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ISSUE BRIEF

U.S. LIVESTOCK INDUSTRIES PERSIST IN HIGH-INTENSITY ANTIBIOTIC USE

CURBING OVERUSE IS CRITICAL TO SLOW THE SPREAD OF ANTIBIOTIC RESISTANCE

Antibiotic resistance is a global crisis, having risen to dangerous levels in all parts of the world.[1] In the United States alone, more than 2.8 million people fall ill with antibiotic-resistant infections annually.[2] At least 35,000 of them die, and likely many more.[3]

Antibiotic-resistance occurs when bacteria, due to prolonged exposure to antibiotics, evolve the ability to withstand them, often acquiring resistance to several antibiotics at a time.[4] These "superbugs," as they are sometimes called, spread without respect to national borders.[5] It is now harder—and, for a rising number of cases, impossible—to effectively treat people suffering from superbug-caused infections; more deaths ensue as a result.

The more we use antibiotics, the faster drug-resistant bacteria will spread, increasing the global threat. All antibiotic use contributes to the problem.[6] So while some uses of antibiotics are essential and can be lifesaving, many others are unnecessary or avoidable and therefore constitute overuse.[7] Expert warnings have become ever more urgent:

If we continue taking precious antibiotics for granted by overusing them, they will increasingly fail when we need them most.[8]

Tackling overuse is a public health imperative. But curbing overuse in human medicine alone is insufficient because these same antibiotic classes are often used excessively in raising livestock such as cattle, pigs, and other food-producing animals.[9] Worldwide, an estimated 73 percent of all medically important antibiotics are sold for livestock use rather than for people, and just three countries are thought to account for 60 percent of these livestock sales: China (45 percent), Brazil (8 percent), and the United States (7 percent).[10,a] Livestock antibiotics, according to experts, are used mostly to make food animals grow more quickly or as a cheaper surrogate for on-farm changes, such as improvements to animal nutrition and hygiene, known to boost animal health and prevent disease, thereby avoiding the need for antibiotics in the first place.[11]

Reducing antibiotic overuse in livestock requires that data first be collected on where and how antibiotics are being used and at what intensity. This holds true at the individual farm level as well as at the national level. Comparison of different countries' success in curbing antibiotic use is optimal because levels of bacterial resistance are already dangerously high worldwide, and antibiotic resistance spreads across national borders. Every country has a public health stake in knowing which nations are leading or lagging in antibiotic stewardship and the degree to which their individual livestock sectors have reduced the intensity of antibiotic use.

a Hereafter, when *antibiotics* is used in this brief in reference to livestock, it should be understood as referring to medically important antibiotics, unless otherwise indicated.

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Ideally, these data would come from comprehensive on-farm tracking of antibiotic use, which can help identify patterns of overuse. In fact, many experts now recognize the public health urgency for countries to build national surveillance systems to closely track antibiotic use, including veterinary antibiotic use at the farm level.[12] Yet most countries, including the United States, have failed to do so. The exception is countries in Europe. In 2009, at the direction of the European Commission, the European Medicines Agency (EMA) launched a major region-wide initiative to standardize the collection and reporting of national data on sales and use of livestock antibiotics.[13] In 2022 new European legislation took effect with an accelerated timeline that will soon require all European Union member countries to track antibiotic use at the farm level.

Even where farm-level data are lacking, estimates of livestock antibiotic use can be derived from national sales data. The United States and at least 40 other countries, most of them in Europe, already collect and report national sales data.[14] The EMA and other public health experts, along with the World Organization of Animal Health (WOAH), consider weight-adjusted antibiotic sales to be an appropriate basis for estimating the actual use of antibiotics in livestock.[15] The EMA has issued annual reports on antibiotic sales for dozens of countries on both a raw (unadjusted) and weight-adjusted basis for more than a decade.

Using annual sales data already available from the U.S. Food and Drug Administration (FDA) and the EMA, this issue brief compares how patterns of livestock antibiotic use in the United States and Europe changed from 2011 to 2020. Our analysis found that:

