, and ... we don't expect this to have a material impact on our future financial results.”
- The president of the animal health division of Eli Lilly, the fourth largest

animal pharmaceutical company in the country, stated “we do not see this announcement being a material event.”

- According to Bimeda, another animal pharmaceutical company, “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” by the new FDA guidelines.

**Experience with similar rules in Europe shows that the FDA should have implemented stronger recommendations.**

- From 1972 to 2006, European regulators took action similar to the FDA's by banning the practice of feeding antibiotics to animals for “growth promotion.” In the Netherlands—which keeps records of antibiotic consumption—the total use of antibiotics fed to animals did not decline because farms increased the antibiotics fed to animals for “disease prevention.” In 2011, the European Parliament adopted a resolution stating that the ban was insufficient to protect human health from the overuse of antibiotics.
- With the ban on antibiotics for growth promotion failing to reduce the overuse of antibiotics on factory farms, the Netherlands enacted regulations, embraced by industry, calling for a 70 percent decline in antibiotic consumption by 2015. As a result, the amount of antibiotics fed to animals for therapeutic uses, such as disease prevention, dropped by more than 50 percent over five years.

- From 1994 to 1999, Denmark took a series of steps that led to a ban on the practices of feeding animals antibiotics for “growth promotion” *and* “disease prevention.” Consequently, farmers adopted better practices to prevent disease, such as allowing piglets to nurse longer before being weaned. As a result, from 1992 to 2008, use of antimicrobials declined 51 percent on pig farms while pork production increased 47 percent, and antimicrobial use declined 90 percent on chicken farms, even as production increased slightly.

**State governments, the FDA and other branches of the federal government should take steps to protect human health from the antibiotic-resistant bacteria that can develop on factory farms.** Specifically, these authorities should:

- Restrict the use of antibiotics in livestock production to cases of animal sickness or direct disease exposure. The use of antibiotics on factory farms for “disease prevention” should be banned.
- Ban the farm use of certain antibiotics that are especially valuable

to human medicine, including fluoroquinolones, glycopeptides, macrolides, and third- and fourth-generation cephalosporins—all considered critically important by the World Health Organization.

- Create transparency over the antibiotics fed to animals by managing a registry of industrial farms’ usage of antibiotics. The registry should be accessible online and provide the public with information on the types, doses and purposes of antibiotics administered farm-by-farm.
- Require that the administration of antibiotics to animals on factory farms be overseen by a qualified veterinarian who has been to the farm or ranch and assessed the animals.
- Provide funding for research and development of antibiotic and non-antibiotic treatments. As today’s antibiotics become less effective in treating infections, scientists and pharmaceutical companies should be encouraged to discover new antibiotic classes to cure human diseases.



# Introduction

When Alexander Fleming discovered penicillin in 1928, the drug was heralded as a miracle cure, capable of treating strep infections, staph infections and more.<sup>1</sup> Following this discovery, scientists and doctors developed numerous new antibiotics such as azithromycin, ciprofloxacin and cephalexin that are capable of curing an array of life-threatening infections. Today, antibiotics are vital to human medicine. The Centers for Disease Control and Prevention (CDC), for instance, reports that doctors prescribe antibiotics to four out of five Americans per year.<sup>2</sup>

The danger of antibiotics losing their effectiveness, however, has been noted since their discovery. When Fleming won the Nobel Prize in 1945, he warned that the improper use of penicillin could create bacteria resistant to the drug. Fleming said that exposing bacteria to penicillin in “concentrations not sufficient to kill them” can “make [the] microbes resistant to penicillin.”<sup>3</sup> In other words, bacteria are able to mutate to survive exposure to antibiotics, and the more we use the drugs—especially at low doses—the more antibiotic-resistant bacteria we create.

In the 1950s, as antibiotic use in humans increased, scientists and farmers discovered that feeding antibiotics to livestock created benefits other than curing sickness. In fact, they found that adding the drugs at low doses to animal feed caused livestock to grow faster and prevented diseases on large farms. As the cost of antibiotics declined, more and more farms began to take advantage of these properties and feed their livestock antibiotics important to human medicine.<sup>4</sup>

In 1977, the U.S. Food and Drug Administration (FDA) concluded that this practice could, as Fleming predicted, create and spread antibiotic-resistant bacteria.<sup>5</sup> These bacteria could travel off the farm and into our food, water and communities. Infections created by such resistant bacteria can be more difficult and expensive, and sometimes impossible, to cure.

Finally, in December 2013—36 years after warning us about the threats of antibiotic-resistant bacteria—the FDA attempted to reduce the formation of these “superbugs” on factory farms by issuing *Guidance for Industry #213*, which urges pharmaceutical companies to voluntarily

stop labeling their antibiotics as appropriate for making livestock grow faster.<sup>6</sup> Unfortunately, as this paper explores, this guidance will likely fail to significantly

reduce the quantity of antibiotics used on farms and thus tackle the critical issue of antibiotic resistance.



*The misuse of antibiotics has created resistant bacteria that threaten public health by compromising the ability of these drugs to cure infections. Part of the problem is the overuse of antibiotics on factory farms, where 80 percent of America's antibiotics are given to livestock to speed their weight gain and keep them healthy in crowded conditions, such as at this Wisconsin swine farm. Credit: Bob Nichols/USDA NRCS.*

# Overuse of Antibiotics on Factory Farms Creates Antibiotic-Resistant Bacteria

The discovery of penicillin in the early 20<sup>th</sup> century was one of the great advances in modern medicine, and enabled doctors to treat infections that otherwise often led to death. The misuse of antibiotics, however, has created resistant bacteria that threaten public health by compromising the ability of these drugs to cure infections. Adding to the problem is the overuse of antibiotics on factory farms, where 80 percent of America's antibiotics are given to livestock to speed their weight gain and keep them healthy in the unsanitary, disease-laden conditions common on factory farms.

