



## The Ticking Time Bomb

Few of those living today in the United States have known the terror of standing by helplessly as untreatable infection rages through the body of a loved one. Few of us remember the time when infectious diseases such as typhoid and childhood diseases such as whooping cough and scarlet fever swept through populations. In the early part of the century, such diseases were the major cause of death. Then in the 1940s, when antibiotics and other antimicrobials<sup>1</sup> became commercially available, their ability to banish infectious disease caused by bacteria seemed miraculous. But as we move into the 21st century, the miracle is under threat as bacteria increasingly develop resistance to those drugs.

The reason that antimicrobial resistance is becoming more common is simple: evolution. Microorganisms are so numerous and

so adept at exchanging genetic traits that a few always escape the killing effects of antimicrobials. Over time, these hardy strains come to predominate in the population and the drugs are no longer effective against them. Diseases that once were easily cured by antimicrobials are becoming more difficult to treat. Physi-

cians turn to other drugs, but evolution works against those drugs as well. As the number of effective antimicrobials diminishes, the time bomb is ticking. When the pharmacy runs out of drugs, diseases will once again become untreatable scourges.

It is always a temptation to let the future take care of itself in the hope that new antimicrobials will become available to replace the old. But after decades of evolution, the future has arrived. The pipeline for new antimicrobials has slowed to a trickle and infectious

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<sup>1</sup> Antimicrobials comprise all drugs that kill or inhibit the growth of any microorganism. The category includes antibiotics, naturally occurring substances that kill or inhibit the growth of bacteria.

disease agents are exhibiting resistance to more and more antimicrobials.

Antimicrobial resistance is attracting worldwide attention. The World Health Organization (WHO) sees the threat of increasing antimicrobial resistance, especially in medical settings, as ominous. In its most recent report, WHO fears that the window of opportunity to control and eliminate many of the infectious diseases, including those caused by antimicrobial-resistant bacteria is closing (WHO 2000). In the United States, the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the US Department of Agriculture (USDA), and the National Institutes of Health recently developed an interagency task force action plan on antimicrobial resistance. The medical community is also becoming alarmed. The prestigious *New England Journal of Medicine* has, in the last few years, carried numerous reports, editorials, and commentaries on the issue (e.g., Molbak et al. 1999, Linares et al. 1999, Gorbach 1999, Fey et al. 2000).

Serious attention to the problem of antimicrobial resistance is welcome. But we should not underestimate how difficult the solution—which involves fundamental changes in physicians' behavior, patients' expectations, and hospital procedures—will be to implement. Nevertheless, the momentum is building to address the overuse and misuse of antimicrobials in human medicine.

But the use of antimicrobials in humans is not the only source of antimicrobial-resistant bacteria. Enormous amounts of antimicrobials are also used in agriculture, subjecting microorganisms to the same forces of evolution as occur when antimicrobials are used in humans. Humans may encounter bacteria from animals through the food supply, through direct contact with animals, or through water. Because many of the antimicrobials used in animals are also used in human medicine, the use of antimicrobials in animals is part of the global problem of antimicrobial resistance.

Society has been even slower in responding to the problems caused by agriculture than to those caused by human medicine. The contribution of agricultural use to the overall problem of antimicrobial resistance is harder to pin down than the contribution of human use for two reasons. Public health officials have had a tough time compiling the data needed to document the link between animal use of antimicrobials and human illness,

and increased resistance has not, until recently, compromised the treatment of humans.

But the time bomb has been ticking away. Resistance has emerged in drugs commonly used in humans and now the evidence demonstrating ties between animal agriculture and human illness has accumulated to the point that it cannot be ignored.

A good example is the recent article in the *New England Journal of Medicine* (Molbak et al. 1999), which reported a foodborne outbreak of Salmonellosis that made scores of people sick and led to the death of two people. The outbreak was caused by *Salmonella typhimurium* DT104, which was resistant to five different antibiotics and had reduced susceptibility to fluoroquinolones. In nearly half the hospitalized patients, the powerful drug ciprofloxacin (a fluoroquinolone) was not effective, and one of the deaths occurred in spite of multiple treatments with this and other antimicrobial drugs. This outbreak was traced back through the food system to its source: a herd of swine infected with the same multidrug-resistant strain of bacteria. According to Dr. Abigail Salyers, the president-elect of the American Society for Microbiology, the study is the “closest that anyone has come to a smoking gun” linking agricultural use of drugs to antimicrobial resistance that contributed to a particular human death (Ferber 2000).

“Smoking guns” are difficult to come by because the terrain between the livestock facilities and a particular patient dying in a hospital is occupied by a complex food system. Tracing bacteria through that territory is daunting. The only way to navigate the terrain is with good surveillance and monitoring, timely use of sophisticated methods to track resistant bacteria by their genetic fingerprints, and lots of data crunching.