- **The U.S. livestock sector as a whole uses far more antibiotics each year than are used in human medicine, as reflected by raw sales data** (Figure 1A).
- **Raw antibiotic sales for European livestock production, 2011 to 2020, dropped further and more consistently than they did in the United States.** Raw U.S. sales declined by 27.3 percent, while raw sales for livestock production aggregated across 25 European countries fell by 42.9 percent (Figure 1B).
- **The intensity of antibiotic use in European livestock production during those same years fell further and more consistently than it did in the United States.** The intensity of use in the U.S. livestock sector as a whole (measured as milligrams per kilogram of livestock) declined 30.4 percent, while it fell 43.2 percent among livestock producers aggregated across 25 European countries. This decline in Europe, however, is in addition to presumed reductions that accompanied the European Commission's much earlier (2006) ban on the use of antibiotics for livestock growth promotion. In the U.S., reductions in antibiotic use intensity took place from 2015 to 2017, when the FDA asked animal drug makers to voluntarily stop marketing their medically important antibiotic products for growth promotion purposes. There has been no net decline since then (Table 1).
- **High-intensity antibiotic use persists within the U.S. livestock sector.** In 2020 the intensity of antibiotic use in the U.S. livestock sector was an estimated 170.8 mg/kg-livestock, nearly twice as high as the overall rate reported that year for the European livestock sector (91.6 mg/kg-livestock) (Figure 2).

These findings should ignite a sense of urgency for U.S. policymakers. A more effective U.S. response to antibiotic resistance can be modeled after Europe, where stewardship has consistently improved and reductions in antibiotic use exceeding 50 percent are commonplace. On page 7 are three key changes that could put U.S. antibiotics policy back on course to protecting public health.

OUR APPROACH

Since 2018 NRDC has been comparing the FDA's efforts to track and respond to livestock antibiotic use and overuse with the efforts of European officials.[16] This issue brief updates previous analyses using the most recent U.S. and European data. More details can be found in the accompanying Appendix.

Both the FDA and the EMA started 2009 initiatives to collect and report data pertaining to antibiotic use in livestock production.[17] They began with national sales of these antibiotics, information that is relatively easy to collect. As a result, U.S. sales data are currently available for 2009 through 2020.[18] European sales data are available for up to 31 countries, as far back as 2005 for some of them; 25 countries have been providing national sales data to the EMA continuously since 2011.[19] Worldwide, at least 41 countries now report national sales data, including the United States; Denmark was the first country to do so, starting in 1996.[20]

Merely knowing the annual volume of livestock antibiotics sold, however, does not provide any information about whether there is growth in the number of animals receiving antibiotics from one year to the next, or whether the species makeup of those animals has changed. With a straightforward adjustment, however, sales data can serve as the basis for estimating actual antibiotic use in livestock populations. The WOAH has long endorsed using national sales data for precisely this purpose when data on actual antibiotic use are not being collected or otherwise available.[21,b] So it is not surprising that soon after the EMA's 2009 launch of its European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, it quickly developed and began using a method to normalize, or weight-adjust, national antibiotic sales by the size of the animal population likely to have received those antibiotics.[22]

Weight-adjusted sales are estimates of the rate of antibiotic use by livestock producers for the year in question. They are expressed on a mg/kg basis, or alternatively as mg/PCUs (population correction units). ESVAC refers to them as rates of antibiotic "consumption," but our issue brief refers to them

b The United States is one of 182 WOAH members, and the FDA's Center for Veterinary Medicine is a WOAH "Collaborating Center".

instead as measures of the "intensity" of antibiotic use. Each ESVAC report to date has included both raw (unadjusted) and weight-adjusted versions of the national sales data collected from participating countries; an online ESVAC database contains the most recent updates to these data.[23]

In 2017 an independent commission of physicians, veterinarians, and public health experts agreed with the EMA that antibiotic sales data are most policy-relevant when expressed using a weight-adjusted metric to facilitate comparisons across time or among countries.[24] The commission urged the FDA to begin weight-adjusting its own sales figures, ideally using the methods and mg/kg metric already devised and long used by the EMA. That same year, the FDA issued a public proposal for weight adjustment of sales data, but it then failed to follow through.[25]

Five years later, just as this issue brief went into production, the FDA finally published some weight-adjusted sales data, albeit on a very limited basis.[26] The agency weight-adjusted U.S. sales figures only for 2016 through 2019, and only for individual animal species. Notably, the FDA did not weight-adjust national antibiotic sales across the entire livestock sector, which is how the EMA has reported weight-adjusted sales since 2010. Further, FDA leaders say they have no intention to retrospectively weight-adjust raw national sales figures already issued for 2009 through 2015, nor do they plan to issue annual sales reports that include both raw and weight-adjusted sales figures, side by side, as does the EMA.[27]

When the FDA finally did issue weight-adjusted sales data, it used its own unique method and terminology rather than the already validated method the EMA has been applying since 2010 to sales data from as many as 31 European countries. Whatever the FDA's reasoning, its decision clearly hinders the ability to compare different countries' success around antibiotic stewardship on an equivalent basis. Accordingly, our analysis does not incorporate the new FDA numbers and instead continues to use data derived using the same methods as the EMA. The figures and discussion below summarize our results.

