Chapter 15
The Political Economy of US Antibiotic Use in Animal Feed

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Abbreviations

ADAA Animal Drug Availability Act
AHI Animal Health Institute
AMS Agricultural Marketing Service
APHIS Animal and Plant Health Inspection Service
AR Antibiotic resistance
ARDs Antibiotic-resistant determinants
ARMS Agricultural and Resource Management Survey
CDC Centers for Disease Control and Prevention
CR Consumer Reports
CSPI Center for Science in the Public Interest
ERS Economic Research Service, USDA
FACT Food Animal Concerns Trust
FAO United Nations’ Food and Agriculture Organization
FDA US Food and Drug Administration
FSIS Food Safety and Inspection Service, USDA
GFI Guidance for Industry
IOM Institute of Medicine
MRC UK Medical Research Council
NAE No Antibiotics Ever
NAHMS National Animal Health Monitoring System
NARMS National Antimicrobial Resistance Monitoring System—Enteric Bacteria
NASS National Agricultural Statistics Service
NRDC Natural Resources Defense Council

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15.1 Introduction

Antibiotic resistance has been widely recognized as a serious public health problem. Hence, there is a major public good to be realized in safeguarding the effectiveness of existing antibiotics and creating new ones. Antibiotics are used to treat human infections and used in animal agriculture. While many drugs are dual-use, others are animal- or human-use specific. The production benefits of sub-therapeutic levels of antibiotics in animal agriculture have been recognized since the late 1940s (CAST 1981). In animal agricultural production, antibiotics are used at therapeutic levels to treat infections and at sub-therapeutic levels to prevent infections and promote animal growth (Sneeringer et al. 2015; Van Boeckel et al. 2017; WHO 2017).

As the organizational complexity of the animal agricultural supply chain increased, the number of economic stakeholders in on-farm antibiotic use has also increased. The major stakeholders include pharmaceutical companies, production integrators, feed suppliers, farm groups, producers, restaurants, food retailers, the public, the medical community, the scientific community, government regulators and policy makers. Each of these stakeholders faces a different set of incentives and disincentives related to on-farm use of antibiotics in animal agriculture. Knowledge of these incentives and disincentives has evolved with the accumulation of scientific and economic research. To understand the regulatory outcomes governing antibiotic use in agriculture, it is important to recognize the political economy context in which they are developed. The various stakeholders are driven by the relative benefits they receive under policies as they affect their industry segment (Zilberman et al. 2014).

15.2 Context of Antibiotic Resistance

Alexander Fleming, who discovered penicillin, warned that “…misuse of the drug could result in selection for resistant bacteria” (Rosenblatt-Farrell 2009). Antibiotic resistance (AR), a term sometimes used interchangeably with antimicrobial
resistance, occurs when bacteria change in ways that make antibiotics less effective in treating infections, thereby allowing the bacteria to survive, multiply, and cause additional harm. AR has been recognized as a serious public health problem among the medical and scientific communities. Antibiotics are used to treat human infections and used in animal agriculture. Particularly concerning is resistance for those antibiotics that are of value in treating human health issues, the so-called medically important antibiotics.

The use of antibiotics along with other advances in agricultural technology has facilitated the concentration of animal production on farms in the United States (US) and elsewhere. For example, in 2012, 88% of all US sales of hogs and pigs were by the 13% of farms with 5,000 or more head, and 66% of all layers were produced on the less than 1% of farms that sold 100,000 or more to egg producers (NASS 2014). The majority of the production of hogs, broilers, and eggs occurred under contractual arrangements between growers and integrators, with the integrators prescribing certain production practices, including the use of antibiotics for treating infections, for disease prevention and for promoting growth.

Many of the antimicrobial drugs administered to food-producing animals are also important in treating humans, worldwide. Domestic sales of medically important antimicrobial drugs for use in food-producing animals in the United States accounted for 62% of the domestic sales of all antimicrobials approved for use in food-producing animals. And, 28% of domestic sales of all medically important antimicrobials approved for use in food-producing animals are labeled for therapeutic use only (FDA 2015). Importantly, animal drug sales data represent products sold or distributed by manufacturers through various outlets for intended sale to the user. Since veterinarians and others in the supply chain may have substantial inventory on hand for possible use, these numbers do not accurately reflect the amount of product ultimately administered to animals. Given the number of humans versus a much larger number of animals in each of the species, as well as other confounding factors, no definitive conclusions from any direct comparisons between the quantities of antimicrobial drugs sold for use in humans versus animals can be drawn (FDA 2016a).

There are obvious situations where antibiotics are required to treat sick animals in agriculture, but the proper therapeutic use versus prophylactic use remains in question among stakeholders. Farm groups and others in the food animal supply chain recognize that antibiotics in animal feed keep animals healthy and meat costs down. But over 1000 medical doctors and other healthcare providers signed petitions to Congress asking for new legislation to reduce non-therapeutic antibiotic use in food animals (Miller 2011). The animal health industry is very concerned that needed preventative use will be threatened by the recent FDA ban on use of medically important antibiotics for growth. FDA classifies as therapeutic those antimicrobials targeted for treatment, control, and prevention of bacteria or disease identified on the product label. FDA explicitly states that the use of antibiotics in animal feed for growth promotion is not allowed.

Those who characterize preventative use as routine overlook the difference between treating animals versus humans. If preventative measures are not taken and
a disease outbreak occurs and spreads rapidly within a flock or herd, it risks large numbers of animals developing a deadly, high mortality disease. Waiting until a disease is clearly evident makes successfully treating the active infections very difficult due to the large number of animals involved. By contrast, a human patient can generally be quickly diagnosed and treated. While some are concerned that producers will continue to use antibiotics for growth under the guise of prevention, the FDA-approved label is specific about dose and duration for a specified bacterium or disease. Off-label use of antibiotics in animal production is illegal, and FDA only allows a veterinarian to decide whether to use or not to use a preventative treatment based on their judgment of a disease threat (Carnevale 2016).

In an economic framework, antimicrobial resistance can be considered as an unwanted side effect, or externality, associated with the use of antibiotics. The efficacy of antibiotics can be considered as a public good that must be managed with government involvement. This is because the costs of overuse by any single individual are borne by society and, in the case of antibiotics, globally. Hence, not only is there a role for government involvement with the animal agriculture industry in managing the stock and use of antibiotics as an important public good, but it must be done cooperatively across countries.

15.3 Challenges in Recognizing the Problem

In 1969, the United Kingdom’s (UK) Parliament received the Swann Report, which concluded that using antimicrobials at sub-therapeutic levels in food-producing animals created risks to human and animal health (Joint Committee on the use of Antibiotics in Animal Husbandry and Veterinary Medicine 1969). It noted a dramatic increase in numbers of animal-origin bacteria strains which showed resistance to one or more antibiotics and that these strains could transmit resistance to other bacteria. It recommended that only antimicrobials that are not medically important for humans should be used without prescription in animal feed and that antimicrobials should only be used for therapeutic purposes under veterinary supervision. The primary reason that producers were using these sub-therapeutic doses of antibiotics was to promote faster weight gain in the animals.

In 1970, a US Food and Drug Administration (FDA) task force was charged to do a comprehensive review of antibiotic use in animal feed (FDA 2012). Its report found that sub-therapeutic use of antimicrobials in food-producing animals was associated with development of resistant bacteria and that treated animals might provide a reservoir of antimicrobial-resistant pathogens capable of causing human disease. The task force recommended that medically important antimicrobial drugs meet certain guidelines they identified or be prohibited from growth promotion or other sub-therapeutic use by certain dates. Further, antimicrobials not meeting the guidelines should be limited to short-term therapeutic use only under veterinarian control.

In the 1970s, the Animal Health Institute (AHI), a US trade association for the animal drug industry, funded an on-farm study to determine the impact of adding
low-dose antibiotics to chicken feed. Within 1 week of adding tetracycline, the intestinal flora in the chickens “…contained almost entirely tetracycline-resistant organisms” (Levy et al. 1976). The antibiotic resistance was not located in the DNA of the bacteria which is hard to transfer among bacteria but in plasmids located on the outside surface of the bacteria. Plasmids are easily exchanged among bacteria living in the intestine. Importantly, the tetracycline-resistant bacteria in the chicken’s intestines were resistant to multiple antibiotics. Furthermore, some members of the farm families began to harbor these same antibiotic-resistant bacteria in their intestines within 6 months.

In 1977, the FDA proposed withdrawing the new animal drug approvals for the sub-therapeutic uses of human medically important penicillin and tetracycline in animal feed based on lack of evidence to show they were safe. However, the US Congress intervened and asked for more research first. The AHI was one of the groups advocating in Congress to delay regulation pending additional research, then and now. In 2010 Congressional Testimony, Richard Carnevale, vice-president at AHI, testified that while it is possible for human antibiotic resistance to be caused by antibiotic use in farm animals, “…it does not happen enough that we can find it and measure it” (Carnevale 2010). This statement contradicted the data produced by the AHI-funded study by Levy (Levy et al. 1976) that was published in the prestigious New England Journal of Medicine in 1976.