The study in the *New England Journal of Medicine* was able to document most of the steps in the food chain between a herd of swine and the death of two people because the Danish government operates first-class surveillance and monitoring programs. These programs sample flocks of chickens and herds of swine throughout the country for *Salmonella* and test *Salmonella* isolates for antimicrobial resistance. Thus public health officials were able to act rapidly to trace the antimicrobial-resistant *Salmonella* back through the food supply when reports came of a cluster of patients suffering from drug-resistant disease. They rapidly learned that many of the patients had bought pork from groceries supplied by a single slaughterhouse, and records showed which farms supplied the slaughterhouse. Officials collected *Salmonella* isolates from the

implicated slaughterhouse and farms and rapidly confirmed that the resistant strains in the patients, including those who died, the stores, the slaughterhouse, and the farms had identical molecular fingerprints.

The United States has only rudimentary surveillance programs for the livestock and food systems, making definitive evidence harder to come by and usually more circumstantial. Nevertheless, in a recent case, a 12-year-old Nebraska boy came down with a multidrug-resistant strain of *Salmonella* that was identical to strains isolated from cattle on his family's and neighbors' farms (Fey et al. 2000). The strain was also resistant to ceftriaxone, a powerful human drug related to a drug commonly used to treat diarrhea in cattle. Although the boy recovered, the identification of ceftriaxone-resistant *Salmonella* sent shock waves through the pediatric

community. Ceftriaxone is a third-generation cephalosporin, a class of drugs essential for treating serious infections in children. What was important was not the near miss for this lucky boy, but the demonstration that drug use in animal systems can have important consequences in human medicine.

More evidence of the human health consequences of the use of antimicrobials in food animals comes from the state of Minnesota. Scientists showed that the rapid rise (1 percent to 10 percent) in fluoroquinolone-resistant *Campylobacter* cultures in Minnesotans followed upon the 1995 approval of fluoroquinolones for use in poultry (Smith et al. 1999). The fluoroquinolone antibiotics are essential for the treatment of serious infections in adult humans. Using molecular techniques like those used in Denmark, scientists determined that strains of *Campylobacter* found in people matched those found in animals. Again the study confirms that antimicrobial use in animals may result in resistance that can be transmitted to humans.

Concern about the emergence of fluoroquinolone resistance led the CDC to oppose the approval of fluoroquinolones for animal use, but the FDA approved them anyway. A risk assessment done by the FDA in 1998 estimated that nearly 5,000 people were infected with *Campylobacter* resistant to fluoroquinolones, sought medical care, and were treated with ineffective fluoroquinolones (FDA 2000a). By 1999, about 11,000 people infected

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with *Campylobacter* were receiving less effective or ineffective treatment with fluoroquinolones. The rising risks of difficult-to-treat disease prompted the FDA to announce its intention to withdraw approval for enrofloxacin, one of the two fluoroquinolones used in poultry (FDA 2000d). The manufacturer of the other fluoroquinolone, sarafloxacin, withdrew the drug from the market voluntarily.

With an ever-increasing body of evidence strengthening the link between animal use and human illnesses, public health researchers and scientists are now beginning to collect data documenting the presence of antimicrobials and resistant bacteria in the nation's streams and rivers. In 1999, for example, the US Geological Survey began to collect baseline information on human and veterinary antimicrobials in US streams (USGS 2000). In other surveys that began in the late 1990s, scientists in the Midwest began to document the occurrence and spread of resistant bacteria in the nation's waterways (Bennett and Kramer 1999, Schroeder and Bennett 1999, Christian and Bennett 2000). These new data suggest that antimicrobial-resistant bacteria have spread widely in the environment and raise concerns about a new route of human exposure—drinking water.

The most obvious problems deriving from livestock use of antimicrobials are evident with foodborne illnesses caused by *Salmonella* and *Campylobacter*. But evidence is also accumulating for connections between livestock use of antimicrobials and serious hospital-centered infections. In the May-June 1999 issue of the CDC journal *Emerging Infectious Diseases*, a team of Danish scientists traced in detail the evidence showing that avoparcin, an animal growth promoter, had triggered a dramatic increase in vancomycin-resistant *Enterococcus faecium* in hospitals (Wegener et al. 1999). Avoparcin is chemically related to vancomycin, an important drug in human medicine. It is now banned in Europe.

In the United States, the FDA is exploring the connection between virginiamycin, an animal growth promoter, and resistant enterococcal infections. Enterococcal infections cause 20 to 30 percent of over 2 million hospital-acquired infections every year. About 14 percent of those infections are now resistant to vancomycin, the drug of last resort. In 1999, the FDA approved a new drug for use against vancomycin-resistant enterococci called Synercid. Unfortunately, virginiamycin, an antimicrobial closely related to Synercid, has been used in livestock feed for growth promotion for over 25 years. Scientists believe that Synercid-

resistant enterococci may have been generated in livestock facilities as the result of the use of virginiamycin and transferred to humans on contaminated meat. Perhaps not surprisingly, patients in hospitals are already exhibiting resistance to Synercid. Because Synercid is likely to be given to 70,000 patients per year who have vancomycin-resistant infections, the FDA is currently attempting to assess the impact of virginiamycin use in livestock on the evolution of resistance (FDA 2000b).