We begin by comparing raw U.S. antibiotic sales for raising livestock and for use in human medicine from 2011 to 2020; then we compare U.S. livestock antibiotic sales to those in Europe over the same span of time (Figures 1A and 1B). The principal aim of our analysis is to use weight-adjusted sales, calculated on an apples-to-apples basis, to compare the intensity of antibiotic use in the United States and Europe over roughly the same time frame (Figure 2). Details of our analysis can be found in the Appendix.


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U.S. ANTIBIOTIC SALES ARE PERSISTENTLY HIGHER FOR LIVESTOCK USE THAN FOR HUMAN MEDICINE

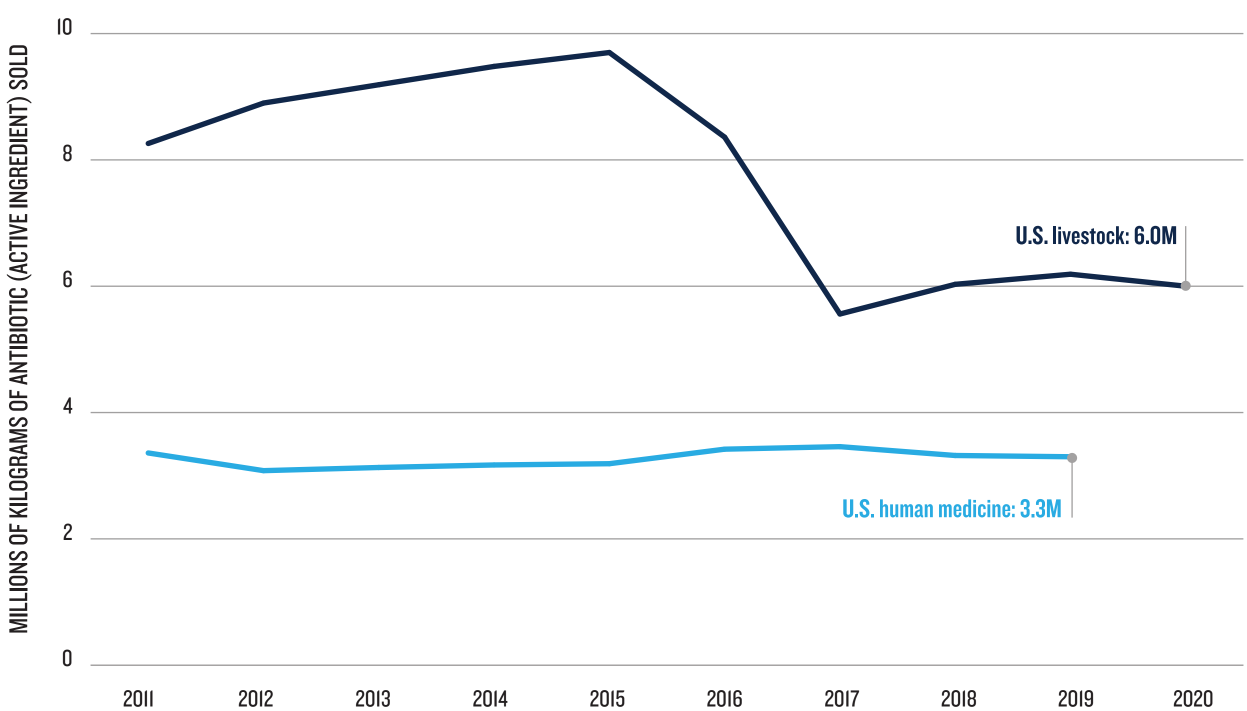
Figure 1A shows that U.S. sales of medically important antibiotics for livestock use since 2011 have remained persistently high relative to sales for use in human medicine. At their peak, in 2015, nearly three times more medically important antibiotics (74.9 percent of the U.S. total) were sold for livestock use than were sold for use in human medicine. (See the data table accompanying Figure 1A in the Appendix.) In 2019, the last year for which human sales are currently available, almost twice as much of these precious medicines were still being sold for livestock as for use in human beings.