Richard Carnevale also mentioned in his 2010 testimony that prior to joining AHI he was Deputy Director of New Animal Drug Evaluation in FDA and had worked at USDA in the Food Safety and Inspection Service (FSIS). His testimony illustrates two points in the political economy of food production: (1) how industry has an opportunity to influence regulators’ decision-making via the revolving door of employment and (2) how industry carefully selects its facts to present a point of view that bolsters their profits, namely, for drug companies in this case (Oreskes and Conway 2010).

Another example of the political economy in action involved USDA prohibiting an agency research microbiologist from talking about the significant levels of antibiotic-resistant bacteria detected in the air near Midwest hog confinement operations (Union of Concerned Scientists 2004). A third element of the political economy is shown by industry efforts to influence policy makers through campaign contributions and strong lobbying of proposed legislation which may affect their bottom line. Pharmaceutical companies spent at least $135 million and agribusiness companies another $70 million during 2009, in large part to fight possible limits on antibiotic use in animal feed (Mason and Mendoza 2009).

In response to Congressional pressure in the late 1970s, FDA withdrew its proposal and instead funded three studies to determine the impact of using low levels of antibiotics in animal feed (industry won this round, obtained a delay in regulations, and funded more reports):

1. In 1980, the National Academy of Sciences reported that there was limited epidemiological research on the topic. Available evidence at that time did not prove nor disprove dangers of seven therapeutic antimicrobials in animal feed, but that did not preclude the existence of hazards (National Academy of Sciences 2009).
2. In 1984, the FDA funded the Seattle-King County Department of Public Health to analyze *Salmonella* and *Campylobacter*, which were chosen as models to estimate the flow of potentially pathogenic bacteria from animals to humans through the food chain. Their report was based on sampling retail meat and poultry and investigating *Salmonella* and *Campylobacter* enteritis cases in humans. Isolates from human illness cases and retail foods were analyzed for antibiotic resistance of these pathogens, using plasmid analysis and serotyping. The report found that *Campylobacter* was a more common cause of enteritis than *Salmonella* and appeared to flow from chickens to humans through consumption of poultry products, with tetracycline resistance being plasmid-mediated (Seattle-King County Department of Public Health 1984).

3. In 1988, the Institute of Medicine (IOM) undertook a FDA-requested independent quantitative risk assessment of human health impacts from sub-therapeutic use of penicillin and tetracycline in animal feed. Based on a risk-analysis model of *Salmonella* infections that resulted in human death, the IOM did not find substantial direct evidence that sub-therapeutic use in animal feed posed a human health hazard. However, they found a considerable body of indirect evidence implicating both sub-therapeutic and therapeutic use of antimicrobials as a potential health hazard and strongly recommended additional study of the issue (Institute of Medicine 1988).

### 15.4 Global Concern About Antibiotic Resistance

Numerous research results quantifying the extent of the antimicrobial resistance problem have been published in the scientific literature and indicate a growing and serious threat to human health. The many channels for AR to affect humans are shown in Fig. 15.1. The two main channels for food animals are (1) AR bacteria in the food animal’s gut can contaminate the meat or poultry eaten and (2) environmental contamination, such as manure used to fertilize fields that contain AR bacteria, may contaminate the environment and some of the food crops grown on these fields. *Consumer Reports* (CR) tested products sold in US supermarkets and found resistance to multiple antibiotics in the following percent of samples: beef 14%, shrimp 14%, turkey 83%, and chicken 57% (Consumer Reports 2016). CR also found that ground beef from conventionally raised cows was twice as likely to contain antibiotic-resistant pathogens as ground beef from cows raised without antibiotics.

Like other threats to human health, AR is best managed across national boundaries. Increasing international trade may spread antibiotic resistance through imported food products as more trade agreements are approved. This scenario could be exacerbated to the extent FSIS approves additional international facilities, local regulations, and inspections as “equivalent to the United States.” Future trade agreements will need to include provisions which address reduced use of medically important antibiotics in producing food animals.
Numerous trusted institutions from the United States (US) and the United Kingdom (UK) as well as international organizations such as the World Health Organization (WHO), the United Nations’ Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE) have acknowledged the threat of antibiotic resistance related to use in producing food animals. The fol-

Fig. 15.1 How antibiotic resistance happens and spreads. Source: The US Centers for Disease Control and Prevention, AR-infographic.508c.pdf
lowing excerpts from a few recent reports highlight the role that low-dose antibiotic use in animal feed plays in spreading AR.

The Centers for Disease Control and Prevention (2013b) reported that:

Each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections. Many more die from other conditions that are complicated by an antibiotic-resistant infection.

Antibiotic-resistant infections add considerable and avoidable costs to the already overburdened U.S. healthcare system. In most cases, antibiotic resistant infections require prolonged and/or costlier treatments, extend hospital stays, necessitate additional doctor visits and healthcare use, and result in greater disability and death compared with infections that are easily treatable with antibiotics. The total economic costs of antibiotic resistance to the U.S. economy has been difficult to calculate. Estimates vary but have ranged as high as $20 billion in excess direct healthcare costs. Adding on the costs for lost productivity brings the total societal costs (sic) for AR to $35 billion a year (2008 dollars). (CDC 2013a, p. 11)

This CDC report also indicates that foodborne cases are responsible for 20% of human AR infections (Fig. 15.1). Thus, societal costs of these AR foodborne illnesses could total $7 billion annually of the $35 billion/year total costs to the US economy. These societal costs could be prevented if the foods were free of contamination with AR pathogens. There may be additional costs associated with environmental pathways of human contamination from use of antibiotics in meat production, such as exposure to contaminated water.

In 2014, WHO stated: “Antimicrobial resistance (AR) is an increasingly serious threat to global public health. AR develops when a microorganism (bacteria, fungus, virus or parasite) no longer responds to a drug to which it was originally sensitive. This means that standard treatments no longer work; infections are harder or impossible to control; the risk of the spread of infection to others is increased; illness and hospital stays are prolonged, with added economic and social costs; and the risk of death is greater—in some cases, twice that of patients who have infections caused by non-resistant bacteria. The problem is so serious that it threatens the achievements of modern medicine. A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the 21st century” (WHO 2014, p. 3).

In 2015, OIE noted: “Today, in many countries, including developed countries, antimicrobial agents are widely available, directly or indirectly, practically without restriction. Of 130 countries recently evaluated by the OIE, more than 110 do not yet have relevant legislation on the appropriate conditions for the import, manufacture, distribution and use of veterinary products, including antimicrobial agents. Consequently, these products circulate uncontrolled like ordinary goods and are often falsified.”

To date, there is no harmonized system of surveillance on the worldwide use and circulation of antimicrobial agents. That information is necessary, however, to monitor and control the origin of medicines, obtain reliable data on imports, trace their circulation, and evaluate the quality of the products in circulation. It is in this context that the OIE was mandated by its member countries to gather that missing information
and create a global database for monitoring the use of antimicrobial agents, linked to
the OIE’s World Animal Health Information System (WAHIS). That mandate is also
supported by FAO and the WHO within the framework of the WHO’s global action
plan on antimicrobial resistance. The database will form a solid basis for the three
organizations’ work to combat antimicrobial resistance (OIE 2015, p. 2).

In 2016, a UK evaluation of 139 academic, peer-reviewed research articles
addressing antibiotic use in agriculture determined that only 5% found no link and
75% found a positive link between antibiotic use in animals and antibiotic resis-
tance (AR) in humans (O’Neill 2016). Taken together, these and numerous other
scientific findings show an indisputable relationship between antibiotic use on farms
and drug-resistant infections in people (Van Boeckel et al. 2017; Silley and Stephan
2017; Tang et al. 2017; Webb et al. 2017).

15.5 Farm-Level and Public Health Economic Impacts

To evaluate proposals to ban the use of growth-promoting or sub-therapeutic levels
of antibiotics in food animals, USDA’s Economic Research Service (ERS) econo-
mists added questions on antibiotic use to the Agricultural and Resource Management
Survey (ARMS). ARMS is a nationally representative survey of farms administered
jointly by ERS and USDA’s National Agricultural Statistics Service (NASS). Hog
producers were surveyed in 2006 and 2009, and broiler producers were surveyed in
2006 and 2011. ERS also drew upon their research using data in the National Animal
Health Monitoring System (NAHMS) to develop a model to estimate the impacts of
withdrawing antibiotics for other than therapeutic use in food animals. Using Monte
Carlo simulations, ERS estimated the impacts of eliminating antibiotic use for
growth promotion of poultry and pork, not just the FDA-specified “medically impor-
tant” antibiotics (Table 15.1). Simulation results showed less than 0.5% reduction in
output and an approximate 0.75% increase in wholesale prices, netting pork produc-
ers greater total revenue of 0.29% and poultry producers 0.42%. ERS concluded that
these small effects were not statistically significant (Sneeringer et al. 2015).

Table 15.1 Ban on antibiotics used for growth promotion has statistically insignificant impact

| Impact of Ban on Growth Promotion Antibiotics (%) | Hogs  | Broilers |
|--------------------------------------------------|-------|---------|
| Percent change in output                         | −0.47 | −0.31   |
| Percent change in wholesale price                | 0.77  | 0.73    |
| Percent change in value of production            | 0.29  | 0.42    |

Source: Data from Sneeringer et al. (2015)
These ERS results are consistent with research studies post-2000 indicating that productivity gains from using antibiotics for growth promotion were lower than earlier research had found (Teillant and Laxminarayan 2015). Another report suggested that phase out of growth promotion use in food animals over a 5-year period would avoid most of the 67% projected global growth in such use and cost agricultural sectors a small portion of the costs of AR in each country. Further, reduced infection risk and costs of medications would cover most farm-level costs of improving animal husbandry practices to offset loss of antimicrobials for production purposes (Laxminarayan and Chaudhury 2016).