## Antibiotic-Resistant Bacteria Endanger Public Health

For decades, antibiotics like penicillin, streptomycin and erythromycin have been critical drugs for treating infections and protecting public health. Before the

advent of antibiotics, 90 percent of children who contracted bacterial meningitis died.<sup>7</sup> Common ailments such as pneumonia and tuberculosis often were fatal illnesses. Today, these are largely curable, thanks to antibiotics. In addition, antibiotics have made possible many advances in modern medicine by preventing and treating infections from surgery, organ transplants and joint replacements.

However, infectious bacteria are increasingly becoming resistant to antibiotics. When people get sick, physicians have fewer medicines—and sometimes none at all—to help them recover. For example:

- In U.S. hospitals, a standard antibiotic used for treating infected wounds has become ineffective in over 50 percent of cases.<sup>8</sup>
- Globally, 3.6 percent of tuberculosis cases being treated today and 20.2 percent that have already been treated are resistant to treatment.<sup>9</sup>

- In 2005, drug-resistant infections by methicillin-resistant *S. aureus* (MRSA) caused 20,000 deaths, or one of out of five affected patients, in the United States.<sup>10</sup>

When bacteria are exposed to an antibiotic, most of them are susceptible to the drug and die. Some of the organisms, however, possess traits that allow them to survive. Left without competition for food from their more vulnerable counterparts, these resistant bacteria replicate very quickly.

In total, more than 2 million people in the United States each year are infected by antibiotic-resistant bacteria and more than 23,000 people die as a direct result of those infections.<sup>11</sup> Additional deaths occur when drug-resistant infections complicate treatment of other illnesses.<sup>12</sup>

Providing care to U.S. patients with antibiotic-resistant infections costs the nation at least \$20 billion annually. Lost productivity due to hard-to-treat infections costs the nation another \$35 billion per year.<sup>13</sup>

Data from the Centers for Disease Control and Prevention show that the development of newly resistant bacteria has sped up in recent years. Signs of bacterial resistance to the three most recently developed antibiotics—linezolid in 2000, daptomycin in 2003 and ceftaroline in 2010—all appeared within just a few years of each drug's introduction.<sup>14</sup>

As the problem of drug-resistant bacteria has grown, the development of new antibiotics has slowed. From 1962 to 2000, researchers introduced no new chemical classes of antibiotics.<sup>15</sup> New antibiotics in that period were variations of existing classes of drugs, to which bacteria were able to adapt with relative ease.

## Bacteria Develop Resistance to Antibiotics on Factory Farms

Bacterial resistance to antibiotics has been hastened by overuse of antibiotics. Much of the inappropriate use of antibiotics has occurred in the raising of animals in crowded conditions.

Bacteria exposed to sub-lethal doses of antibiotics are able to survive and adapt instead of being destroyed. Drug-resistant bacteria pass along their resistance to the next generation by reproducing and to other bacteria by sharing genetic material, enabling resistance to spread rapidly.<sup>16</sup> As a result, the recipient bacteria can become resistant to an antibiotic without direct exposure to that drug. In addition, resistance to one antibiotic can confer resistance to other antibiotics in the same class.

Giving low doses of antibiotics to farm animals for extended periods of time—as is common on factory farms—creates ideal conditions for the growth of drug-resistant bacteria. Operators of large livestock facilities give antibiotics to their animals for four reasons, two of which facilitate the growth of drug-resistant bacteria:

- When animals are kept in crowded, unsanitary conditions, disease spreads easily. To avoid this, operators give antibiotics to livestock to stave off infections and ensure the survival of more animals.
- The second reason for regularly dosing healthy animals with antibiotics is to facilitate weight gain while feeding animals less food, thereby saving money.<sup>17</sup>
- Farmers give antibiotics to sick animals to treat infection, an appropriate use of antibiotics.

- Farmers also give antibiotics to healthy animals to control disease outbreaks, a reasonable use of antibiotics if certain conditions are met.<sup>18</sup>

These two unnecessary uses of antibiotics—to prevent infection and hasten growth—encourage development of drug-resistant bacteria, which then can spread from animals to people.<sup>19</sup> This has been documented by multiple studies:

- Researchers of a 2013 study published in the journal *PLOS One* sampled bacteria from workers at swine and poultry operations in North Carolina. People who worked at facilities where antibiotics were given regularly to animals carried multi-drug resistant *S. aureus* (MDRSA) bacteria at twice the rate of workers at facilities where animals were not given antibiotics.<sup>20</sup>
- Fields fertilized with swine manure can cause antibiotic-resistant infections in people, according to a 2013 study of patients in Pennsylvania. Researchers at Johns Hopkins University concluded that 11 percent of the methicillin-resistant *S. Aureus* (MRSA) infections that patients acquired outside of a health care setting could be attributed to the use of swine manure to fertilize crops.<sup>21</sup> Given that there were more community-acquired MRSA infections than health care-acquired infections, the link to swine manure application is significant.
- A study of patients admitted to the Veterans Affairs hospital in Iowa City found that veterans who lived within one mile of a large factory farm with pigs were nearly three times as

likely as other patients to be carrying MRSA bacteria.<sup>22</sup>

- A study published in 1976 documented that when chickens were given antibiotics mixed with their feed, they produced antibiotic-resistant *E. coli* bacteria in their feces. Subsequently, the same antibiotic-resistant bacteria were found in people living nearby.<sup>23</sup>
- Drug-resistant bacteria can also be carried from livestock through the air. Researchers who measured airborne bacterial contamination found antibiotic-resistant bacteria in higher concentrations downwind from factory farms than upwind.<sup>24</sup>

These studies are part of a growing body of research showing that giving animals regular low doses of antibiotics fosters the creation and spread of drug-resistant bacteria.

## Antibiotic Use at Factory Farms Is Rising

Despite the fact that regular antibiotic use in animals is harmful to public health, the practice is widespread and growing.