The intent and manner of antibiotic use is very different in people and in food animals. In human medicine, antibiotics are almost always given by mouth, injection, or IV to treat an infection diagnosed in a sick patient. Just 6 percent of livestock antibiotics sold in the United States are in an injectable form, while 92 percent are products to be given via feed or drinking water to groups of animals.[28] Worldwide, treatment of sick animals represents only a very small portion of total livestock antibiotic use. Instead, antibiotics are most often used to promote faster growth or for mass disease prevention, both of which involve exposing healthy animals to low-dose antibiotics in feed over long periods.

For decades, experts have raised alarms that routine and avoidable uses of antibiotics in livestock contribute to development and spread of antibiotic-resistant bacteria. The biomass of livestock in the United States and around the world far exceeds human biomass, and in many countries outside Europe—including the United States—antibiotic use typically is more intense in livestock, which translates into a greater likelihood that antibiotic-resistant mutations will arise in these animal populations than in human settings.[29] In addition, the extended use of low-dose antibiotics in feed for healthy animals creates ideal conditions for antibiotic-resistant strains of bacteria to thrive, multiply, and spread into the human population.[30] In fact, the science has long been clear that antibiotic-resistant bacteria do spread from livestock animals to human populations, including directly via the farmers and other workers handling those animals and indirectly through bacteria-contaminated water, soil, and air as well as on contaminated meats.[31]

For these reasons, there is public health value in comparing raw U.S. sales of antibiotics for use in humans against sales for use in food animals. We can clearly see that stewardship efforts have succeeded in keeping human sales steady despite a general increase in the U.S. population. By contrast, raw livestock sales have increased nearly every year since 2011 (with only a small drop from 2019 to 2020, and a somewhat more significant drop from 2015 to 2017, which will be discussed in later sections).

FIGURE 1A: SALES OF MEDICALLY IMPORTANT ANTIBIOTICS FOR U.S. LIVESTOCK PRODUCTION AND HUMAN MEDICINE, 2011 TO 2020



Sources: U.S. livestock sales are from the U.S. Food and Drug Administration, Annual Summary Reports on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, www.fda.gov/industry/animal-drug-user-fee-act-adufa/adufa-reports; U.S. human antibiotic sales are from One Health Trust (previously the Center for Disease Dynamics, Economics & Policy), which obtained them from IQVIA, a private company, as described in D Wallinga, E Klein, and A Hamilton, US Livestock Antibiotic Use is Rising, Medical Use Falls (blog), NRDC, www.nrdc.org/experts/david-wallinga-md/us-livestock-antibiotic-use-rising-medical-use-falls-0.

ANTIBIOTIC SALES HAVE FALLEN FURTHER AND MORE CONSISTENTLY IN EUROPE THAN IN THE UNITED STATES

Figure 1B shows that raw antibiotic sales for livestock aggregated across the 25 European countries providing data, and despite brief upticks in sales in 2014 and in 2020, declined further and more consistently from 2011 to 2020 than did U.S. sales. The only declines in U.S. sales occurred from 2019 to 2020 and from 2015 to 2017, the latter being the period leading up to the FDA's 2017 ban on further use of these antibiotics to promote growth.

The 25 European countries represented in Figure 1B cover "approximately 95 percent of the food-producing animal population in the EU/EEA area," according to the EMA, making them a reasonable stand-in for Europe as a whole.[32] As explained in the Appendix, however, the size of the livestock population aggregated across these 25 countries in 2020 was 56.5 billion kilograms, or around 61 percent larger than the calculated size of the U.S. livestock population that same year (35.1 billion kilograms).

Since 2012, Europe's livestock producers collectively have consumed fewer antibiotics than have their U.S. counterparts in every year but one. Europe's thriftier use of antibiotics is even more impressive because its livestock population is around 61 percent larger than the U.S. population, and is produced on a landmass much smaller than the size of the continental U.S.[33]