These studies confirm what scientists and public health officials have long believed: use of antimicrobials in animal agriculture is an important source of antimicrobial-resistant disease in humans. Thus, the public health community has seen the problem of resistance coming. It has watched as pathogens such as *Salmonella typhimurium* DT104 have become resistant to a growing list of antimicrobials and as these resistant strains have spread globally. But as long as effective antimicrobials remained, few individuals died for lack of therapy. Drug companies used the paucity of clinical failures and smoking guns to argue for inaction—and inaction won the day. But the time bomb has continued to tick. Now *Salmonella typhimurium* DT104 is resistant to seven antimicrobials and the antimicrobial cupboard for it and other diseases is almost bare. Although drug manufacturers are again beginning to turn their attention to antimicrobials, it is likely to take a decade or more for new drugs to be discovered, tested, approved, and brought to market. When the drugs do arrive, they will be patented and expensive.

## Time to Act

The time has come to contain antimicrobial resistance by reducing the misuse and overuse of antimicrobials in agriculture. The public health community is leading the way. The recent WHO report forcefully restated its recommendation, first made in 1998, that antimicrobials important for human medicine be banned from use as growth promoters in animals. The CDC has had a program for preventing emerging infectious diseases since 1994, which includes an effort to promote the judicious use of antimicrobials (CDC 1998). Even the FDA's Center for Veterinary Medicine now considers antimicrobial resistance its top priority, as evidenced by its recent efforts to ban fluoroquinolones used in poultry (Sundlof 2000).

What can be done? Since the problem is a consequence of overuse and misuse, the solution is obvious: use antimicrobials

only where medically necessary. A first step is to identify nonessential uses of antimicrobials. Agriculture is a good place to look for uses of antimicrobials that could be eliminated because much of the antimicrobial use is for nontherapeutic purposes such as growth promotion. Unlike in human and veterinary medicine, where antimicrobials are used to treat sick individuals, in agriculture, antimicrobials are also used in the absence of disease to produce primarily economic benefits. These economic benefits can be produced in other ways, which if implemented would reduce the use of antimicrobials and thereby prolong their effectiveness.

It is long past time to examine agricultural systems for opportunities to reduce antimicrobial use.

## Flying Blind

As the public health and public interest communities gird themselves for the push to address the looming health crisis of antimicrobial resistance, they face a major stumbling block. Public health officials and regulators have only a hazy picture of where, how much, and for which purposes antimicrobials are used in animal agriculture.

Astonishingly, even the most basic information on antimicrobial usage is not available—not from industry, not from the FDA, not from the CDC. To illustrate, the FDA does not have the information it needs to do the risk assessment on virginiamycin mentioned above. *Despite the fact that virginiamycin has been used in food-producing animals for 26 years, the agency does not know how much is being used in cattle, swine, and poultry.* Since this information is essential for its risk assessment, the FDA is requesting that industry voluntarily come forward with “virginiamycin use information including the proportion of food-producing animals in each class that receive virginiamycin” (FDA 2000b). Unfortunately, the lack of information is not confined to virginiamycin: it exists across the board.

The Union of Concerned Scientists (UCS) at first thought that antimicrobial use information would be publicly available, so we commissioned two consultants, Charles and Karen Lutz Benbrook, to do a small study to ferret it out. They scoured the academic literature, all of the major reports on veterinary antimicrobials, and various industry publications. They also interviewed officials in the FDA and the CDC. And they came up dry. With one small exception—USDA’s data on antimicrobials used as pesticides in vegetables and fruit orchards—no entity has compiled publicly available,

comprehensive data on the use of antimicrobials in agriculture. As it turns out, even the often-cited 50-million-pound figure for total antimicrobial production is not based on current data. As we discuss below, the estimate is an extrapolation of data 20 years old that has gained legitimacy simply through repetition. The most basic data on how much of which antimicrobials are used in cattle, swine, and poultry and how use patterns have changed over time are simply unavailable to the public, the public health community, or regulators.

## The Purpose of This Study

We undertook this study to begin to fill in the chasm of unavailable data on the quantities of antimicrobials used in animal systems. In this report, we estimate the usage of antimicrobials in three sectors of US animal agriculture: cattle, swine, and poultry.

*Rough as they may be, our estimates are the best available on the usage of antimicrobials in US animal agriculture.*

Because these data are not publicly available, UCS worked with consultants to devise a methodology to estimate the pounds of specific antimicrobials used by livestock producers in these three sectors. We started with verifiable pieces of publicly available information, such as the number of animals slaughtered in a year, the list of antimicrobials approved for use on various kinds of livestock, and the

dosage for approved antimicrobials. Then, with the help of assumptions and informed judgments, we used these data to estimate the quantities of antimicrobials used in cattle, swine, and poultry.

In developing our methodology, we sought guidance from many expert reviewers. We wanted to be sure that we were producing the most accurate estimates possible given the information available. The resulting estimates are good ballpark figures. We make no apologies for using assumptions and judgments; had the needed data been available from a reliable source, we would have used them. But they are not. *The estimates in this report, as “rough” as they may be, are the best available on the usage of antimicrobials in US animal agriculture.* It remains for those critical of our results to provide transparent data to facilitate better estimates.