Presuming that any new antibiotic classes probably will not be made available for veterinary medicine, it is important to preserve the effectiveness of existing antibiotics which are necessary for treatment of infectious diseases to maintain animal health (Teillant and Laxminarayan 2015). An alternative to encourage development of new antibiotics would be to delay or not approve drugs which mimic others, but for which the applicant company has not performed antibiotic research (Amábile-Cuevas 2016). Even better, several production practices may be used to enhance animal health in the absence of using antimicrobials for growth or for prophylactic disease prevention (Sneeringer et al. 2015; WHO 2017; MacDonald and Wang 2011). These include:

- Improved management practices, such as more space per animal and better control of the housing environment
- Tightened biosecurity to prevent diseases and improve productivity by avoiding introduction of infectious agents by wild animals, domestic pets, and nonessential workers or other humans; through increased cleanliness of production facilities; and from timely removal of dead animals
- Optimized nutrition to increase growth and mitigate stress-related factors and provide vitamin and mineral supplements to reduce disease susceptibility
- Improved gut microflora to improve feed efficiency by providing enzymes, organic acids, prebiotics, probiotics, and immune modulators
- Vaccinations to prevent some diseases
- Hazard Analysis Critical Control Point plans to improve productivity in the absence of using sub-therapeutic antibiotics in animal production

Generally, these practices may raise production costs modestly at the farm level because of the need for more resources required to successfully manage them. Since ERS found no statistically significant evidence that antibiotics reduce the costs of producing pork or broilers, we conclude that there are small or no costs to producers from withdrawing growth-promoting or prophylactic uses of antibiotics in production of food animals.

In contrast, the public health benefits of withdrawing these antibiotics from agriculture are significant. As reported above, CDC estimates that the medical costs and productivity losses of AR illnesses attributed to agriculture are $7 billion US dollars annually. The benefit/cost analysis becomes $7 billion in public health protection benefits vs. the very small costs to animal production from withdrawing antibiotics from non-therapeutic use. In other words, the protection of the public health will
come at little or no cost to agriculture. Furthermore, this benefit/cost analysis provides a conservative estimate of public health protection benefits. The CDC public health protection benefits do not include estimates for protection from an increasing number of “superbugs” that would be created if low-level antibiotics would continue to be used. And CDC does not include the costs of long-term health outcomes caused by foodborne pathogens (see Chap. 8).

15.6 Other Societal Costs

Aside from costs to agricultural producers, there are also other societal costs related to AR and connected to antimicrobial use in animal production, both in their production and use/misuse, affecting human and environmental health. In economic terminology, these costs are considered negative externalities to society from the individual use of antibiotics. Moreover, since the science of AR is unfolding, there may be additional unknown human health and environmental risks associated with the use of antibiotics in food animal production.

Pharmaceutical Production. A major issue involved with manufacturing of active ingredients for antibiotics and the effluent from factories producing them is the potential to contaminate nearby water systems. Pharmaceutical factories often contaminate the environment, since guidelines for pharmaceutical waste discharge focus on chemicals used in manufacturing, rather than active pharmaceutical ingredients. This is a primary concern in countries outside the United States, but international trade makes it a worldwide problem.

Use and Misuse. Worldwide, antibiotics are used heavily in animal agriculture. This practice has created resistance problems transmissible from animals to humans. For example, China has mrc-1 colicin resistance in pork and Salmonella resistance to cephalosporins at higher levels than in the United States (Zhang et al. 2016). Their practice of applying human waste on fields and the closeness of population centers to agriculture contribute to cross-mixing of pathogens in China. Parasites are common in Chinese soil and can contaminate pork. And low levels of chlorine in Chinese water supplies allow accumulation of biofilms containing antibiotic-resistant pathogens in water pipes. In India, manufacturing of pharmaceuticals and waste disposal practices lead to contamination of water and soil. Further, over-the-counter antibiotics are available and heavily used there.

Farm antibiotic use is of concern in India and China in poultry and pigs (APUA Newsletter 2016). The threat of superbugs via food is worldwide, due to the distribution of animal food products from China (Zhang et al. 2016; Zhu et al. 2013). Rosenblatt-Farrell (2009) drew upon existing literature to identify additional environmental paths to exposure to antibiotic resistance. Veterinary antibiotics are frequently excreted intact from food animals (Table 15.2). For the widely used tetracycline, 60–80% of the antibiotic is excreted in the feces or urine and not metabolized by the food animal. The transfer of this animal waste to croplands may transfer antibiotics and possibly AR pathogens. In one study, AR genes in soil
increased fourfold after manure from hog and dairy farms was applied to the soil (Moyer 2016). Runoff from farms, feedlots, or cropland can lead to antimicrobial resistance problems in soil, surface water runoff, and groundwater. Animal waste held in lagoons allows birds and insects to become contaminated with antibiotic-resistant bacteria, and flies around food animal facilities can carry antibiotic-resistant enteric bacteria which increases potential human exposure. Migratory birds and seagulls which become infected with antibiotic-resistant bacteria or viruses can widely transmit resistance to other birds as well as marine life.

Others note that antibiotics should never be used to compensate for poor hygiene and husbandry practices or conditions in livestock production (Van Boeckel et al. 2017). Veterinary medicine should only use antibiotics to treat diagnostically determined bacterial infections not otherwise treatable and only those antibiotics authorized for the diagnosed pathogenic indication and the specific bacteria involved. Further, given the potential for acute diseases that require immediate treatment, it is important that routine testing (surveillance) be carried out for farm-specific pathogens for all relevant antibiotic classes (Silley and Stephan 2017). WHO also emphasizes the need for surveillance and monitoring antimicrobial use in food-producing animals to evaluate the extent to which their guidelines are implemented.

### 15.7 US Policy Response

FDA has increased regulation of antibiotic use in food animals. As noted in Sect. 15.3 above, FDA attempted to withdraw new animal drug approvals for sub-therapeutic uses of human medically important penicillins and tetracyclines in animal feed based on lack of evidence to show they were safe. After industry opposition and Congressional intervention to require further study, this early policy response was withdrawn. Subsequently, the US Congress gave something to each group when it enacted the Animal Drug Availability Act (ADAA) in 1996. This Act both

| Drug class and example | Quantity sold for veterinary use (kg) | Fraction not metabolized (%) |
|------------------------|---------------------------------------|-------------------------------|
| Aminoglycosides/neomycin | 270,342                               | 80–90                         |
| Cephalosporins/ceftiofur | 28,337                                | <10                           |
| Ionophores/monensin     | 4,434,657                             | 50–80                         |
| Lincosamides/lincomycin | 236,450                               | 10–50                         |
| Macrolides/tylosin      | 563,251                               | 10–80                         |
| Penicillins/penicillin G | 828,721                               | 80                            |
| Sulfonamides/sulfadimethoxine | 384,371                 | 20–50                         |
| Tetracyclines/chlortetracycline | 6,514,779               | 60–80                         |

Source: Data from Aga et al. (2016)
facilitated the approval and marketing of new animal drugs and medicated feeds and
gave FDA new regulatory controls. The Act created a new category, Veterinary Feed
Directive (VFD), for drugs used in animal feed that could only be used under the
professional guidance of a licensed veterinarian. FDA implemented the ADAA VFD
provisions through final regulations published in 2000. However, subsequent
feedback from various stakeholders led FDA to seek public input on improvements
needed in the regulations. Following lengthy delays as shown in Table 15.3, FDA in
recent years issued three core documents to implement a policy framework for judi-
cious use of medically important antimicrobial drugs in food animals:

Table 15.3 US policy actions to reduce antibiotics in animal feed

| Year   | Policy action                                                                 | Comments                                                                                          |
|--------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| 1951   | FDA approved antibiotics in livestock feed                                   | Production purposes and therapeutic uses                                                          |
| 1970s  | FDA proposed ending production-purpose use                                    | FDA 1970 report: antibiotic use might pose human health threat                                  |
| 1975   | Antibiotic drug sponsors required to show that products not a human health threat | Result of the 1970 FDA report                                                                    |
| 1977   | FDA proposed withdrawal penicillin, tetracycline sub-therapeutic feed use     | Congress directed FDA wait for further study to be conducted                                      |
| 1980   | FDA-contracted National Academy of Science report issued                      | Available data could neither prove nor disprove human health hazards                             |
| 1980–2003 | FDA continued research support into safety of sub-therapeutic antibiotic use | Reviews of research that associated antimicrobial livestock use and human disease resistance     |
| 2003   | FDA guidance, requiring risk assessment for any new antibiotics for livestock agriculture | Not applicable to majority of antibiotics used in meat production, approved before 2003       |
| 2005   | FDA withdrew enrofloxacin (type of fluoroquinolone) for poultry production    | Lengthy and challenging process to withdraw approval of specific drug use                         |
| 2010   | FDA voluntary guidelines: medically important antibiotics in livestock limited to nonproduction use, with veterinary oversight | Allowed disease treatment, control, or prevention purposes; FDA to rely on voluntary industry response |
| 2011   | FDA draft guidance: “judicious use” of antimicrobial drugs in livestock production | Concern that production-purpose use of medically antimicrobial drugs adversely affects human public health |
| 2012   | FDA Guidance for Industry # 209 finalized                                    | Limit medically important antibiotic use to assuring animal health; veterinary oversight          |
| 2013   | FDA guidance document # 213                                                  | Detailed information to pharmaceutical manufacturers on withdrawing production uses; veterinary oversight of remaining OTC uses |
| 2014   | As of June 2014, all 26 producers of antibiotics used in livestock feed agreed to FDA’s request in guidance # 213 | It only took 44 years, starting in 1970, to stop production use of antibiotics in food-producing animals |

Source: Sneeringer et al., pp. 12–14
• Guidance for Industry (GFI) #209 “The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals” was published in April 2012, citing primary scientific literature they considered (FDA 2012). It identified several steps for ensuring appropriate judicious use by eliminating feed and water use of medically important antimicrobial drugs for production purposes and bringing remaining therapeutic uses under the oversight of licensed veterinarians.