HIGH-INTENSITY ANTIBIOTIC USE PERSISTS IN THE U.S. LIVESTOCK SECTOR

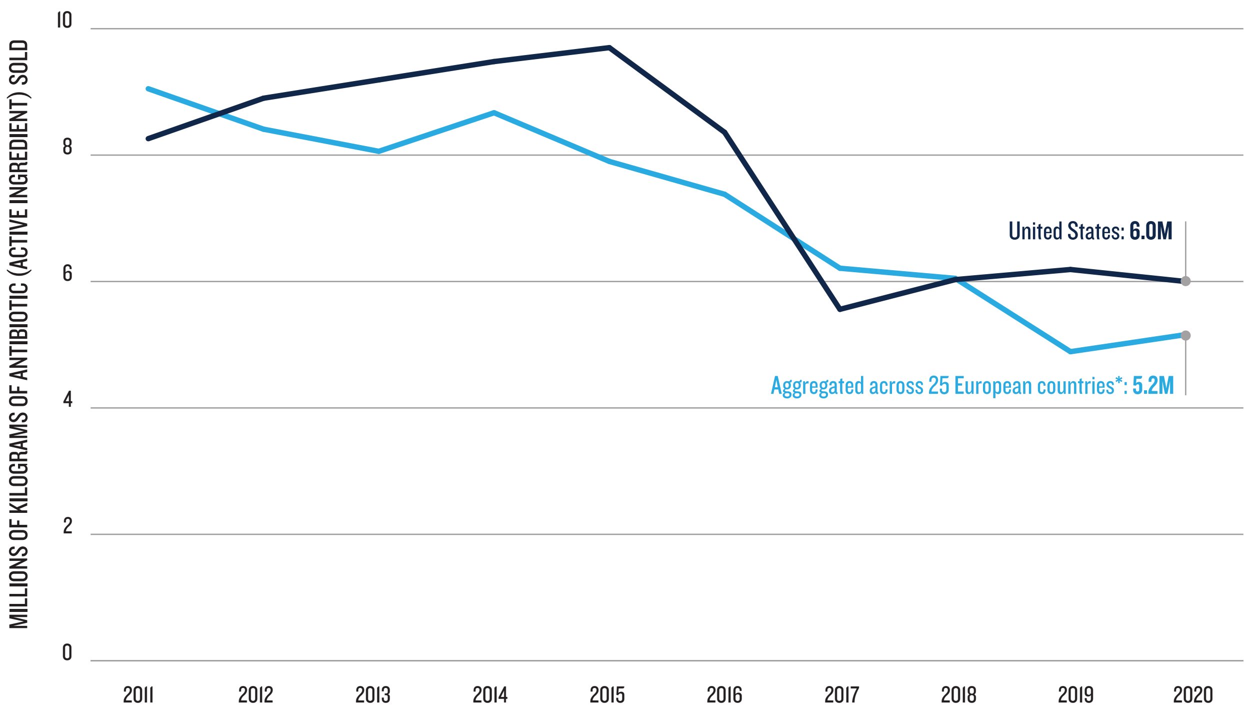
High-intensity antibiotic use has persisted in the U.S. livestock sector for longer than it has in Europe, as shown in Figure 2.

From 2011 to 2020, the intensity of livestock antibiotic use aggregated across 25 European countries fell further than in the United States (a decline of 43.2 percent versus 30.4 percent). It dropped even more in continental Europe's top three livestock-producing countries, Germany (60.4 percent), Spain (54.1 percent), and France (50.5 percent). In fact, six of Europe's top seven livestock producers reduced their intensity of antibiotic use by at least 50 percent from 2011 to 2020. (See the Appendix for more details).

TABLE 1: DECLINE IN INTENSITY OF ANTIBIOTIC USE IN LIVESTOCK PRODUCTION IN THE U.S. AND SELECT EUROPEAN COUNTRIES, 2011 TO 2020

Country	% decline
United States	−30.4
All 25 European countries	−43.2
France	−50.5
Spain	−54.1
Germany	−60.4