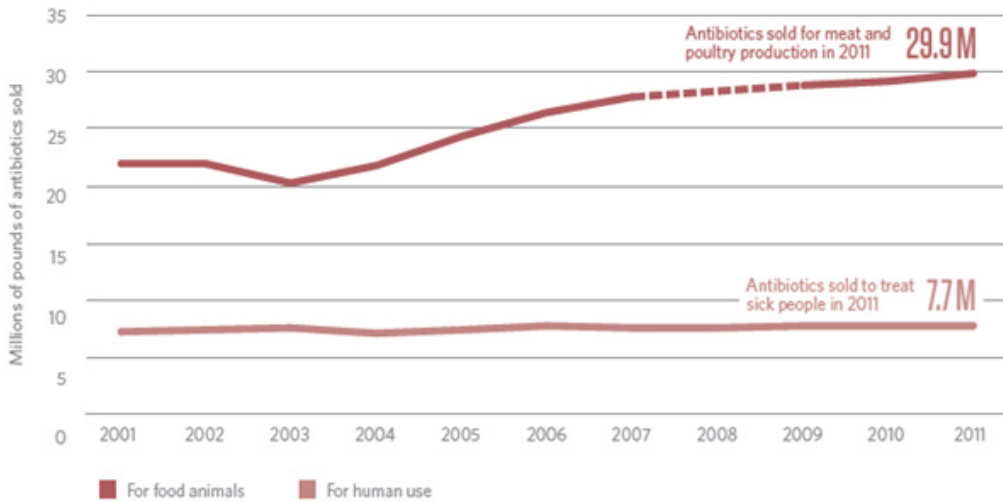
The vast majority of antibiotic use in the U.S. is in animals. In 2009, livestock operations consumed nearly four times as many antibiotics, by weight, as was used by humans.<sup>25</sup> Looking only at antibiotic classes used in human medicine, livestock operations consume more than twice the amount of antibiotics used by humans.<sup>26</sup> The use of antibiotics in livestock has been approved by the Food and Drug Administration, with 685 drugs approved by the agency as additives to animal feed.<sup>27</sup>

Routine use of antibiotics at factory

farms is increasing, even as use by people stays steady. Figure 1 shows that the amount of antibiotics sold for meat and poultry production increased by

approximately 35 percent from 2001 to 2011.<sup>28</sup> In the same period, use in humans was essentially flat, despite a 9 percent increase in population.<sup>29</sup>

**Figure 1. Amounts of Antibiotics Sold for Animal and Human Use, 2001-2011<sup>30</sup>**



# The FDA's Recommendations Are Unlikely to Stop the Overuse of Antibiotics

The Food and Drug Administration's *Guidance for Industry #213* is unlikely to reduce the overuse of antibiotics because farmers will still be allowed to feed large amounts of antibiotics to animals to keep livestock healthy in the unsanitary, disease-laden conditions common on factory farms. According to pharmaceutical companies, the FDA's recommendations are unlikely to reduce the sale of antibiotics to farms, meaning that they are unlikely to meaningfully slow the development of antibiotic-resistant bacteria. Data from the Netherlands show that European Union rules similar to *Guidance for Industry #213* did not reduce the use of antibiotics there, suggesting that the FDA guidance is also unlikely to have a major impact.

## The FDA's Recommendations Will Change the Labels on Antibiotics

In December 2013, the FDA published *Guidance for Industry #213* in an attempt

to reduce the use of antibiotics on factory farms. Under *Guidance #213*, pharmaceutical companies will voluntarily remove labels from antibiotics that authorize the drugs to be fed to animals to make them grow faster with less feed.

Specifically, the recommendations state: “the use of medically important antimicrobial drugs for production purposes in food-producing animals does not represent a judicious use of these drugs. ... FDA believes that production use indications such as ‘increased rate of weight gain’ or ‘improved feed efficiency’ are no longer appropriate for the approved conditions of use for medically important antimicrobial drugs.”<sup>31</sup>

The FDA has also proposed changes to the rules regarding veterinary oversight. Fewer antibiotics would be available over the counter and instead more would require a veterinarian's approval before being added to animal feed or water.<sup>32</sup> However, under proposed revisions to rules concerning the veterinary-client-patient relationship, veterinarians may be allowed to prescribe antibiotics without having visited the facility or examined the animal in the recent past.

*Guidance #213* has set a target of three years for animal pharmaceutical companies to comply with the new recommendations, and while companies are under no legal obligation to follow the guidelines, all 26 affected companies have agreed to comply.<sup>33</sup>

## Pharmaceutical Companies Will Continue to Sell Antibiotics to Factory Farms

The FDA's new recommendations may change the rationale under which factory farms use antibiotics without meaningfully affecting the amount that is used.

Before the recommendations, farmers purchased the vast majority of antibiotics under rules that allowed them to feed their livestock drugs to prevent disease. The Animal Health Institute, the trade association that represents large animal pharmaceutical companies, estimates that the antibiotics purchased under rules that allowed farmers to feed their livestock drugs for growth promotion made up a small fraction—"only 10-15

percent at best"—of all antibiotics administered to livestock.<sup>34</sup> In other words, the new recommendations can affect at most 10 to 15 percent of antibiotics given to animals.<sup>35</sup>

Even for these antibiotic sales targeted by the new rules, farmers can continue to administer the drugs by claiming that the antibiotics will be used for disease prevention purposes. According to the FDA recommendations, "FDA considers uses that are associated with the treatment, control, and *prevention of specific diseases* [emphasis added] to be therapeutic uses that are necessary for assuring the health of food-producing animals."<sup>36</sup>

With the exception of penicillin for chickens, all classes of antibiotics that the FDA has approved to promote growth in livestock have also been approved to prevent diseases in chickens, cows and pigs. (See Table 1.) In order for factory farms to give penicillin to chickens, pharmaceutical companies would need to get approval from the FDA by showing that the antibiotic class has prophylactic uses for the birds.