• GFI # 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” was published in December 2013. It detailed a process and timeline for implementing GFI #209 measures. When fully implemented, feed use of antimicrobial drugs would transition from over-the-counter (OTC) to VFD marketing status (Veterinary Feed Directive 2015).

• The third element in this process is the VFD regulation issued in June 2015. The FDA amended regulations for Veterinary Feed Directive (VFD) drugs used in animal feeds to improve the efficiency of the program but still protect human and animal health. VFD drugs are new animal drugs for use in feed, allowed only under professional supervision of a licensed veterinarian who issues an order (VFD) under a valid veterinarian-client-patient relationship (VCPR). The VFD rule is the final document to implement FDA’s policy framework for judicious use of medically important antimicrobial drugs in food-producing animals. It eliminates feed and water use of medically important antimicrobial drugs for production purposes. Remaining therapeutic uses of these drugs are brought under oversight of licensed veterinarians. The final rule provides accountability through important controls regarding distribution and use of VFD drugs. It facilitates transition of the currently large number of over-the-counter (OTC) feed-use antimicrobial drugs to a new VFD status (Veterinary Feed Directive 2015).

On January 3, 2017, FDA announced that it had completed implementation of the Guidance for Industry #213. This means that medically important antimicrobials provided to food-producing animals may no longer be used for growth promotion purposes and may be used to treat, prevent, or control animal illnesses only under direction of a veterinarian. FDA worked with industry participants to implement this voluntary compliance to slow development of antimicrobial resistance and preserve effectiveness of medically important antibiotics. More than 70 percent of 292 new drug applications subject to GFI #213 were converted from over-the-counter to prescription status, 84 applications were withdrawn, and all 31 applications indicating production use withdrew that specified use. FDA also indicated plans to work with industry stakeholders to support antimicrobial stewardship in food animal production and to evaluate the effectiveness of strategies to reduce antimicrobial resistance development under the allowed uses (FDA 2017).


15.8 Industry Stakeholders and Responses

Some industry stakeholders in the supply chain are actively engaged in responding to consumer and general public health concerns about AR in the food supply chain amidst mounting scientific evidence, but responses vary considerably by country, place in the supply chain, and individual company. Aside from farm groups, stakeholders include feed companies, pharmaceutical companies, integrators or meat processors, restaurant chains and other retail outlets, and consumer and other interest groups.

Pharmaceutical Companies. In the case of pharmaceutical companies, little evidence exists that they are responding to the AR problem yet. As described earlier, most antibiotics are produced in India and China, and their production has resulted in significant risk, especially environmental risk. Regulators need to set minimum standards for the treatment of manufacturing waste before it is released into the environment. Other industries which purchase these pharmaceuticals need to establish higher standards through their supply chains to help correct this environmental pollution (O’Neill 2016).

Furthermore, the drug companies are not required to compensate victims who become ill or die from either the environmental or food exposure. The drug companies and their trade associations have resisted more regulation to prevent misuse of antibiotics. The companies therefore have been getting a “free ride” at the expense of the ill consumers and the general public.

Integrators and Meat Processors. Some chains and food retailers have recently responded to customer concerns by restricting the use of antibiotics in their food supply chains. Large meat processors committing to judicious use of antibiotics have already led many producers to eliminate the use of antibiotics for production enhancement purposes.

In a case study of voluntary labeling in the broiler industry, “Raised without Antibiotics” (RWA) label claims by Tyson Foods and by Perdue Farms in 2007, respectively, numbers one and three in total broiler production, resulted in mixed outcomes. At that time, USDA FSIS had not published a standard for such claims, nor was a clear definition established. Perdue and Tyson developed their own standards and submitted the label claims to FSIS for approval along with supporting documentation. After initially approving both firms’ label claims, FSIS determined in September 2007 that Tyson’s claim was false and misleading and gave them the opportunity to submit a revised label claim. However, Tyson continued their advertising of the RWA claims. The diverse label claims in which Tyson and their competitors were using different standards for their claim resulted in consumer confusion, and eventually court challenges were filed jointly by Sanderson Farms, the fourth largest producer, and Perdue against Tyson. The suit was upheld in court in April 2008. Tyson was found not to have delivered the RWA attribute promised to the marketplace and to thereby have harmed competitors, while Tyson profited from introducing a false and misleading claim. In June 2008, FSIS rescinded Tyson’s qualified RWA label claim and required its removal within 2 weeks, after the claims
and advertising had continued for more than a year. The authors found no evidence that the events had any impact on Tyson’s brand, suggesting that companies may have incentives to introduce misleading label claims since the size of penalties is uncertain (Bowman et al. 2016).

Perdue Farms Inc. was the only major chicken producer to eliminate all medically important and animal-specific antibiotics from use in its chicken production as of 2016. By replacing antibiotics with vaccines and improving its production facilities and practices, it has been able to produce chicken at virtually the same cost as when using antibiotics. Perdue estimates that its conventional chicken sales are increasing by not more than 3% annually, while sales for product raised without antibiotics are growing 15–20% annually (Bunge 2016).

GNP Company, a leading provider of premium natural chicken products, is adopting antibiotics-free production of chicken products. Its Gold’n Plump brand will feature a “No Antibiotics-Ever” claim. This will go well beyond what many companies are currently focusing on—eliminating the use of medically important antibiotics, rather than all antibiotics. USDA regulations allow this label claim only for chicken never having received antibiotics, even inside the egg. The company will continue to treat flocks for illness as necessary, but not market them under their premier Gold’n Plump brand. The company plans extensive media and in-store support to educate consumers about the transition to its chicken products raised totally without antibiotics (GNP Company 2015).

Tyson Foods, a leading producer of chicken, pork, and beef and products thereof, adopted a position to eliminate the use of human-use antibiotics in broiler production by September 2017. They stopped the human antibiotic use in their hatcheries and reduced usage in producing broilers by 80% since 2011. They also have worked with farmers and others in the beef, pork, and turkey supply chains to explore ways to reduce human antibiotic use at the farm level. Tyson is employing alternative husbandry strategies such as use of probiotics and essential oils, improved housing, and selective breeding to offset the potential impact of eliminating the use of the antibiotics. They are also interacting with the food industry and other involved supply chain participants, as well as academics, to increase research on disease prevention and alternatives to replace antibiotics (Tyson Foods 2017).

Feed Companies. The feed companies are also getting into the discussion to address public health concerns about antibiotic resistance and the relationship to livestock production uses of antibiotics. Phibro Animal Health Corporation recently launched a website AnimalAntibiotics.org to “…provide accurate and credible information while still creating open dialogue about animal agriculture in the use of antibiotics.” It will address all issues involving animal antibiotics and changes underway within the industry to promote responsible use of antibiotics in livestock (Johansen 2016). This is very consistent with the historical pattern of the animal agriculture industry making its case in the political economy in reaction to the strong push to limit use of antibiotics to help quell rising antibiotic resistance of medically important drugs.

Restaurant Chains. An interesting example of restaurant chains and poultry producers working together is provided by Panera Bread Co. and Perdue Farms Inc.
Panera is one of the restaurant companies for which Perdue supplies chickens raised without antibiotics. When Panera pioneered antibiotic-free chicken in its restaurant products over 10 years ago, they paid a 50% premium versus chicken produced using antibiotics. With improved production practices, the cost differential has virtually disappeared (Bunge 2016) and is thus consistent with the ERS estimates cited earlier.

**Consumer and Other Interest Groups.** In the process of developing these new FDA regulations, activist groups petitioned the Federal Courts. For example, in May 2011, the Natural Resources Defense Council (NRDC), Center for Science in the Public Interest (CSPI), Food Animal Concerns Trust (FACT), Public Citizen, and Union of Concerned Scientists (UCS) filed a case against the FDA. They charged that FDA failed to ban penicillins and tetracyclines used at low doses in animal feed for growth promotion, despite evidence FDA put forth in 1977 that penicillin and most tetracyclines were not shown to be safe and may pose a risk to human health (APUA 2016). In 2012, the Federal Court ruled in favor of these petitioners. In a later ruling in 2012, the Federal Court directed FDA to reexamine its decision on five other classes of “medically important drugs” used as growth promoters addressed in two citizen petitions (filed in 1999 and 2005) to ensure the safety and effectiveness of all drugs sold in interstate commerce (Ibid).