## The Use of Usage Data

Estimates of the quantities of antimicrobials used are fundamental in directing appropriate interventions to reduce their overuse and misuse. Without basic information on how much is being used, public health officials are flying blind as they try to formulate rational strategies to address this threat to public health.

The following questions—all fundamental to public health policy on appropriate use of antimicrobials—cannot be accurately answered with the currently inadequate state of data.

- What is the total quantity of antimicrobials used annually in the United States?
- What share of the total quantity of antimicrobials is used in animals and what share is used in humans?
- What portion of antimicrobial use is for nontherapeutic purposes?
- What portion of the antimicrobials used in agriculture is delivered in feed and what portion in water?
- Which uses are increasing and which are decreasing?

The US public health community has complained of the lack of reliable data on antimicrobial use in the United States for more than 30 years. Industry has long relied on the lack of such data to justify inaction on the basis of its belief that the link between use of antimicrobials in animals and human health consequences was unproved. This has always been a cynical position, since industry possesses the data that would make the link more apparent.

For example, at a 1998 WHO consultation on fluoroquinolones, there was much discussion about whether the observed increase in fluoroquinolone resistance in human pathogens was due to the increased use of the drugs in animals. The key piece of information needed to answer the question was whether animal use had indeed increased and whether the time at which the drug was introduced correlated with the onset of the rise in resistance rates in human pathogens. The industry possessed the data and, in fact, provided it at the meeting, but refused to allow it to be published in the meeting's proceedings. Not surprisingly, the data strongly implicated animal use as a source of resistance traits (WHO, personal communication).

As evidence in the clinical literature mounts indicating the human health consequences of using antimicrobials in animals, such stonewalling by the animal drug industry is increasingly untenable. If the public health community is right, and antimicrobial

resistance continues to rapidly emerge and spread, we may soon reenter the era of untreatable infectious diseases. Lack of detailed information should no longer provide cover for business as usual. We have a serious human health problem, and we need information now to fashion effective solutions before it becomes too late.



## USING ANTIMICROBIALS IN LIVESTOCK

*Antimicrobials are routinely added to the feed or water of healthy animals.*

It comes as a surprise to many people that antimicrobials—including familiar antibiotics that are commonly used in humans such as penicillin and tetracycline—are routinely added to the feed or water of healthy animals. Producers use antimicrobials at low doses—too low to treat diseases—because they appear to promote faster animal growth on less feed. That antimicrobials could have that effect was first suggested in 1946 in an article published in the *Journal of Biology and Chemistry* by a team of scientists working with poultry (Moore et al. 1946). By 1950, research reports had appeared in several journals claiming to document the benefits of so-called subtherapeutic doses of tetracyclines and penicillins in other systems including swine (Cunha et al. 1950) and calves (Loosli and Wallace 1950).

Despite more than 50 years of routine use for this purpose, just *how or to what extent* antimicrobials work to promote animal growth has not been demonstrated. Several theories have been advanced but consensus remains elusive. Some suggest that they work through impacts on microorganisms, others by mechanisms that are unrelated to antimicrobial activity, for example, through shifts in energy metabolism or the immune system. Of course, the mechanisms might overlap, i.e., growth promotion could be the result of preventing the growth of microorganisms or could work by two methods at the same time, or by one mechanism early in life and a different one later on. For whatever reason, the exact mechanisms by which antimicrobials stimulate growth have never been worked out. Despite the lack of well-understood mechanisms, livestock producers routinely use them for growth promotion in the belief that they increase profit margins.

Thus, antimicrobials used for growth promotion are given to healthy animals to increase the pounds of gain per unit of feed consumed. In theory, the faster the animals grow, the fewer days

they remain on feed before reaching slaughter weight and the more profitable the production system, all other things being equal. Shorter times on feed improve feed efficiency per pound of weight gain because animals burn most of the calories they consume each day—between 70 and 85 percent—just maintaining bodily functions.

Livestock and poultry farmers have also come to believe that relatively low concentrations of antimicrobials in feed and water can help avoid disease-driven losses in livestock. Such losses are a constant threat in the confinement systems that are common in American agriculture. The trend toward these large-scale, concentrated housing systems has been driven by economics. Producers can lower labor, feed, and housing costs by raising more animals in existing spaces and precisely controlling what and when they are fed. The feed industry contributes to the trend by providing a steady flow of feeds that include appropriate mixtures of vitamin and mineral supplements, calories, protein—and antimicrobials.