In a report to Congress, the Government Accountability Office (GAO) quoted a veterinary expert to explain how this

**Table 1: Almost All Antibiotic Classes Used to Promote Animal Growth Are Already Used to Prevent Diseases<sup>37</sup>**

Antibiotic Class	Chickens	Cows	Pigs
Tetracyclines	X	X	X
Macrolides	X	X	X
Lincosamides	X		X
Penicillin	X		X
Streptogramins	X	X	X

An X marks antibiotic classes that are used to promote animal growth. A shaded cell marks antibiotic classes that are also used to prevent animal diseases. The list of antibiotic classes excludes those that are used on factory farms, but not used in human medicine.



would work. According to the GAO, “if FDA withdrew an antibiotic’s approval for growth promotion, he [the veterinarian] could continue to give the antibiotic to the animals under his care at higher doses for prevention of a disease commonly found in this species. The veterinarian stated that there is an incentive to do so because using an animal antibiotic can help the producers he serves use less feed, resulting in cost savings.”<sup>38</sup> In other words, farmers could simply change the stated purpose of the drugs (from “weight gain” to “disease prevention”) to continue feeding animals the same antibiotic.

According to the FDA’s recommendations, factory farms can administer some antibiotics only with a prescription or veterinary-feed directive (often shortened to “VFD,” a prescription for antibiotics in animal food). Fewer drugs would be available on an over-the-counter basis than has historically been the case. However, factory farms are allowed to feed antibiotics to their animals without having a veterinarian-client-patient relationship, meaning that the antibiotics can be administered without a veterinarian ever assessing the animal in person.

While industrial agriculture companies typically have veterinarians on their staff and payroll, those staff oversee millions of animals. For example, both Foster Farms and Purdue Farms’ have corporate veterinarians who “oversee poultry health and welfare.”<sup>39</sup> However, according to the American Association of Avian Pathologists, “a corporate poultry veterinarian may be responsible for the health of several million birds spread across a number of production complexes that may be located in several states. Therefore, it is physically impossible for the corporate poultry veterinarian to be directly involved in every single diagnosis of disease.”<sup>40</sup>

## Pharmaceutical Executives Do Not Believe the FDA’s Recommendations Will Reduce Sales

Animal pharmaceutical companies do not believe *Guidance #213* will be effective in reducing the antibiotics fed to animals.

Since animal pharmaceutical companies profit from the sale of animal antibiotics, these companies could be expected to be concerned about government regulations that would lead to a dramatic reduction in sales—which would need to occur in order to effectively confront the threat of antibiotic resistance.

Several industry leaders, however, have publicly stated that they do not expect the new guidelines to have a major effect on their business.

In a presentation to shareholders, Juan Ramón Alaix, the CEO of Zoetis (which is the largest animal health care company in the world) said “Zoetis supports the U.S. FDA’s efforts, and ... we don’t expect this to have a material impact on our future financial results.”<sup>41</sup> A spokeswoman for Zoetis reinforced the CEO’s message, saying “we believe the impact of the FDA Guidances and [veterinary feed directive] on our revenues will not be significant.”<sup>42</sup>

Likewise, Jeff Simmons, president of the animal health division of Eli Lilly, the fourth largest animal health company in the world, stated “we do not see this announcement being a material event.”<sup>43</sup> When the company held a call in April 2014 announcing its acquisition of Novartis’ animal health business, the FDA guidance was not mentioned.<sup>44</sup>

According to Bimeda, a pharmaceutical company that sells drugs to factory farms, “growth uses of medically important antibiotics represent only a small percentage of overall use, so even if all other factors are

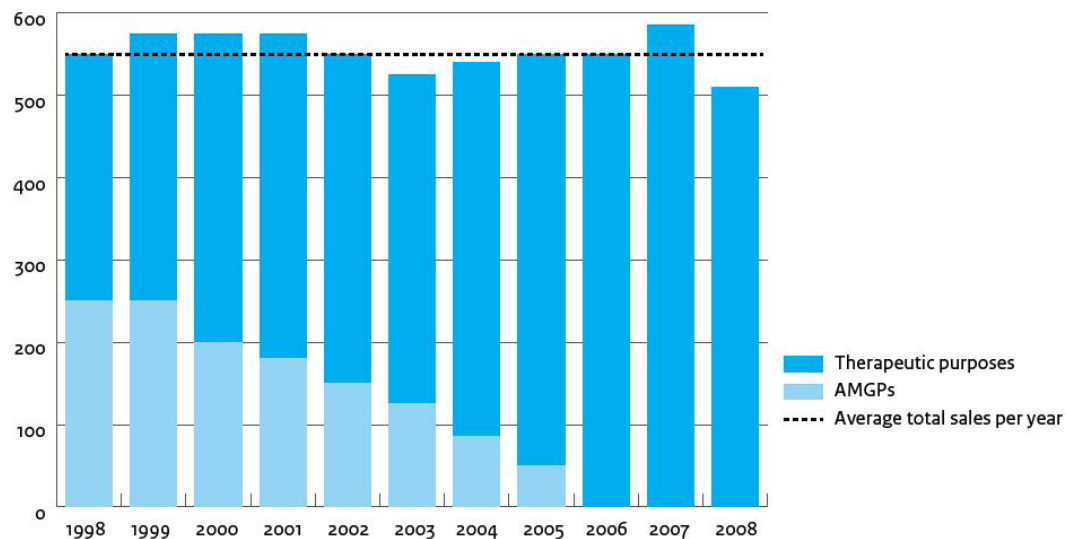
static it's unlikely overall use would be greatly affected" by the new FDA guidelines.<sup>45</sup>

Reflecting the comments from company officials, stock prices for animal pharmaceutical companies remained steady after the FDA's announcement on December 12, 2013, suggesting that investors were unconcerned about the impact of the FDA's recommendations on the companies' profitability. Instead, among the five largest animal health care companies in the world—Zoetis, Merck Animal Health, Sanofi (owns Merial), Eli Lilly (owns Elanco), and Bayer (owns Bayer Animal Health)—stock prices stayed level in the days after the announcement and generally increased in the following months.<sup>46</sup>

## Similar Rules in Europe Show that the FDA Should Have Implemented Stronger Recommendations

The European Union's ban on antibiotics for growth promotion—similar to the FDA's—did not significantly reduce the consumption of antibiotics on factory farms. Denmark's ban on antibiotics for growth promotion *and* disease prevention, on the other hand, significantly reduced the consumption of antibiotics.