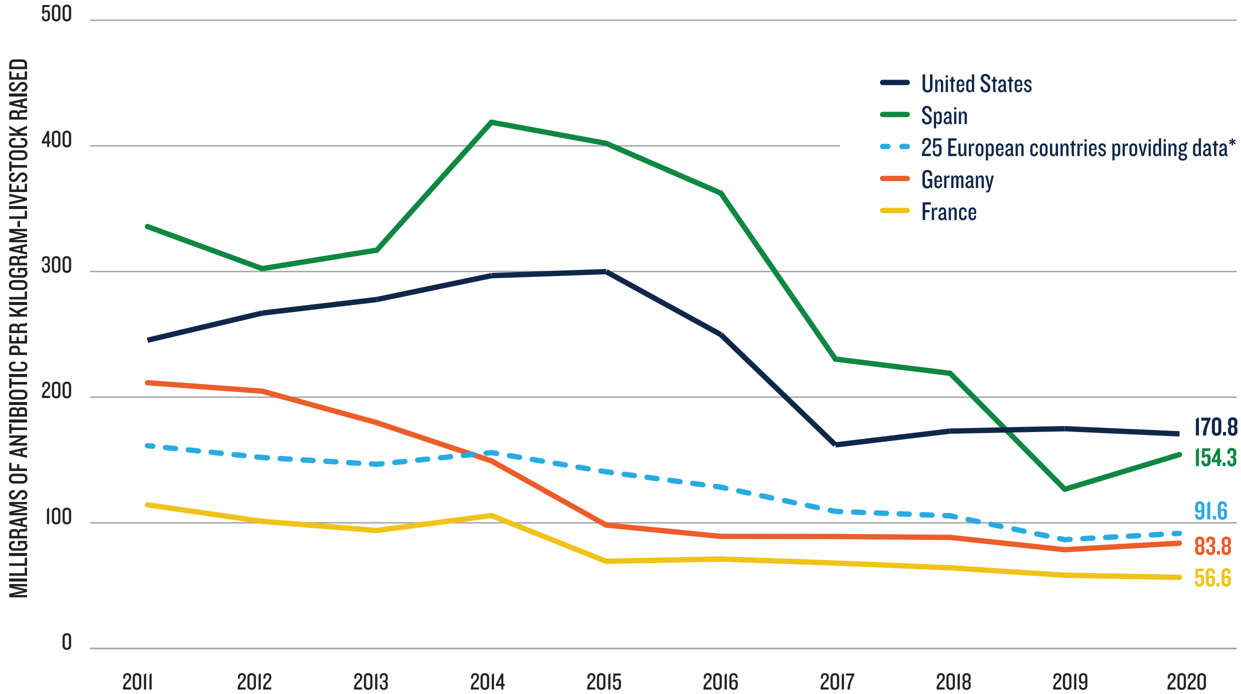
FIGURE 1B: SALES OF MEDICALLY IMPORTANT ANTIBIOTICS FOR U.S. AND EUROPEAN LIVESTOCK PRODUCTION, 2011 TO 2020



* The 25 countries providing national sales data to the European Medicines Agency for this time period were Austria, Belgium, Bulgaria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Sources: US livestock sales are from the U.S. Food and Drug Administration, Annual Summary Reports on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, https://www.fda.gov/industry/animal-drug-user-fee-act-adufa/adufa-reports; European data are from European Medicines Agency, European database of sales of veterinary animicrobial agents, accessed May 30, 2022, https://esvacbi.ema.europa.eu/analytics/saw.dll?Dashboard.

FIGURE 2: INTENSITY OF MEDICALLY IMPORTANT ANTIBIOTICS USED IN U.S. AND EUROPEAN LIVESTOCK PRODUCTION, 2011 TO 2020 (MILLIGRAMS OF ANTIBIOTIC ACTIVE INGREDIENT PER KILOGRAM OF LIVESTOCK RAISED)



* The 25 countries providing national sales data to the European Medicines Agency for this time period were Austria, Belgium, Bulgaria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Sources: European Medicines Agency, European database of sales of veterinary animicrobial agents, accessed May 30, 2022, https://esvacbi.ema.europa.eu/analytics/saw.dll?Dashboard; U.S. Food and Drug Administration, Annual Summary Reports on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, https://www.fda.gov/industry/animal-drug-user-fee-act-adufa/adufa-reports.

It is likely that reductions in antibiotic use among European countries since 2011 are due at least in part to the European Commission's region-wide commitment to slowing the spread of resistance through better antibiotic stewardship. As a result of this commitment, European agencies have elevated the importance of primary disease prevention: keeping animals healthier in the first place by improving animal breeds and husbandry, greater use of vaccines, and changes to other on-farm practices, thus avoiding disease along with the subsequent need for antibiotics to treat that disease.[34] Another key component of the EC strategy was the creation of ESVAC in 2009 to standardize European collection and reporting of national data on antibiotic sales and use. By using common methods and metrics, this regional surveillance program has provided the means for measuring progress toward better antibiotic stewardship in individual countries and across the region as a whole. The reductions in antibiotic use intensity shown in Figure 2 suggest this approach has worked well.

By contrast, the FDA's goal, as spelled out in its current action plan, is to "foster" veterinary antibiotic stewardship through education and voluntary actions by pharmaceutical companies and by U.S. livestock producers and their veterinarians.[35] The 2017 ban on the use of medically important antibiotics for growth promotion was an exception to the FDA's largely voluntary program. As Figure 2 indicates, the program has produced no net improvement in veterinary antibiotic stewardship since 2017. In fact, the intensity of antibiotic use in U.S. livestock production as a whole was 5.5 percent higher in 2020 than in 2017, as shown in Table 2.