Given that most governments have neglected to acknowledge and address the problem of increasing antibiotic resistance, international organizations with a role in health issues have been stymied from doing so. It will take more concerted action by societies around the globe to successfully address this cross-border issue (Amábile-Cuevas 2016).

### 15.9 Consumer Demand for Labeling of Antibiotic Use

US consumers, in general, have much less information about the product than does the seller (Chaps. 2 and 3). This asymmetric information can offer opportunity for the selling firm behavior that is detrimental to the interests of the consumer, as when a product is labeled as containing or not containing certain desirable or undesirable attributes. In the case of many products known as credence goods, it is impossible to determine whether the attributes are as stated, even when the product is used or consumed. This market failure can be addressed either through government regulations or through voluntary steps by the sellers to assure that the stated attributes are factual. The latter could be accomplished through advertising to build and maintain the firm’s brand and reputation, and competition with other sellers could result in consumers having increased variety of product choices. However, some consumers may not trust private companies’ word about product attributes and prefer certification programs which monitor products against some standard established either by the private sector or by government agencies.

Lusk (Lusk 2013) argues that voluntary labels are dynamically efficient in responding to changes in market conditions and encouraging innovation more than
mandatory labels implemented through regulations, since the latter are more subject to manipulation by those with vested interests. Further, USDA’s Agricultural Marketing Service (AMS) process-verified and certification programs are very effective in helping to assure the credibility of voluntary labeling, while accommodating innovation from the private sector. GNP’s adoption of antibiotics-free production discussed in 15.8 is an example of dynamic market efficiency through use of voluntary labeling to innovate in response to changing consumer demand.

USDA’s Food Safety Inspection Service (FSIS) currently employs an animal production claims protocol for evaluating and allowing or denying labeling claims. Labeling applications must provide supporting documentation such as operational protocols detailing production practices and affidavits or testimonials about production practices. FSIS then evaluates whether protocols support the accuracy of the proposed label. Also, feed formulations must be provided and reviewed to ensure they do not include substances not permitted by the claim. Commonly approved claims relevant to the use of antibiotics include “raised without added hormones” (only allowed for use in beef cattle and lamb production) and “raised without antibiotics.” Claims not allowed include that animal products are antibiotic-, hormone-, or residue-“free” (FSIS 2016). Given the current trend among meat producers, restaurants, and retail livestock product marketers, it can be anticipated that there will be increasing attention to labeling the lack of antibiotic use for other than therapeutic purposes. This will likely result in animals that have been raised with antibiotics to promote growth and uniformity of size consistent with processor contract agreements being diverted to marketing outlets where such promises do not exist. The impact of labeling in this manner will vary according to how much consumers know about the use of antibiotics in livestock production and their ability to currently purchase antibiotic-free livestock products (Lusk et al. 2006).

O’Neill and his British colleagues emphasize improving transparency as a major step in addressing antimicrobial resistance related to the livestock production. Recent attention by companies such as food retailers, wholesale producers, and fast-food chains, as well as investors, for reducing antibiotic use in their supply chains, has been in response to consumer pressure. Providing greater transparency through voluntary approaches is helpful in the short term, but it may be necessary to mandate transparency requirements about how antibiotics are used in the supply chains to have longer-term impacts. Labeling that refers to antibiotic use could improve consumer knowledge to allow them to make better informed decisions. They also argued that third-party validation of support from independent institutions to monitor progress may be beneficial (O’Neill 2016).

15.10 Surveillance, Data Gaps, and Transparency

Improved transparency by food producers about antibiotics used in producing meat could help consumers make better informed purchasing decisions. But there are large gaps in data needed to allow monitoring of types and quantities of antibiotics
used in animal agriculture and their impacts (CFI 2016), as well as on emergence and spread of resistance in animals. The WHO also identified major gaps in surveillance and data sharing on emergence of antibiotic resistance in bacteria and its impact on animal and human health. WHO called for integrated surveillance systems harmonized across countries to enable better comparison of data from food-producing animals, food products, and humans (WHO 2014).

In the United States, FDA requires drug companies to voluntarily submit data on drugs sold for use in food animals. The publicly available data are not detailed, and 97% of the sales of medically important antimicrobials are over-the-counter (OTC). Tetracyclines are primarily added to feed and accounted for 71% of domestic sales of animal drugs that are “medically important” to human medicine in 2015 (FDA 2016b). From 2009 to 2015, domestic sales and distribution of tetracycline products approved for use in food-producing animals increased by 31%. While Levy et al. (1976) discovered how rapidly tetracycline created antibiotic resistance in the gut of chickens, 40 years later, the public does not have access to information on what antibiotics are used in which food animals at what stage of life.

This will change somewhat in FDA implementation of GFI # 213 (FDA 2017) that will identify whether the sales are intended for use in cattle, sheep, hog, or poultry. FDA (2016b) issued a final rule amending an existing requirement that sponsors of drug products containing antimicrobial active ingredients report annually the amount of each such ingredient in the drug products sold or distributed for use in food-producing animals. Effective July 11, 2016, drug sponsors were required to submit species-specific estimates of product sales as a percent of their total sales. Additional reporting requirements are expected to facilitate better understanding of antimicrobial drug sales for specific food-producing animal species and the relationship between such sales and antimicrobial resistance. As reported above, drug sponsors have all adopted voluntary revision of FDA-approved labels for use of new medically important antimicrobial animal drugs administered through feed or water. Under this rule, sponsors all voluntarily removed the growth promotion and feed efficiency uses and brought the remaining therapeutic uses under veterinarian oversight by the end of December 2016. The rule makes it illegal to use medically important antibiotics for production purposes. Despite the scientific and economic evidence, many comments to the proposed final regulation reflected ongoing resistance to the elimination of food animal production use of medically important antibiotics.

Data available on antibiotics used in the US livestock industry is derived primarily from two nationally representative surveys of farms conducted by the USDA’s Economic Research Service (ERS) and National Agricultural Statistics Service (NASS). The Agricultural and Resource Management Survey (ARMS) is designed to collect information on farm finances, production practices, and resource use focuses on three commodities annually, livestock included. Different types of livestock are resurveyed every 5–6 years and represent commercial producers in states producing 90% of production for that livestock type. Some questions have been included in these surveys on antibiotic use for hogs and broilers. The hog surveys ask about use of antibiotics in feed or water for growth promotion, disease preven-
tion, and/or disease treatment in breeding, nursery, and finishing hogs. Given the widespread use of hog production contracts under which farm operators may receive feed from integrators, the surveyed operators may not know if antibiotics are included in it. For broilers, there is only a single question about whether they were raised without antibiotics in feed or water other than for therapeutic treatment of illness. Production contracts dominate the broiler industry, so surveyed farm operators are in a similar situation as hog producers in not necessarily knowing whether antibiotics are included in the feed provided. A further complication is that ARMS does not separate traditional antibiotics and ionophores, which are not used in human medicine (Sneeringer et al. 2015).

The National Animal Health Monitoring System (NAHMS) consists of national studies to provide essential information on livestock and poultry health and management. Major food livestock species are surveyed about every 5 years to provide current and trend information important to industry participants, researchers, and policy makers. Each study includes states that represent at least 70% of the targeted animal population and at least 70% of the farm operations involved and provides statistically sound information for decision-making. A NAHMS study is a collaborative, voluntary, confidential, scientifically sound product. Descriptive reports are prepared along with information sheets which briefly address very specific topics, such as biosecurity practices (APHIS 2016). The NAHMS focuses on animal health and management, providing information on disease occurrence and disease prevention practices, as well as more detailed information on antibiotics used in production, including by specific purpose. However, the information collected on antibiotics varies greatly across commodities, as well as over time with the same commodities. Further, ARMS focuses on hog production operations with 25 or more head versus NAHMS focus on 100 or more head. This complicates comparison of statistics across surveys, assuming smaller operations may have different characteristics than larger ones (Sneeringer et al. 2015).

To track antimicrobial resistance changes over time, the National Antimicrobial Resistance Monitoring System—Enteric Bacteria (NARMS) was established by CDC in 1996. The program is a collaboration between state and local public health departments and three federal agencies to monitor changes in antimicrobial susceptibility for certain enteric bacteria from ill people (CDC), retail meats (FDA), and food animals (USDA) in the United States. It provides information about emergent bacterial resistance, the ways resistance is spread, and how resistant infections differ from susceptible ones (NARMS 2016).

15.11 Global Responses to Antimicrobial Use in Livestock

The World Organization for Animal Health (OIE) plans to address antimicrobial resistance as a major risk to the international community, in the face of concern about agriculture’s role in increased antimicrobial resistance. The goal is to preserve effectiveness of antimicrobials used in animal medicine, protect animal welfare, and
help maintain important antimicrobials for use in human medicine. OIE has already developed international standards, most recently revised in 2015. The new strategy introduced at the 84th OIE General Session in May 2016 outlines plans to help nations improve legal frameworks to preserve antibiotics, communicate about the AR problem, train animal health workers, and monitor antibiotic use in animals. They are currently working to create a database of information on the use of antimicrobial agents in animals and develop performance indicators to assist countries by increasing information flow and transparency in their use of antimicrobials. Further, the OIE expert network is working to reinforce scientific knowledge about new technologies and replacement solutions for current antimicrobials (Mitchell 2016).