Animals in intensive agricultural settings are more susceptible to infectious diseases: they are crowded together, share feeders, and are periodically subjected to environmental extremes. Coping with the health consequences of intensive systems incurs costs that may offset their economic advantages. Common circumstances leading to stress and disease include unseasonably warm, dry, damp, or cold weather; a malfunctioning water- or manure-handling system; or a batch of feed that has not been mixed properly or was contaminated with bacteria. It is in these settings that antimicrobials are often used. As pointed out by the 1999 National Research Council report *The Use of Drugs in Food Animals*, the “beneficial effects of subtherapeutic drug use are found to be greatest in poor sanitary conditions” (NRC 1999). Under such circumstances, producers could suffer significant losses in a matter of days. In the face of such potential losses, producers often treat *all* animals in a flock or herd with antimicrobial-supplemented feed when they believe animals are susceptible to disease—even without any manifestation of disease.

Feed efficiency and growth-promotion benefits can, however, be achieved by other means than reliance on antimicrobials. These include efforts directed at reducing stress and increasing cleanliness, ventilation, and comfort. Such changes can also reduce the need for therapeutic administration of antimicrobials.

Although antimicrobial usage is closely linked with confinement agriculture, the two are not inextricable. Experience in Europe has

shown that low-level antimicrobials are not *necessarily* required for confinement systems—at least moderate-scale systems—if the systems are designed to provide the good hygiene and relatively comfortable living conditions that are key to avoiding stress and disease.

As the June 2000 World Health Organization report *Overcoming Antimicrobial Resistance* emphasized, “antimicrobials [should] not be used as an alternative to high-quality animal hygiene. Evidence shows that farmers who stopped relying on antimicrobials as growth promoters in livestock have experienced no economic repercussions—provided animals were given enough space, clean water, and high-grade feed” (WHO 2000). Small-scale operations offer even more opportunities for avoiding stress and disease.





## **Total Quantity of Antimicrobials Used**

Antimicrobials have many uses in human and veterinary medicine, agriculture, and consumer products. They are used as medicines to treat human and animal diseases, as growth promoters and for disease prevention in livestock systems, as pesticides in vegetables and fruit orchards, and as disinfectants in consumer products (Table 1).

The most commonly cited estimate of total quantity of antimicrobial production and use in the United States is at least 50 million pounds annually. What is the source of this figure? It is an extrapolation from the US production estimates offered in Table IV-4 of the 1989 Institute of Medicine (IOM) report *Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feed*. This table, which reports US antibiotic production from 1950 to 1986, is in turn based on older National Research Council reports and data from the US International Trade Commission. The table reports US production as

- 0.9 million pounds in 1950
- 4.7 million pounds in 1960
- 16.9 million pounds in 1970
- 24.6 million pounds in 1980
- 31.9 million pounds in 1985
- 44.3 million pounds in 1986

The IOM committee considered the 44.3-million-pound number to be an anomaly and stated that the production in the low 30-million-pound range was typical for the late 1980s. When the rate of increase in the 1970s and 1980s is extrapolated to the late 1990s, the resulting figure is about 50 million pounds.

In several places, the IOM committee stated how little confidence it placed in the data on which the extrapolation was based. For example, regarding the data in Table IV, the committee noted that sales reported by the International Trade Commission

**Table 1. Uses of Antimicrobials**

Subject	Use
Human	Therapeutic (i.e., medical) Consumer (soaps, toys, etc.)
Animal  Livestock (cattle, swine, poultry, turkey, goat, etc.)	Nontherapeutic (growth promotion, disease prevention) Therapeutic (i.e., medical)
Aquaculture	Nontherapeutic (disease prevention) Therapeutic (i.e., medical)
Companion animals	Therapeutic (i.e., medical)
Plant (orchards, vegetables)	Pesticidal

totaled just 11.3 million pounds in a year when production of 44.3 million pounds was reported.

Despite the obvious deficiencies in Table IV, upon which the 50-million-pound estimate is based, the figure has bounced around long enough to attain a degree of legitimacy. But the figure is no more than an extrapolation of almost 20-year-old production information, which is itself of questionable accuracy.

*The 50-million-pound figure rests on nothing more than extrapolation and repetition.*

The fact that the 50-million-pound figure rests on nothing more than extrapolation and repetition is indicative of the dismal absence of information on quantities of antimicrobials used. The lack of firm figures for total antimicro-

bial production also hampers attempts to calculate what share of the total quantity of antimicrobials is used in animals or humans.

## **Quantity of Antimicrobials Used in Human Medicine**

Considering the lack of information on the total quantity of antimicrobials produced, it is not surprising that information on quantities used for specific purposes in agriculture and human medicine is also limited—even in the important category of human drug use.

As it turns out, survey-based systems are in place to track prescriptions issued by physicians and filled by pharmacists.

Information on the number of prescriptions written and the courses of treatment delivered can be used to estimate the quantity of antimicrobials used in human medicine with reasonable accuracy. But no one has, to our knowledge, produced such estimates. The calculations require estimates of the average quantity of antimicrobial delivered in each course of treatment and simple multiplication by the number of courses delivered.

The National Center for Health Statistics (NCHS), a division of the CDC, has compiled data on the number of prescriptions of antimicrobials given to people following visits to their doctors, commonly referred to as “outpatient” use. According to NCHS, outpatients receive 120 million courses of treatment of antimicrobials annually (NCHS 2000). We reviewed many articles describing recent surveys of outpatient antimicrobial prescriptions and use and consulted with several experts. Based on this input, we project that an average course of treatment includes two doses a day for ten days, at a dose that typically falls between 250 and 500 mg. These parameters translate into between 5 and 10 grams of antimicrobial delivered per outpatient course of treatment.