**Figure 2: The European Union's Ban on Antibiotics for Disease Prevention Failed to Reduce Antibiotics Fed to Farm Animals in the Netherlands (sales of antibiotics in metric tons)<sup>50</sup>**



"Therapeutic purposes" include disease prevention. AMGP stands for Antimicrobial Growth Promoters.

## **The EU’s Ban on Antibiotics for “Growth Promotion” Was Insufficient in Protecting Human Health**

In the early 1970s, Europe banned the use of tetracycline, penicillin and streptomycin to make animals grow faster.<sup>47</sup> In the decades following, Europe banned other antibiotics for growth promotion purposes, culminating in an across-the-board ban on antibiotics for “growth promotion” by 2006—similar to the FDA’s 2013 recommendations.<sup>48</sup>

While many European countries did not track the effects of these bans, in the Netherlands—where data exist—the total use of antibiotics on farms did not decline. Farmers in the Netherlands simply reduced the antibiotics fed to animals for “growth promotion” and increased the antibiotics fed to animals for therapeutic purposes such as “disease prevention.”<sup>49</sup> (See Figure 2.)

After Europe’s ban on all growth-promotion antibiotics in 2006, total antibiotic consumption declined, though officials do not know the degree to which the ban contributed to the decline, if at all.

Across the eight European countries that recorded data between 2005 and 2009, the amount of antibiotics consumed per kilogram of animal decreased 8.2 percent.<sup>51</sup> Across the 20 European countries that recorded data between 2010 and 2011, 19 saw a decrease in animal antibiotic use, and the antibiotics consumed per kilogram of animal decreased 10.3 percent.<sup>52</sup> While this reduction is a step in the right direction, it still leaves the majority of antibiotic use unchanged.

In 2011, the European Union concluded the ban on antibiotics for growth promotion was not sufficient to reduce the threat of antibiotic-resistant bacteria and protect human health. A resolution adopted by the European Parliament found that “despite the ban on the use of antibiotics as

growth promoters ... additional efforts are ... required to improve the agricultural practices so as to help minimize the risk associated with the use of antibiotics for veterinary purposes and the development of resistance in humans.”<sup>53</sup>

## **Denmark’s Ban on Antibiotics for “Disease Prevention” Has Reduced Antibiotic Consumption and Protected Public Health**

In a step-by-step process from 1994 to 1999, Denmark banned the practice of feeding animals antibiotics for the purposes of preventing disease and accelerating growth.<sup>54</sup>

How did farmers in Denmark adapt to the new policies? They adopted better disease-prevention practices such as allowing piglets to nurse longer before being weaned, reducing overcrowding, creating airflow systems to lower the transmission of diseases, and raising animal breeds that are less likely to contract diseases.<sup>55</sup>

As a result, Denmark’s farms reduced their use of antibiotics.<sup>56</sup> From 1992 to 2008, antimicrobial use declined 51 percent on pig farms while pork production increased 47 percent, and antimicrobial use declined 90 percent on chicken farms, even though production slightly increased.<sup>57</sup>

This reduction in antibiotic use came with a very low price tag. According to the Danish Agriculture and Food Council, the average cost of raising pigs increased 1 euro per animal since the ban on antibiotics took effect.<sup>58</sup> Researchers at Iowa State University estimated the ban increased costs by 4.5 percent at most.<sup>59</sup>

In Denmark, the reduction in antibiotics fed to animals led to a reduction in antibiotic-resistant bacteria. By 1997—two years after the enactment of a ban on avoparcin—the prevalence of enterococci resistant to vancomycin, an antibiotic with a similar chemical structure to

avoparcin, had fallen significantly in pigs and humans.<sup>60</sup> (Enterococci are bacteria that cause urinary tract and other infections.<sup>61</sup>)

Initially, when farmers reduced the volume of antibiotics fed to pigs, more

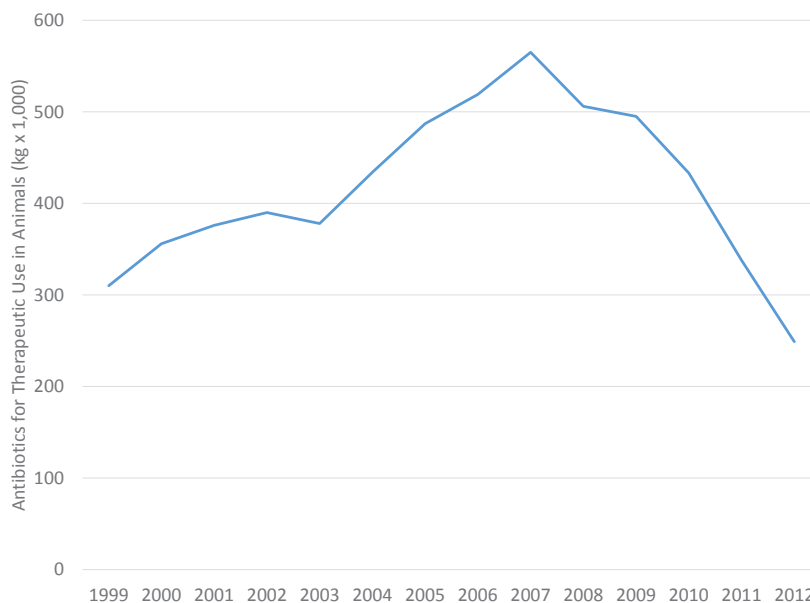
animals become sick, causing farmers to administer more valuable antibiotics to cure the illnesses. For example, use of third- and fourth-generation cephalosporins—which are used to cure strep throat in people—increased more than 300 percent.<sup>62</sup> In