The EU has banned the use of antimicrobials in food animal production, other than by veterinarian prescription for specific therapeutic use. Some other countries have adopted similar bans, and, as discussed above, the United States fully implemented voluntary guidelines in 2016 requiring current drug sponsors to withdraw antibiotics for growth promotion. However, the Animal Health Institute’s Carnevale has said that the new FDA guidance on antibiotics may not decrease the total quantities of antibiotics used in animal food production (Moyer 2016). Generally, variations among countries in implementing regulations have resulted in the spread of resistance. There is ample evidence to support the need for global coordination to prevent continued spread of antimicrobial resistance, and elements of a framework to make such global coordination effective have been posited (So et al. 2015).

The UK Review on Antimicrobial Resistance Final Report proposes three broad steps to deal with reducing unnecessary use of antibiotics in animals. First, establish 10-year targets for reduction in use, with milestones to support progress consistent with countries’ economic development. This could encourage farmers to reduce non-therapeutic use to be able to allocate the resulting reduced amounts of antibiotics to treating sick animals. Second, implement restrictions or bans on certain types of highly critical last-line antibiotics for humans from being used in agriculture. This would require a harmonized approach to identify the most important human health antimicrobials across countries and good systems of veterinarian oversight to assure compliance. Third, improve transparency from food producers on antibiotic use in meat production to allow consumers to make better informed buying decisions. Voluntary industry efforts may be one of the most practical approaches to reduce antibiotic use in the near term, but third-party validation to monitor progress would be beneficial (O’Neill 2016). Generally, voluntary industry approaches require monitoring by an outside party to assure both industry participants and consumers that standards are being met as required.

The UK Medical Research Council (MRC) recently made three large grants focused on antimicrobial resistance through an initiative established in 2014 to address the growing AR issue. The projects will use new technology to exploit natural compounds, develop a better and faster diagnostics tool, and study how the body’s immune system can be harnessed to better fight infections. The goal is not only to develop antibiotics but also explore alternatives to antibiotic use, working with other UK research councils to bring to bear a wide range of disciplines to tackle AR (MRC 2016).
The need to focus increased attention to developing new antibiotics is supported by CDC data which shows that many of the most widely used drugs have developed resistance. The number of years to develop resistance varies greatly but never extends more than a couple of decades, and more recent antibiotic introductions have been resistant for only a year or two. For example, the widely used tetracycline was introduced in 1950 and developed resistance to *Shigella* by 1959. This is near the midrange of years to resistance reported (CDC 2013a). Given this scientific fact, the slow pace of adopting policies to proscribe use of human-use antibiotics in animals and to encourage greater investment in developing newer antibiotics or alternatives is unacceptable. Increasing detection of bacteria resistant to last-resort drugs has driven stakeholders to countenance accelerating government efforts to increase surveillance of drug use and to develop new antibiotics (FDA Week 2016). Promising approaches which provide more rapid assessment utilizing newer technologies such as genomics are now being utilized by scientists.

Microbiologists are embracing high-throughput genomics to quickly examine individual organisms or entire microbial communities. A project underway at the University of California, Davis, the 100 K Foodborne Pathogen Genome Sequencing Project, will sequence 100,000 foodborne isolates for the most important worldwide foodborne illness outbreak organisms. It involves a consortium of academic, government, and industry to create a massive database of genome signatures for the most significant foodborne disease-causing microbes. The goal is to allow public health agencies and the food industry supply chain to trace any foodborne illness outbreaks to their source. By comparing the pathogen genome to the database which includes millions of pieces of information on previously detected strains, including their exact location, the contamination source will be positively identified. Bioinformatics and the analytics involved can be used to turn the vast amount of genomic information into actionable knowledge. These event sequencing approaches will enable new diagnostic and public health approaches to manage foodborne disease to facilitate improved public health. The database will increase ability to detect and mitigate pathogenic organisms in food, the environment, and livestock. That capacity is now constrained by continual genetic evolution of pathogens which hinders the ability to defend the food supply. This project will facilitate speedy testing of raw ingredients and finished products from outbreak investigations with precision and accuracy unparalleled using existing methods of analysis. Genomics enabled diagnostics with molecular tools will allow surveillance, risk assessment, and diagnosis of foodborne pathogens directly throughout the global food chain. The result will be a genetic catalog for some of the most important outbreak organisms impacting human health. The database will provide insights into molecular methods of infection and drug resistance for use in creating new vaccines and therapies. And importantly, it will assist in systematic definition of biomarker gene sets associated with antibiotic resistance (Weimer 2016).

A recent innovative metagenomics study also provides new insights on possible impacts of antibiotic use in food animal production and AR in humans. The research investigated antimicrobial resistance potential—the resistome—by tracking specific pens of intensively managed cattle from feedlot through slaughter to market-ready
beef products. Study results found no antibiotic-resistant determinants (ARDs) in the beef products beyond the slaughter facility. This suggests that intervention during slaughter minimizes potential for antibiotic-resistant determinants passing through the food chain. The results also highlight potential risks through indirect environmental exposures to the feedlot resistome through wastewater runoff, manure application on cropland, and wind-borne particulate matter. The insights provided can be used to better inform future agricultural and public health policy. However, this first of its kind study suggests the scientific community must develop a better understanding of the risk of different resistomes and resistance genes. It also identifies a pressing need to standardize ARD nomenclature so that databases and analyses are comparable across studies (Noyes et al. 2016).

The World Health Organization has recently developed guidelines to mitigate human health consequences from use of medically important antimicrobials in food-producing animals (WHO 2017). The guidelines are evidence-based recommendations and include best practices for use of medically important antimicrobials in food-producing animals, especially antimicrobials deemed critically important to human medicine. They also can help preserve effectiveness of antimicrobials for veterinary medicine. The recommendations include:

- An overall reduction in use of all classes of medically important antimicrobials in food-producing animals.
- Complete restriction for use in growth promotion.
- Complete restriction of use to prevent infectious diseases that have not yet been clinically diagnosed.
- Antimicrobials designated as critically important for human medicine should not be used to control spread of clinically diagnosed infectious disease identified within a group of food-producing animals, nor for treatment of food-producing animals with a clinically diagnosed infectious disease.
- For best practices, any new class of antimicrobials for use in humans will be considered critically important for human medicine unless otherwise categorized by WHO. Further, medically important antimicrobials not currently used in food production should not be so used in the future.

These guidelines apply universally, and improved animal health management can be used to reduce the need for antimicrobials including improvements in disease prevention strategies, housing, and husbandry practices as noted in Sect 15.5 above.

Economic incentives in regulations were addressed in a recent article. In some European countries, capping total antimicrobial use per animal through regulations has been successful in reducing use by more than half while maintaining competitive livestock sectors. The second option was to impose user fees on veterinary antimicrobials, applied at the point of manufacture or wholesale purchases for imported products, which could also reduce use significantly. As a policy option, some combination of these two strategies would significantly reduce antimicrobial use in food animal production (Van Boeckel et al. 2017). Finally, as discussed in Chap. 12, Sweden does not allow use of antibiotics in broiler production. If there is the political will, strong regulations can provide strong economic incentives to control antibiotic use.
15.12 Need for Producer Education

To promote the understanding and implementation of the FDA's new Veterinary Feed Directive, the Farm Foundation and the Pew Charitable Trusts sponsored a series of meetings with livestock and farming communities throughout the United States. Twelve educational workshops provided livestock producers, feed suppliers, veterinarians, and support service organizations information and insights on the new policies. The workshops also provided opportunity for participants to interact with FDA and USDA’s Animal and Plant Health Inspection Service (APHIS) personnel about implementation challenges.

Among livestock producers attending the workshops, small- and medium-sized operators, as well as many veterinarians, were unaware of the pending requirements. Lack of understanding about responsibilities under the revised VFD rule means that producers and veterinarians need education. Some land grant university extension services are now offering balanced education programs to inform these audiences about their obligations going forward, rather than having interested parties in the food animal industry be the primary source of information to producers and veterinarians about the requirements.

While seeing positives of improved public perception and livestock management as result of the new rules, workshop participants were concerned about increased costs in animal health due to restrictions on access to antibiotics and lack of veterinary services. Perhaps the biggest challenge is that many small producers do not have established relationships with veterinarians needed to establish a veterinarian-client-patient relationship (VCPR). This may be particularly challenging in remote rural and urban fringe areas where fewer veterinarians are available to treat food-producing animals.

In sum, workshop participants saw a need for education and outreach; continuing dialogue between industry representatives, consumers, and state or federal regulators; and the need to provide better access to veterinary services for food animals.

15.13 Conclusions

There is widespread agreement that the scientific evidence indicates a global human health and environmental crisis due to antibiotic resistance, in part resulting from production practices in animal agriculture. Government action in regulating the animal agriculture industry, to date, has done little to slow the advance of AR. Most countries still need to pass legislation to establish appropriate conditions for the import, manufacture, distribution, and use of veterinary products, including antimicrobial agents. Continued easy access to antimicrobial drugs for use on the farm is not acceptable. Important stakeholders in the animal production industry include pharmaceutical companies, feed companies, livestock production integrators, and some farm groups, each with their own set of incentives and supporters. They must
be engaged in the effort to reduce agriculture’s role in contributing to development of AR, which CDC estimates at 20% (Fig. 15.1). Even so, other major industry groups must be engaged to significantly reduce their 80% contribution to resistance development.