Multiplied by the NCHS figure—120 million courses—the total quantity of antimicrobials used in outpatients is between 1.3 and 2.6 million pounds. We are using a “most likely value” of 2.1 million pounds, just above the midpoint in our range of estimates set forth in Table 2.

Our estimate for inpatient or hospital use is based on a survey found in the *US Hospital Anti-infective Market Guide*, January-June 2000 edition (AMR 2000).<sup>2</sup> The survey indicates 22 million courses over a six-month period. To be conservative, we have decided to use an annual figure of 50 million courses of treatment.

**Table 2.**  
**Antimicrobials Used in Human Medicine (in pounds)**

	Low End	High End	Most Likely Value
Outpatient Use	1,322,774	2,645,547	2,100,000
Inpatient Use	551,156	1,102,311	900,000
Total Treatment	1,873,930	3,747,858	3,000,000

<sup>2</sup> The *US Hospital Anti-infective Market Guide* is a semiannual syndicated clinical audit of inpatient antibacterial and antifungal use in the US hospitals. The audit is based on anti-infective census data from representative hospitals and review of randomly selected inpatient records.

The *Market Guide* survey states that the average length of an inpatient course of treatment is 7.8 days; we used 8 days in our calculations. We used the same average dose (250 to 500 mg) and doses per day (2) in estimating both inpatient and outpatient use. We are aware that antimicrobial drugs in hospitals are most often delivered by injection, a generally more efficient delivery mechanism than pills. That suggests that the average inpatient (hospital) dose would be lower than the average outpatient dose. But we also know that hospitalized patients tend to be sicker and treated more aggressively; hence they may require somewhat higher concentrations of antimicrobials in their systems.

To be conservative, we have used the same dose range in estimating inpatient use that we used for outpatients. The calculation yields a range for total inpatient use from 550,000 to 1,100,000 pounds, with a “most likely value” of 900,000 pounds. Inpatient and outpatient uses together add up to 3 million pounds of antimicrobials for human medical use, as shown in Table 2.

## **Agricultural Use of Antimicrobials**

This report focuses on the quantity of antimicrobials that are given to cattle, swine, and poultry for nontherapeutic purposes. We have made no attempt to calculate quantities used for therapeutic uses in agriculture and to treat companion animals. In some cases, however, the distinction between therapeutic and nontherapeutic uses is not easy to draw. Antimicrobials given for nontherapeutic purposes are usually given to animals mixed in feed. Some antimicrobials given in feed for therapeutic purposes have been excluded. Antimicrobials administered by injection, boluses, or other routes besides feed are usually administered when illness is present in the herd, flock, or individual. Thus, we have considered these therapeutic and have not included them in this report. (The one exception is our discussion of the injection of day-old and “in-egg” chicks for disease prevention.)

In addition, this report does not address the amounts of antimicrobials used in raising minor species, such as goats and turkeys, or the amounts used in aquaculture. However, we do present data on antimicrobials used as crop pesticides, one of the few sectors for which credible data can be found.

A limited number of surveys on antimicrobial use in beef feedlots and swine production were conducted in the mid-1990s and published by the US Department of Agriculture (APHIS 1995b, APHIS 1996b). Even for these major livestock species, publicly

available data paint only an incomplete picture of total antimicrobial use. For poultry, there are virtually no publicly available data on the quantity of antimicrobials used. Nor are there publicly available data on the quantity of antimicrobials used in aquaculture or for minor species like sheep, goats, rabbits, and horses.

In February 2000, the Animal Health Institute (AHI) posted a press release on its website containing information on the quantity of antimicrobials used in agriculture (AHI 2000a). It contained the first-ever estimate of the pounds sold by major category of antimicrobial product—a welcome step in the direction of disclosure. Unfortunately, these data, which were presented in summary form with no discussion of methodology, are far too incomplete to contribute to the interpretation of antimicrobial surveillance data. It is not even clear which categories of use are included and which are left out. Furthermore, the veracity of the AHI data has not been established and no mechanism is available to verify their data. In June 2000, the AHI placed on its website an information kit on antimicrobial use in agriculture; this provides a few new pieces of information but no new quantitative data on use (AHI 2000b).

### **Limitations of Sales Data**

Because so little information is available on the quantity of antimicrobials used in animals, we reviewed data on the sale of drugs, hoping that it might serve as a proxy for quantity used. Each year, AHI releases a report on the sale of animal drugs. The report breaks all drugs into three classes: feed additives, biologicals,<sup>3</sup> and pharmaceuticals. The feed additive category includes antimicrobials added to feed, but does not include all antimicrobials used for nontherapeutic purposes. The third class includes therapeutic and some nontherapeutic antimicrobials, as well as certain vaccines, antifungal agents, antihelmintics, growth hormone implants, and other drugs.