## The Dutch Approach to Reducing the Overuse of Antibiotics on Factory Farms: 2008 to Today

With the ban on antibiotics for growth promotion failing to reduce the overuse of antibiotics on factory farms, the Netherlands government convened a task force in 2008 to address the problem. The result: reduction targets for the antibiotics consumed by livestock. Dutch farmers needed to reduce antibiotic consumption by 20 percent by 2011, 50 percent by 2012, and 70 percent by 2015 (from 2009 levels).<sup>67</sup>

These national targets were then translated into more specific goals for each herd, supported through inspections, improved reporting of antibiotic use, and potential disciplinary action for veterinarians. As a result, antibiotic use on farms fell. From 2007 and 2012, the amount of antibiotics fed to animals for therapeutic uses, such as disease prevention, was cut by more than 50 percent. (See Figure 3.)

**Figure 3: The Netherlands Reduced the Consumption of Antibiotics on Factory Farms for Therapeutic Purposes<sup>68</sup>**



response, Danish pig farmers implemented a voluntary ban on cephalosporins in 2010 at the same time the government began imposing better disease prevention measures at farms with the highest antibiotic use per pig.<sup>63</sup> By the next year, the amount of cephalosporins administered to pigs dropped close to zero.<sup>64</sup> As a result, in 2011,

the occurrence of cephalosporin-resistant bacteria declined from 11.8 percent to 3.6 percent at slaughterhouses and from 11 percent to 0 percent on farms.<sup>65</sup> Better disease prevention measures, such as greater use of vaccines, and slightly lower production helped maintain animal health.<sup>66</sup>

## Policy Recommendations

While the FDA has recommended that pharmaceutical companies no longer sell antibiotics to farms for “growth promotion,” this action is unlikely to put a serious dent in the amount of antibiotics fed to livestock. Without a reduction in the antibiotics used on factory farms, the development and spread of antibiotic-resistant bacteria will not slow down, and drugs important in human medicine will rapidly become less effective. To reduce antibiotic use on factory farms and protect our health, state governments, the FDA and other branches of the federal government should:

- Restrict the use of antibiotics in livestock production to cases of animal sickness or direct disease exposure. The use of antibiotics on factory farms for general “disease prevention” purposes should be banned.
- Ban the farm use of certain antibiotics that are especially valuable to human medicine, including fluoroquinolones, glycopeptides, macrolides, and third- and fourth-generation cephalosporin. The World Health Organization considers these drugs “critically important” due to the large number of people who rely on the antibiotics and for other reasons.<sup>69</sup>
- Create transparency over the antibiotics fed to animals by managing a registry of industrial farms’ usage of antibiotics. The registry should be accessible online and provide the public with information on the types, doses and purposes of antibiotics administered farm-by-farm. The data should be easily searchable and downloadable.
- Require that the administration of antibiotics to animals on factory farms be overseen by a qualified veterinarian who has been to the farm or ranch and assessed the animals in the recent past.
- Provide funding for research and development of antibiotic and non-antibiotic treatments. As today’s

antibiotics become less effective  
in killing infections, scientists and  
pharmaceutical companies should be

encouraged to discover new  
antibiotic classes to cure human  
diseases.

## Notes

- 1 Howard Markel, “The Real Story Behind Penicillin,” *PBS*, 27 September 2013.
- 2 “CDC: 4 out of 5 Americans Prescribed Antibiotics Each Year,” *CBS*, 11 April 2013.
- 3 Alexander Fleming, *Penicillin: Nobel Lecture*, 11 December 1945.
- 4 R.H. Gustafson and R.E. Bowen, “Antibiotic Use in Animal Agriculture,” *Journal of Applied Microbiology*, 83: 531-541, 1997.
- 5 Peter Lehner, Natural Resources Defense Council, *Superbug Suit: Antibiotics Victory Will Preserve Medicines for Sick People, Not Healthy Livestock* (blog), 23 March 2012.
- 6 Food and Drug Administration, *FDA Takes Significant Steps to Address Antimicrobial Resistance* (press release), 11 December 2013.
- 7 American Academy of Pediatrics, “The History of Antibiotics,” *HealthyChildren.org*, 31 March 2014.
- 8 “The Drugs Don’t Work: Running Out of Ammunition in the War on Germs,” *The Economist*, 3 May 2014.
- 9 World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance*, 2014, 5.
- 10 Katherine Xue, “Superbug: An Epidemic Begins,” *Harvard Magazine*, May-June 2014.
- 11 Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013*, 23 April 2013, 6.
- 12 *Ibid.*, 11.
- 13 Alliance for Prudent Use of Antibiotics (APUA), *The Cost of Antibiotic Resistance to U.S. Families and the Health Care System*, September 2010.