In the United States, some progress was made with the passage of the Animal Drug Availability Act in 1996 and its very gradual implementation through various regulations over the past two decades. However, there are serious gaps in these regulations. Given the gridlock that has prevailed in the US Congress and the power of the pharmaceutical lobby at the national level, state actions are leading the way to responsive regulation in the public interest. For example, California is the first US state to prohibit all human antibiotic use in food animal production.

In contrast to the halting actions of governments and industry, consumer and interest group actions are being at least partially successful in getting fast-food and retail establishments to not market animals fed human-use antibiotics for growth-promoting purposes. This suggests that a productive approach may be finding ways to provide information to and educate consumers about the risks of antibiotic resistance to enable them to make better informed decisions. There is an important role for educators to extend scientific information in a nontechnical way to the lay public.

The drive to use antibiotics more responsibly and in the public interest may be facilitated by recent economic results that show that reducing antibiotic use in animal production need not come at a significant economic cost to producers or consumers. Since the benefits of using antibiotics for livestock growth promotion appear to have resulted in increasingly smaller productivity gains, independent producers where input mix is a farmer-driven choice based on farm-level economics may be better off to substitute good management practices rather than using antibiotics for prophylactic disease prevention. However, much of meat animal production on US farms is produced under contract, where the integrator provides inputs, often including antibiotics, that the grower is required by contract to use. Recent actions by integrators and meat processors to reduce antibiotic use and substitute alternative strategies to protect animals from diseases and maintain productivity are an important development, especially since production-purpose use of antibiotics is now prohibited.

Presuming that any new human-use antibiotic classes will probably not be made available for veterinary medicine, it is important to preserve the effectiveness of existing antibiotics. Some policy makers and industry now recognize the urgency to identify new antibiotics. This will require increased antibiotic research funding and judicious use of existing antibiotics. The ban of human-use antibiotics in animals for production purposes is expected to help slow the growth of antimicrobial resistance, giving more time to discover new antibiotics for animal uses and for human health uses. To the extent they can be developed and used separately, the potential for animal antibiotic use leading to antimicrobial resistance for important human antibiotics will be mitigated.

The ban on antibiotics used for humans also being used for animal production purposes will necessitate adopting improved cultural practices to reduce the poten-
tial for disease and to increase feed efficiency. This calls for research on best management practices to accommodate today’s supply chain requirements for food safety, production efficiency, and attribute verification. Moreover, there is a need to educate producers—for example, through the USDA-State Cooperative Extension Service—about safe production practices for managing AR. This will allow producers to maintain efficiency in their operations and assure that they comply with current regulations to address the growing concern about antimicrobial resistance in the food supply chain. Improved data collection and analysis to allow tracking of potential antimicrobial resistance development are essential to facilitate the food animal industry implementation of cultural practices to reduce the potential for contributing to antimicrobial resistance. It would also allow policy makers to better understand the need for any necessary interventions. These investments in the public good can be very cost-effective, though not without additional public investment or internal agency budget reallocation.

Increasing international trade may spread antibiotic resistance through imported food products as more trade agreements are approved. This scenario could be exacerbated to the extent FSIS approves additional international facilities, local regulations, and inspections as “equivalent to the United States.” In many developed and developing countries, antimicrobial agents are readily available. Policies need to be implemented establishing appropriate conditions for use of veterinary products, including antimicrobial agents. Future trade agreements will need to include provisions which address reduced use of medically important antibiotics in producing food animals.

To date, there is no harmonized system of surveillance on the worldwide use and circulation of antimicrobial agents. That information is necessary to monitor and control the origin of medicines, obtain reliable data on imports, trace their circulation, and evaluate the quality of the products in circulation. The OIE initiative to create a global database for monitoring the use of antimicrobial agents is an important step that can provide valuable information for private sector and public policy leaders worldwide.

The serious implications of growing antibiotic resistance require a concerted effort across all stakeholders and society generally. Increased attention to this issue is emerging in the medical community where overuse of existing drugs and inadequate sanitary precautions account for 80% of the resistance. Lack of development of new antibiotics exacerbates the problem, and industry focus and perhaps government policy are needed to improve this situation. Animal agriculture stakeholders need to improve production practices to reverse the other 20% of resistance attributable to foodborne sources. Government policy and agencies have been slow to acknowledge the seriousness of antibiotic resistance and appropriately address it. Public and private sector collaboration internationally is necessary to successfully deal with this critical societal issue.

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References

Aga DS, Lenczewski M, Snow D, Muurinen J, Sallach JB, Wallace JS. Changes in the measurement of antibiotics and in evaluating their impacts in agroecosystems: a critical review. J Environ Qual. 2016;45:407–19.

Amábile-Cuevas C. Society must seize control of the antibiotics crisis. Nature. 2016;533:439. https://doi.org/10.1038/533439a. Accessed 26 May 2016.

APHIS. National Animal Health Monitoring System (NAHMS). Animal and Plant Health Inspection Service, United States Department of Agriculture. 2016. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/monitoring-and-surveillance/nahms/ct_national_animal_health_monitoring_system_nahms_home. Accessed 10 May 2016.

APUA. Major developments in U.S. policy on antibiotic use in food animals. Alliance for the prudent use of antibiotics. http://emerald.tufts.edu/med/apua/policy/policy_antibiotic_food_animals.shtml. Accessed 26 Dec 2016.

APUA Newsletter. Farm antibiotic use remains worrisome in India. Alliance for the prudent use of antibiotics. APUA Newsletter. 2016;34(1(Spring)):15.

Bowman M, Marshall KK, Kuchler F, Lynch L. Raised without antibiotics: lessons from voluntary labeling of antibiotic use practices in the broiler industry. Am J Agric Econ. 2016;98(2):622–42. https://doi.org/10.1093/ajae/aaw008.

Bunge J. Perdue chickens now free of antibiotics. Wall St J. 2016:B3.

Carnevale R. Antibiotic resistance and the use of antibiotics in animal agriculture: hearing before the subcommittee of the house committee on Energy & Commerce, 1st Sess. (?) (2010). http://www.ahi.org/wp-content/uploads/2011/06/July-14-2010-Testimony-by-Richard-Carnevale.pdf. Accessed 17 July 2016.

Carnevale RA. Across the divide: the importance of antibiotics for animal health. 2016. http://asmcultures.org/3-1/7/. Accessed 3 Apr 2017.

CDC. Antibiotic resistance threats in the United States, 2013. Centers for disease control and prevention. 2013a. http://www.cdc.gov/drugresistance/threat-report-2013/pdf/. Accessed 29 Sep 2016.

CDC. CDC 2011 estimates of foodborne illness in the United States. Centers for disease control and prevention. 2013b. http://www.cdc.gov/foodborneburden/pdfs/factsheet_a_findings_updated4-13.pdf. Accessed 22 May 2016.

CFI. Tracking animal antibiotic use in food animals. The center for foodborne illness research and prevention. 2016. https://www.foodborneillness.org/cfi-library/2016_CFI_Fact_Sheet_Track_animal_antibiotic_use_FINAL.pdf. Accessed 18 May 2016.

Consumer Reports, America’s Antibiotic Crisis. Part 3. 2016. http://www.consumerreports.org/media-room/press-releases/2015/11/consumer-reports-meats-produced-without-antibiotics-harbor-fewer-superbugs/. Accessed 6 Oct 2016.

Council for Agricultural Science and Technology (CAST). 1981. Antibiotics in animal feeds. Report No. 88. Ames, Iowa.

FDA. The judicious use of medically important antimicrobial drugs in food-producing animals. Guidance for Industry #209. 2012. https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM216936.pdf. Accessed 3 June 2016.

FDA. 2014 Summary report on antimicrobials sold or distributed for use in food-producing animals. 2015. https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM476258.pdf. Accessed 3 June 2016.

FDA. 2015 Summary report on antimicrobials sold or distributed for use in food-producing animals. FDA, Department of Health and Human Services. 2016a. https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM534243.pdf

FDA. Anti-microbial animal drug sales and distribution reporting. FDA, Department of Health and Human Services. 2016b. https://www.gpo.gov/fdsys/pkg/FR-2016-05-11/pdf/2016-11082.pdf. Accessed 22 May 2016.
FDA. FDA announces implementation of GFI #213, outlines continuing efforts to address antimicrobial resistance. 2017. https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm535154.htm. Accessed 27 Feb 2017.

FDA Week. Stakeholders: colistin-resistance shows need for congressional action. 2016. http://insidehealthpolicy.com/fda-week/stakeholders-colistin-resistance-shows-need-congressional-action. Accessed 5 June 2016.

FSIS. Animal production claims: outline of current process. FSIS, U.S. Department of Agriculture. 2016. http://www.fsis.usda.gov/OPPDE/larc/Claims/RaisingClaims.pdf. Accessed 06 Oct 2016.