Sales in each class of animal drug are reported for ruminants, swine, poultry, dogs, cats, horses, a miscellaneous category, and the sum across all categories. AHI collects survey data from its dozen or so member companies; the data represent sales of about 80 percent of the animal drug industry, according to AHI's *1999 Market Research Report* (AHI 1999). Data for the years 1994 to the present are available from AHI for a fee.

Although sales data are helpful, they may provide a misleading and inaccurate measure of the use of antimicrobials because they

<sup>3</sup> Drugs used to create immunity, including vaccines and antitoxins.

are influenced by price. In a year when sales data rose, use per animal might actually have fallen if the price per dose went up. In a year when sales data remained constant or fell, the use could actually have increased, if the cost of the average delivered dose fell.

*Sales data are not reliable indicators of the amount of antimicrobials used in any year or over time.*

Furthermore, prices for the same drug may vary with the market into which it was sold. For example, according to AHI, companion animal drug sales totaled \$1.3 billion in 1998, or a remarkable 40 percent of total animal drug sales (AHI 2000c). This conclusion must be interpreted cautiously. The average cost of a pound of antimicrobial mixed in livestock and poultry feed is considerably less than the average cost of a pound administered to pets to treat acute infections. Hence, companion animal use no doubt accounts for a much smaller share of the total quantity of drugs used in animals than suggested by its share of total sales.

Thus, sales data are not reliable indicators of the amount of antimicrobials used in any year or over time. They do not substitute for information on the quantity of antimicrobials produced and used.

### **Growth Promotion vs. Disease Prevention**

As discussed in Chapter 2, scientists do not fully understand the mechanisms by which low concentrations of antimicrobials promote growth. It is also difficult to judge the efficacy of antimicrobials in preventing disease. (If no disease occurs, was it due to antimicrobial use or lack of the infectious agent?) Despite this uncertainty, the commercial world routinely uses the classifications *growth promotion* and *disease prevention*, and hence these terms often appear in the antimicrobial debate. For example, Food and Drug Administration (FDA) approvals often specify an intended use in these terms and sometimes set forth dosage rates and feeding intervals that can vary, depending on whether the purpose is growth promotion or disease prevention. Surveys, too, often ask animal producers to designate the purpose and these are the terms generally used.

Most of the concern about human health consequences of antimicrobial use has focused on growth promotion rather than disease prevention. The rationale is that the benefits of growth promotion are purely economic and often compensate

for and encourage unsanitary conditions. Disease prevention, on the other hand, seems an appropriate use of antimicrobials.

For example, the seminal 1969 Swann Committee report, which was written by a special committee formed by the British Parliament, restricted its call for stricter limits on or an end to the use of antimicrobial feed supplements for growth promotion (Swann 1969). Also, the 1997 World Health Organization recommendations, although calling for a reduction in disease prevention use, specified that antimicrobials “normally prescribed for humans be prohibited as growth promoters in animals” (WHO 1997). The Council of State and Territorial Epidemiologists has adopted a similar position (CSTE 1999).

Not all public health organizations restrict their concern to growth promoters, however. The 1998 report *Protecting the Crown Jewels of Medicine*, from the Center for Science in the Public Interest, called upon the FDA to

...ban *all subtherapeutic* uses of antimicrobial agents that (a) are used in human medicine or (b) might select for cross resistance to antimicrobials used in human medicine. [emphasis added]

In this report, we have decided not to produce separate estimates of growth promotion and disease prevention usage for three reasons. First, the distinction is difficult to apply in practice. There are few commonly agreed objective criteria for the two uses and no way to know what a producer had in mind when choosing to use a particular product.

Second, there are complications arising from the increased use of combination drug packaging. Years ago, two antimicrobials used in a combination feed supplement might have been classified separately, one for disease prevention, the other for growth promotion. Today, the same combination product might be classified as just for disease prevention. Furthermore, a drug might be classified differently at different dosages. For example, at a low dose it might be classified for growth promotion, while at higher doses it might be classified for disease prevention.

Finally, and most importantly from a public health perspective, it does not matter greatly why antimicrobials are given to animals. The problem with both disease prevention and growth promotion usage is the pattern of use: exposure of microorganisms to selective pressure over an extended period. This pattern is the optimal recipe for creating large populations of resistant

bacteria. By contrast, the pattern of use for properly administered therapeutic drugs—short times and high doses—is far less likely to trigger resistance (NRC 1999).

For these reasons, this report makes no attempt to differentiate between disease prevention and growth promotion in uses of antimicrobials. Instead, we have focused on estimating all nontherapeutic uses in the three livestock systems under study. We have chosen to use the term *nontherapeutic* rather than *subtherapeutic* because *subtherapeutic* describes a feature of the

dosage not the purpose for which the drug is used. We define *nontherapeutic* uses as those like growth promotion and disease prevention in which animals are treated in the absence of illness.