- 14 See note 11, 28.
- 15 See note 10.
- 16 Ibid.
- 17 Government Accountability Office, *Antibiotic Resistance: Agencies Have Made Limited Progress Addressing Antibiotic Use in Animals*, September 2011, 28.
- 18 For more information see National Resources Defense Council, *Antimicrobial Stewardship Policy for Poultry*, September 2013.
- 19 University of Minnesota, Food Policy Research Center, *Issue Brief: Balancing the Health Impacts of Antibiotic Use in Animal Feed*, August 2013.
- 20 Jessica Rinsky, et al., “Livestock-Associated Methicillin and Multidrug Resistant *Staphylococcus aureus* Is Present among Industrial, Not Antibiotic-Free Livestock Operation Workers in North Carolina,” *PLoS ONE*, 8(7): e67641, doi:10.1371/journal.pone.0067641, 2 July 2013.
- 21 Johns Hopkins Bloomberg School of Public Health, *Exposure to Pig Farms and Manure Fertilizers Associated with MRSA Infections*, accessed at [www.jhsph.edu/departments/environmental-health-sciences/news-and-events/mrsastudy.html](http://www.jhsph.edu/departments/environmental-health-sciences/news-and-events/mrsastudy.html), 13 August 2014.
- 22 U.S. Department of Veterans Affairs, Health Services Research & Development, *VA/HSR&D Researchers Suggest Veterans Living Near Pig Confinement Operations Are More Susceptible to MRSA*, 30 January 2014.
- 23 Carol Cogliani, Herman Goossens, and Christina Greko, “Restricting Antimicrobial Use in Food Animals: Lessons from Europe,” *Microbe*, 6(6): 274-279, 2011; American Society for Microbiology, *The American Society for Microbiology Honors Stuart B. Levy* (press release), 6 June 2012.
- 24 Shawn Gibbs, et al., “Isolation of Antibiotic-Resistant Bacteria from the Air Plume Downwind of a Swine Confined or Concentrated Animal Feeding Operation,” *Environmental Health Perspectives*, 114(7): 1032-1037, doi: 10.1289/ehp.8910, July 2006.
- 25 Congresswoman Louise M. Slaughter, *Confirmed: 80 Percent of All Antibacterial Drugs Used on Animals, Endangering Human Health* (press release), 23 February 2011.
- 26 Jonathan Kaplan, et al., National Resources Defense Council, *Pharming Chickens: It’s Time for the U.S. Poultry Industry to Demonstrate Antibiotic Stewardship* (issue brief), April 2014, 3.
- 27 Brad Plumer, “Wonkblog: The FDA Is Cracking down on Antibiotics on Farms. Here’s What You Should Know,” *Washington Post*, 14 December 2013.
- 28 The Pew Charitable Trusts, *Antibiotics and Industrial Farming 101*, 5 May 2014.
- 29 Population: U.S. Census Bureau, Population Division, *Table US 2001EST-01 Time Series of National Population Estimates: April 1, 2000 to July 1, 2001*, 27 December 2001, and U.S. Census Bureau, Population Division, *Table 1. Annual Estimates of the Population for the United States, Regions, States, and Puerto Rico: April 1, 2010 to July 1, 2011* (NST-EST2011-01), December 2011.

30 See note 28.

31 Food and Drug Administration, *Guidance for Industry #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 Voluntary Aligning Product Use Conditions with GFI #209*, December 2013.

32 Ibid. and note 27.

33 Three years: see note 31. All 26 affected companies: U.S. Food and Drug Administration, *FDA Secures Full Industry Engagement on Antimicrobial Resistance Strategy* (press release), 30 June 2014.

34 10 to 15 percent: Beth Hoffman, "New FDA 'Rules' Not Likely To Reduce Antibiotic Use On Farm," *Forbes*, 13 December, 2013.

35 Ibid.

36 See note 31.

37 Data for this chart: see note 17. The chart from the Government Accountability Office was amended and updated: Macrolides can be fed to cows and pigs for disease prevention: U.S. Food and Drug Administration, *NADA Number: 012-491*, downloaded from [www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=012-491](http://www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=012-491), 31 July 2014; Lincomycin can be fed to chickens for disease prevention: U.S. Food and Drug Administration, *NADA Number: 097-505*, downloaded from [www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=097-505](http://www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=097-505), 31 July 2014; Penicillin can be

fed to pigs for disease prevention: U.S. Food and Drug Administration, *NADA Number 138-934*, downloaded from [www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=138-934](http://www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=138-934), 31 July 2014; Streptogramins can be fed to pigs for disease prevention: U.S. Food and Drug Administration, *NADA Number: 091-513*, downloaded from [www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=091-513](http://www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=091-513), 31 July 2014; Pleromutilins can no longer be fed to promote growth, so it was removed from the chart: Steve Roach, Food Animal Concerns Trust (FACT), personal communication, 31 July 2014.

38 See note 17.

39 Quote is from: Perdue, *Corporate Responsibility: Our Aspirations to Our Consumers*, downloaded from [www.perduefarms.com/Corporate\\_Responsibility/Our\\_Aspirations/Consumers/Poultry\\_Welfare](http://www.perduefarms.com/Corporate_Responsibility/Our_Aspirations/Consumers/Poultry_Welfare), 21 July 2014; Foster Farms, *How We Raise Foster Farms Poultry*, downloaded from [www.fosterfarms.com/faq/raise.asp](http://www.fosterfarms.com/faq/raise.asp), 21 July 2014.

40 Charles Hofacre, Secretary/Treasurer, American Association of Avian Pathologists, Letter to Food and Drug Administration *Re: Advance Notice of Proposed Rulemaking – Veterinary Feed Directive - (Docket No. FDA 2010-N-0155)*, 17 August 2010. Available at [www.regulations.gov/#!documentDetail;D=FDA-2010-N-0155-0048](http://www.regulations.gov/#!documentDetail;D=FDA-2010-N-0155-0048).

41 Quote: Zoetis, Inc., *Q3 2013 Earnings Call* (corrected transcript), 5 November 2013; Largest animal health company: Bob Sperber, "Animal-Health Pharmaceuticals Are Jumping

the ‘Ethical Channel,’” *Pharmaceutical Commerce*, 2 May 2013.

42 See note 34.

43 Quote: Mark Bittman, “The F.D.A.’s Not-Really-Such-Good-News,” *The New York Times*, 17 December 2013; Kelsey Gee, “Meat Industry Won’t Fight Antibiotics Rule,” *The Wall Street Journal*, 12 December 2013; Fourth largest animal health company in the world: Bob Sperber, “Animal-Health Pharmaceuticals Are Jumping the ‘Ethical Channel,’” *Pharmaceutical Commerce*, 2 May 2013.

44 John Tozzi, “Restrictions on Livestock Antibiotics Don’t Worry the Drugmakers,” *Bloomberg Businessweek*, 7 May 2014.

45 Bimeda, *Effects of FDA’s Proposed New Regulations Regarding: “Judicious Use of Antibiotics in Medicated Feed and Drinking Water of Food Animals”* (Q&A), February 2014.