HIGH-INTENSITY ANTIBIOTIC USE PERSISTS IN U.S. PIG, TURKEY, AND CATTLE PRODUCTION, NOT CHICKEN

NRDC calculated the mg/kg intensities of U.S. antibiotic use by animal species from 2016—the first year for which the FDA asked pharmaceutical companies to estimate national antibiotic sales by species—through 2020.

As shown in Table 2, the intensity of antibiotic use in U.S. livestock production as a whole, and also within the cattle, swine, and turkey industries, was extremely high in 2016, and then dropped significantly in the lead-up to the FDA's 2017 ban on antibiotics for growth promotion. Since 2017, however, that decline has continued only for chicken production, with the 2020 rate of use around half as intense as the already-low 2017 rate. The cattle, pig, and turkey

TABLE 2. CHANGING INTENSITY (% INCREASE [RED] OR DECREASE [GREEN]) OF U.S. ANTIBIOTIC USE OVERALL AND BY SPECIES, 2016 TO 2020 (IN MILLIGRAMS OF ANTIBIOTIC ACTIVE INGREDIENT PER KILOGRAM OF LIVESTOCK RAISED)

	2016	2017	2018	2019	2020	% change 2016–2020	% change 2017–2020
Chicken	55.5	29.6	24.2	20.7	15.2	−72.7	−48.8
Cattle	232.6	153.1	162.8	163.1	161.3	−30.7	5.3
Swine	380.2	239.0	272.9	285.1	267.9	−29.5	12.1
Turkey	478.5	427.0	435.9	435.8	476.6	−0.4	11.6
Overall	249.8	162.0	173.0	174.9	170.8	−31.6	5.5

Source: NRDC analysis, reproduced from David Wallinga, et al., "A Review of the Effectiveness of Current US Policies on Antimicrobial Use in Meat and Poultry Production," Current Environmental Health Reports, 9, no. 2 (June 2022): 339-354, https://doi.org/10.1007/s40572-022-00351-x.

industries, on the other hand, used antibiotics more intensely in 2020 than in 2017—around 12 percent more intensely in turkeys and pigs and more than 5 percent more intensely in cattle. In 2020, their rates of antibiotic use were around 161 mg/kg for cattle, 268 mg/kg for pigs, and 477 mg/kg for turkeys.

While the turkey industry is the most intense user of antibiotics, the much greater size of the cattle and pig industries means the likely negative impact of their little-improved stewardship of antibiotics on public health is greater; these two industries combined accounted for 82 percent of the 6.0 million kilograms of medically important antibiotics sold for food animal use in 2020.[36] Some of Europe's largest pig and cattle industries report rates of antibiotic use that are just a fraction of what their U.S. counterparts have used in recent years.[37]

Since the use of antibiotics to promote faster growth became illegal in 2017, the U.S. livestock sector as a whole has used these precious antibiotics more intensely, not less. This lack of improvement in antibiotic stewardship is putting public health at risk.

CONCLUSION

The United States and Europe have taken divergent policy approaches to address the spread of dangerous antibiotic-resistant bacteria, particularly in tracking and reducing antibiotic use in livestock production. Over the course of a decade, Europe's explicit approach was aimed at improving animal health and preventing illness through changes to on-farm conditions and practices, thereby avoiding the need for antibiotics. That approach coincides with nearly all of Europe's largest livestock producers reducing their intensity of antibiotic use by 50 to 60 percent between 2011 and 2020. European public health agencies, like the EMA, played a crucial role in this reduction by building systems that collect and report data on veterinary antibiotic sales and usage. Those data are essential for tracking rates of antibiotic use and progress toward better antibiotic stewardship.

U.S. policymakers should learn from Europe's experience and public health success. NRDC has long urged three policies—modeled on Europe's—that Congress or the FDA could implement without further delay:

1. ***Set ambitious use-reduction targets.*** The FDA should set a goal of reducing livestock antibiotic use by 50 percent by 2025, relative to a 2010 baseline.
2. ***Closely track antibiotic use in livestock production.*** Robust tracking of antibiotic use is essential to measure improvements in antibiotic stewardship and progress toward national reduction targets. The public health need to robustly track antibiotic use, especially at the farm level, has been recognized in the United States for decades but never acted on. This should be corrected at once. Simultaneously, the FDA should take immediate action to estimate annual antibiotic use in all food-producing animals since 2009 on the basis of weight-adjusted national sales. This approach is endorsed by the World Organization of Animal Health.