GNP Company. Gold’n Plump To Add ‘No Antibiotics-Ever’ and Humane Certified Attributes. 2015. Perishable News.com. http://www.perishablenews.com/print.php?id=0050530. Accessed 6 Oct 2016.

Institute of Medicine. Report of a study: human health risks with the subtherapeutic use of penicillin or tetracyclines in animal feed. Committee on human health. Washington, DC: National Academies Press; 1988.

Johansen J. Accurate, credible info on animal antibiotics. Phibro Animal Health. 2016. AnimalAntibiotics.org. Accessed 5 Aug 2016.

Joint Committee on the use of Antibiotics in Animal Husbandry and Veterinary Medicine. 1969. Report presented to parliament by the secretary of state for social services, the secretary of state for Scotland, the Minister of Agriculture, Fisheries and Food and the Secretary of State for Wales by Command of Her Majesty.

Laxminarayan R, Chaudhury RR. Antibiotic resistance in India: drivers and opportunities for action. PLoS Med. 2016;13(3):e1001974. https://doi.org/10.1371/journal.pmed.1001974. Accessed 5 Aug 2016.

Levy SB, FitzGerald GB, Macone AB. Changes in intestinal Flora of farm personnel after introduction of a tetracycline-supplemented feed on a farm. N Engl J Med. 1976;295:583–8. https://doi.org/10.1056/NEJM197609092951103. Accessed 5 Aug 2016.

Lusk JL. In: Armbruster WJ, Knutson RD, editors. Consumer information and labeling. New York: Springer; 2013.

Lusk JL, Norwood FB, Pruitt JR. Consumer demand for a ban on antibiotic drug use in pork production. Am J Agric Econ. 2006;88(4):1015–33. https://doi.org/10.1111/j.1467-8276.2006.00913.x. Accessed 29 Sep 2016.

MacDonald JM, Wang SL. Foregoing sub-therapeutic antibiotics: the impact on broiler grow-out operations. Appl Econ Perspect Policy. 2011;33(1):79–98. Accessed 1 June 2016.

Mason M, Mendoza M. Pressure rises to stop antibiotics agriculture. PhysOrg. 2009. http://phys.org/news/2009-12-pressure-antibiotics-agriculture.html. Accessed 24 May 2016.

Miller M. Antibiotic discussions intensify in WDC. Pork Network. 2011. http://www.porknetwork.com/pork-news/antibiotic-discussions-intensify-in-wdc-114024789.html. Accessed 24 May 2016.

Mitchell A. World animal health organization sets out action on antibiotic resistance. Poultry News. 2016. http://www.thepoultrysite.com/poultrynews/37091/world-animal-health-organisation-seeks-action-on-antibiotic-resistance/. Accessed 25 May 2016.

Moyer MW. The looming threat of factory-farm superbugs. Sci Am. 2016;315(6):70–9.

MRC. MRC announces cross-council awards worth nearly £10m to tackle antibiotic resistance. Medical Research Council. 2016. http://www.mrc.ac.uk/news/browse/mrc-announces-cross-council-awards-worth-nearly-10m-to-tackle-antibiotic-resistance/. Accessed 25 May 2016.

NARMS. National antimicrobial resistance monitoring system for enteric bacteria human isolates surveillance report for 2014 (Final Report). Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2016. https://www.cdc.gov/narms/pdf/2014-annual-report-narms-508c.pdf. Accessed 29 Sep 2016.

NASS. 2012 Census of Agriculture. United States summary and state data. Vol. 1, Part 51. AC-12-A-51. U.S. Department of Agriculture, National Agricultural Statistics Service. Washington, DC; 2014.
National Academy of Sciences. The effects on human health of subtherapeutic use of antimicrobial drugs in animal feeds. Committee to study the human health effects of subtherapeutic antibiotic use in animal feeds. Washington, DC; 2009.

Noyes NR, Yang X, Linke LM, Magnuson RJ, Dettenwanger A, Cook S. Resistome diversity in cattle and the environment decreases during beef production. eLife. 2016;5:e13195. https://elifesciences.org/content/5/e13195. Accessed 3 Apr 2016.

O’Neill J. Tackling drug-resistant infections globally: final report and recommendations. The review on antimicrobial resistance. 2016. http://amr-review.org/. Accessed 7 July 2016.

OIE. Antimicrobial Resistance. World Organization for Animal Health. 2015. www.oie.int. Accessed 22 May 2016.

Oreskes N, Conway EM. Merchants of doubt: how a handful of scientists obscured the truth on issues from tobacco smoke to global warming. London: Bloomsbury Publishing Plc; 2010.

Rosenblatt-Farrell N. The landscape of antibiotic resistance. Environ Health Perspect. 2009;117(6):A244–50. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2702430/. Accessed 7 July 2016.

Seattle-King County Department of Public Health. Surveillance of the flow of Salmonella and Campylobacter in a community. Prepared for United States Department of Health and Human Services, Public Health Service, Food and Drug Administration, Bureau of Veterinary Medicine; 1984. Contract Number.

Silley P, Stephan B. Prudent use and regulatory guidelines for veterinary antibiotics—politics or science? J Appl Microbiol. 2017;123:1373–80. Accessed 30 Nov 2017.

Snerring S, MacDonald J, Key N, McBride W, Mathews K. Economics of antibiotic use in U.S. livestock production. U.S. Department of Agriculture, Economic Research Service. ERR-200, November. 2015. http://www.ers.usda.gov/publications/err-economic-research-report/err200.aspx. Accessed 1 June 2016.

So AD, Shah TA, Rouch S, Chee YL, Nachman KE. An integrated systems approach is needed to ensure the sustainability of antibiotic effectiveness for both humans and animals. J Law Med Ethics. 2015;43(Suppl 3):38–45. Accessed 30 May 2016.

Tang KL, Caffrey NP, Nóbrega DB, Cork SC, Ronksley PE, Barkema HW, et al. Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. Lancet Planet Health. 2017;1(8):e316–27. https://doi.org/10.1016/S2542-5196(17)30141-9. Accessed 18 Nov 2017.

Teillant A, Laxminarayan R. Economics of antibiotic use in U.S. swine and poultry production. Choices 1st Quarter. 2015;30(1). http://choicesmagazine.org/choices-magazine/theme-articles/theme-overview/economics-of-antibiotic-use-in-us-swine-and-poultry-production. Accessed 5 June 2016.

Tyson Foods. Position statements: antibiotic use. 2017. http://www.tysonfoods.com/media/position-statements/antibiotic-use. Accessed 27 Feb 2017.

Union of Concerned Scientists. Scientific integrity in policymaking: an investigation into the Bush Administration’s misuse of science. Cambridge, MA: 2004. http://www.ucsusa.org/sites/default/files/legacy/assets/documents/scientific_integrity/rsi_final_fullreport_1.pdf. Accessed 1 Mar 2017.

Van Boeckel TP, Glennon EE, Chen D, Gilbert M, Robinson TP, Grenfell BT, Levin SA, Bonhoeffer S, Laxminarayan R. Insights: reducing antimicrobial use in food animals. Science. 2017;357(6358):1350–2.

Veterinary Feed Directive A rule by the food and drug administration on 06/03/2015. 2015. https://www.federalregister.gov/documents/2015/06/03/2015-13393/veterinary-feed-directive. Accessed 3 June 2016.

Webb HE, Angulo FJ, Granier SA, Scott HM, Loneragan GH. Illustrative examples of probable transfer of resistance determinants from food animals to humans: Streptothricins, glycopeptides, and colistin [version 1; referees: 2 approved]. F1000Research. 2017;6:1805. https://doi.org/10.12688/f1000research.12777.1.
Weimer BC 100 K genome project 2016. Veterinary Medicine, UC Davis. 2016. Accessed 5 July 2016; OIE. Fact sheet on antimicrobial resistance. World Organization for Animal Health. 2015. http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Fact_sheets/ANTIBIO_EN.pdf. Accessed 24 Oct 16.

WHO. Antimicrobial resistance: Global Report on Surveillance. 2014 summary. World Health Organization. 2014. http://apps.who.int/iris/bitstream/10665/112647/1/WHO_HSE_PED_AIP_2014.2_eng.pdf?ua=1. Accessed 30 Sep 2016.

WHO. WHO guidelines on use of medically important antimicrobials in food-producing animals. Geneva: World Health Organization; 2017. License: CC BY-NC-SA 3.0 IGO

Zhang WH, Lin XY, Xu L, Gu XX, Yang L, Li W, et al. CTX-M-27 Producing Salmonella enterica serotypes Typhimurium and Indiana are prevalent among food-producing animals in China. Front Microbiol. 2016;7:436. https://doi.org/10.3389/fmicb.2016.00436. Accessed 7 July 2016.

Zhu YG, Johnson TA, Su JQ, Qiao M, Guo GX, Stedtfeld RD, et al. Diverse and abundant antibiotic resistance genes in Chinese swine farms. PNAS. 2013;110(9):3425–40. http://www.pnas.org/cgi/doi/10.1073/pnas.1222743110. Accessed 7 July 2016.

Zilberman D, Hochman G, Kaplan S, Kim E. Political economy of biofuel. Choices. 2014. 1st Quarter 2014;29(1). http://choicesmagazine.org/choices-magazine/theme-articles/theme-overview/economics-of-antibiotic-use-in-us-swine-and-poultry-production. Accessed 7 July 2016.