46 Five largest animal health companies in the world: Bob Sperber, “Animal-Health Pharmaceuticals Are Jumping the ‘Ethical Channel,’” *Pharmaceutical Commerce*, 2 May 2013; Zoetis: Bloomberg, *ZTS: US*, downloaded from [www.bloomberg.com/quote/ZTS:US](http://www.bloomberg.com/quote/ZTS:US), 21 July 2014; Sanofi: Bloomberg, *SAN:FP*, downloaded from [www.bloomberg.com/quote/SAN:FP](http://www.bloomberg.com/quote/SAN:FP), 21 July 2014; Merck, Eli Lilly and Bayer: Google Finance, stock price history is displayed by searching for the companies’ names: Sanofi owns Merial: Merial, *Merial* (mainpage of Merial website), [www.merial.com](http://www.merial.com), 21 July 2014; Eli Lilly owns Elanco: Elanco, *About Us*, downloaded from [www.elanco.com/about/default.aspx](http://www.elanco.com/about/default.aspx), 21 July 2014.

47 Europe banning antibiotics for growth promotion in 1972: Carol Cogliani, Herman Goossens, and Christina Greko, “Restricting Antimicrobial use in Food Animals: Lessons from Europe,” *Microbe*, 6(6): 274-279, 2011.

48 Ibid., and Commission on the European Communities, *Communications from the Commission on a Community Strategy Against Antimicrobial Resistance*, 20 June 2001, 14.

49 Carol Cogliani, Herman Goossens, and Christina Greko, “Restricting Antimicrobial Use in Food Animals: Lessons from Europe,” *Microbe*, 6(6): 274-279, 2011.

50 Netherlands Ministry of Economic Affairs, *Reduced and Responsible: Policy on the Use of Antibiotics in Food-Producing Animals in the Netherlands*, February 2014.

51 European Medicines Agency, *Trends in the Sales of Veterinary Antimicrobial Agents in Nine European Countries: Reporting Period: 2005-2009*, 2011, 52.

52 Statistics derived from Table 5 of European Medicines Agency, *Sales of Veterinary Antimicrobial Agents in 25 EU/EEA Countries in 2011: Third ESVAC Report*, 2013. Note: Due to changes in reporting methods between 2009 and 2010, we were unable to calculate the change in antibiotic consumption between those years per European Medicines Agency, *Sales of Veterinary Antimicrobial Agents in 19 EU/EEA Countries in 2010: Second ESVAC Report*, 2012, 45.

53 European Parliament, *P7\_TA(2011)0473, Public Health Threat of*

*Antimicrobial Resistance, European Parliament Resolution of 27 October 2011 on the Public Health Threat of Antimicrobial Resistance*, 27 October 2011, available at <http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2011-0473+0+DOC+XML+V0//EN>.

54 1994: Ministry of Food, Agriculture and Fishers, Danish Veterinary and Food Administration, *Fact Sheets: On the Danish Restrictions of Non-Therapeutical Use of Antibiotics for Growth Promotion and Its Consequences*, 12 July 2010, 3; 1999: Dan Charles, "Europe's Mixed Record on Animal Antibiotics," *NPR*, 23 March 2012.

55 Dan Charles, "Europe's Mixed Record on Animal Antibiotics," *NPR*, 23 March 2012.

56 Ministry of Food, Agriculture and Fishers, Danish Veterinary and Food Administration, *Fact Sheets: On the Danish Restrictions of Non-Therapeutical Use of Antibiotics for Growth Promotion and Its Consequences*, 12 July 2010, 3.

57 See note 49.

58 Sharon Levy, "Reduced Antibiotic Use in Livestock: How Denmark Tackled Resistance," *Environmental Health Perspectives*, 122(6): A160-A165, June 2014.

59 Dermot Hayes and Helen Jensen, "Lessons from the Danish Ban on Feed-Grade Antibiotics," *Choices: The Magazine of Food, Farm and Resource Issues*, August 2003.

60 See note 58; K.H. Ekborg-Ott, et al., "Evaluation of the Macrocylic Antibiotic Avoparcin as a New Chiral

Selector for HPLC," *Chirality*, 10(7): 627-660, 1998.

61 B.H. Heintz, et al., "Vancomycin-Resistant Enterococcal Urinary Tract Infections," *Pharmacotherapy*, 30(11): 1136-1149, November 2010.

62 See note 55.

63 Statens Serum Institut and Technical University of Denmark, *DANMAP 2011 – Use of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Bacteria from Food Animals, Food and Humans in Denmark*, September 2012, 16.

64 Ibid.

65 Yvonne Agersø and Frank Aarestrup, "Voluntary Ban on Cephalosporin Use in Danish Pig Production Has Effectively Reduced Extended-Spectrum Cephalosporinase-Producing *Escherichia coli* in Pigs," *Journal of Anti-Microbial Chemotherapy*, 68: 569-572, 5 November 2012.

66 See note 63, 36.

67 Ministry of Economic Affairs, *Reduced and Responsible: Policy on the Use of Antibiotics in Food-Producing Animals in the Netherlands*, February 2014, 4; Dik Mevius and Dick Heederik, "Reduction of Antibiotic Use in Animals 'Let's Go Dutch,'" *Journal für Verbraucherschutz und Lebensmittelsicherheit*, 9(2):177-181, 19 February 2014, 179; Note: The 70 percent reduction target by 2015 was set in 2012.

68 Dik Mevius and Dick Heederik, "Reduction of Antibiotic Use in Animals 'Let's Go Dutch,'" *Journal für Verbraucherschutz und*

*Lebensmittelsicherheit*, 9(2):177-181,  
19 February 2014; and Autoriteit  
Diergeenmiddelen, *Usage of Antibiotics  
in Livestock in the Netherlands in 2012*, July  
2013.

69 World Health Organization, *Critically  
Important Antimicrobials for Human  
Medicine: 3<sup>rd</sup> Revision 2011*, 2012, 31 and  
36.