   Our analysis already provides these weight-adjusted sales data. Ideally, however, the FDA would do its own weight adjustments, reporting them each December along with its annual sales summaries. Ultimately, public health goals will best be served if the United States joins other countries in reporting national sales and/or use data using metrics that enable rather than obscure comparisons across countries or regions.
3. ***End antibiotic use in healthy animals for disease prevention.*** Some of Europe's major livestock-producing countries discovered that an essential step to curbing the overuse of antibiotics was to end their use in healthy animals for so-called prevention purposes. Effective January 2022, these avoidable antibiotic uses became illegal across the European Union, with few exceptions. The new law also is consistent with 2017 guidelines published by the World Health Organization.[38] Evidence from Europe to date, supported by published scientific reviews commissioned by the WHO, underscores that preventive antibiotics are not necessary for animal health. In fact, they can be avoided through improvements made to farm practices and animal husbandry that help prevent disease from occurring in the first place.

ENDNOTES

1 World Health Organization (hereinafter WHO), "Antibiotic Resistance," July 31, 2020, http://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance.

2 Centers for Disease Control and Prevention (hereinafter CDC), *Antibiotic Resistance Threats in the United States, 2019*, revised December 2019, https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf.

3 Ibid.; Infectious Diseases Society of America, "Estimate of Annual Deaths Caused by Treatment Resistant Infections Highlights Gaps in Research, Stewardship, Surveillance," press release, December 3, 2018, https://www.idsociety.org/news--publications-new/articles/2018/new-estimate-of-annual-deaths-caused-by-treatment-resistant-infections-highlights-gaps-in-research-stewardship-surveillance/; Antimicrobial Resistance Collaborators, "Global Burden of Bacterial Antimicrobial Resistance in 2019: A Systematic Analysis," *Lancet* 399, no. 10325 (February 2022): 629–55, https://doi.org/10.1016/S0140-6736(21)02724-0 (estimating that antibiotic-resistant bacteria globally may contribute to around four times as many deaths as the number of deaths directly attributed to them).

4 CDC, "How Antimicrobial Resistance Happens," accessed October, 2022, https://www.cdc.gov/drugresistance/about/how-resistance-happens.html; ReAct Group, "Spread of Resistant Bacteria," accessed July 29, 2022, https://www.reactgroup.org/toolbox/understand/antibiotic-resistance/spread-resistant-bacteria/.

5 Laura Shallcross and Dame Sally Davies, "Antibiotic Overuse: A Key Driver of Antimicrobial Resistance," *British Journal of General Practice* 64, no. 629 (December 2014): 604–5, https://www.doi.org/10.3399/bjgp14X682561.

6 Thomas O'Brien, "Emergence, Spread, and Environmental Effect of Antimicrobial Resistance: How Use of an Antimicrobial Anywhere Can Increase Resistance to Any Antimicrobial Anywhere Else," *Clinical Infectious Diseases* 34, supplement 3 (June 2002): S78–84, https://www.doi.org/10.1086/340244; European Medicines Agency (hereinafter EMA), *Trends in the Sales of Veterinary Antimicrobial Agents in Nine European Countries, Reporting Period: 2005–2009*, September 15, 2011, https://www.ema.europa.eu/en/documents/report/trends-sales-veterinary-antimicrobial-agents-nine-european-countries_en.pdf; Tim Landers et al., "A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential," *Public Health Reports* 127, no. 1 (January/February 2012): 4–22, https://www.doi.org/10.1177/003335491212700103; European Commission Notice, *Guidelines for the Prudent Use of Antimicrobials in Veterinary Medicine*, September 11, 2015, https://health.ec.europa.eu/system/files/2016-11/2015_prudent_use_guidelines_en_0.pdf; WHO, "Antibiotic Resistance."

7 CDC, "Antibiotic Use: Questions and Answers," accessed July 8, 2022, https://www.cdc.gov/antibiotic-use/q-a.html; CDC, "Measuring Outpatient Antibiotic Prescribing," accessed July 8, 2022, https://www.cdc.gov/antibiotic-use/data/outpatient-prescribing/index.html. *Overuse* is a term applied to antibiotic use that is unnecessary (as when antibiotics are used for viral infections or to promote faster growth in livestock) or inappropriate (as when an ineffective or too-powerful antibiotic is used for an infection or when the correct drug is administered at the wrong time, in the wrong dosage, or for an excessive duration). CDC states that at least 30 percent of antibiotics prescribed to outpatients are not needed at all; add in the outpatient prescriptions that reflect the wrong choice of medicine, dose, or duration of use and total overuse of antibiotics in U.S. outpatient settings may approach 50 percent.

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