*We define nontherapeutic drug use as treatment of animals in the absence of illness.*

#### **Therapeutic vs. Nontherapeutic Use**

There is also uncertainty in drawing the line between certain therapeutic and nontherapeutic (or subtherapeutic) uses. In general, the term *subtherapeutic* has been simply, but arbitrarily, defined to involve drugs given for more than 14 days at a concentration of less than 200 grams per ton of feed (FDA 2000c). No adjustment is made for differences in drug potency.

Several sources of ambiguity complicate the *therapeutic/nontherapeutic* distinction. One is that some uses of antimicrobials for disease prevention, for example, shipping fever in cattle, involve high rather than low levels of antimicrobials. Also, many cattle feedlot operations mix two antimicrobials separately into feed for the prevention of shipping fever, each at dosages under 200 grams per ton. Thus each of the antimicrobials individually meets the common definition of subtherapeutic use. But when a combination product containing the same two drugs, or some other mixture, is added to feed at 300 grams per ton, does this use become therapeutic? Such ambiguities can lead to inconsistencies in how producers respond to various USDA surveys covering antimicrobial use and in the ways companies report sales data to the AHI.

Although somewhat fuzzy at the margins, the distinction between therapeutic and nontherapeutic use makes sense from a public health point of view, and so we have done our best to draw the distinction between the two for this report. As new reporting systems are established, this line should be drawn as

sharply as possible, so that everyone providing, collecting, and reporting data understands how to make the distinction and properly classify drug use on a given farm.

### **The Difference Between Antimicrobial Use and Reliance**

Two related concepts—use and reliance—describe the impact of antimicrobials on livestock systems.

*Antimicrobial use* is the total amount of a drug administered to a species or an animal across all stages of growth, measured in pounds, grams, or kilograms. Antimicrobial use can be expressed as any of the following:

- Aggregate pounds consumed by all animals
- Average pounds per animal
- Grams per pound or ton of feed and/or unit of drinking water consumed

*Antimicrobial reliance* is a measure of the degree to which livestock production systems depend on antimicrobials. It is usually expressed in terms of amount of a drug administered per animal. Reliance is greater if, on average, individual animals receive a greater amount of a drug per dose or if they receive it for a longer time.

Ideally, reliance estimates should take into account that different antimicrobials have different potencies, or biological response, per unit amount of drug. In the 1960s and 1970s, a relatively small number of products accounted for the lion's share of total use. As newer products replaced those older drugs, average dose rates tended to fall. But this change does not necessarily indicate progress in lessening reliance on antimicrobials: it may simply reflect the increased potency of many newer drugs.

In addition, the dose rates of antimicrobials used in animal feed have changed over time. Generally, the longer an antimicrobial has been on the market, the higher the recommended and common dose rates. Put another way, they have become less effective over time. Because the efficacy and mechanisms of growth promotion are not well understood, it is difficult to know if the loss in potency is real and, if so, the cause. The evolution of resistance is an obvious candidate among many possible causes. Regardless of the reason for loss of potency, the drugs would nevertheless exert selection pressure on microorganisms encountered in the environment and select for resistant pathogens.

In the future, it will become more important to develop an accepted method to adjust estimates of reliance and use for changes

in average potency. Potency considerations could be used to revisit and refine the concentration benchmark of the standard definition of subtherapeutic use: doses up to 200 grams per ton added to feed. It will also become a crucial consideration if policy and regulatory goals, when set, are linked to reductions in the pounds of antimicrobials used in animal production.



# ESTIMATING ANTIMICROBIAL USE IN LIVESTOCK

The method we have constructed to estimate nontherapeutic antimicrobial use in beef, swine, and poultry production calculates use from three kinds of data that are publicly available: the numbers of animals, the drug dosages, and their recommended uses. The methodology employs many assumptions and relies heavily on expert judgment about, for example, the duration of treatment in a given stage of production, the average pounds of feed consumed per pound of gain, and the average dose rates in feed. Nevertheless, this method represents a sound approach to estimating the contemporary total use and reliance on nontherapeutic antimicrobials in the three major livestock systems: cattle, swine, and poultry.<sup>4</sup>

In addition, we have structured this methodology to allow comparisons with the 1985 use estimates reported in the Institute of Medicine report *Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feed* (IOM 1989). The IOM's 1985 estimates of use, by species, are the most authoritative available.

## Background on Methods

The amount of antimicrobial use in livestock systems depends on herd size, extent of use, and intensity and duration of use. The most complete and reliable data are available on the size of animal herds. For each major species, we draw upon two sources of official US Department of Agriculture (USDA) statistics:

- Inventory data on the numbers of dairy cattle, beef cattle, swine, and poultry on farms
- The number of animals slaughtered for meat in a given year

<sup>4</sup> Because of rounding, the percentage numbers in the charts may not add up to 100%. Also, rounding of the figures in the formulas for total amount of antimicrobials used may result in slight discrepancies between the reported totals and calculations based on the numbers presented in the charts.

### **Extent of Use**

Antimicrobial use varies by age of animal and growth stage. *Extent of use* reflects the percent of animals treated at a given growth stage. Reasonably good data are available on the extent of use in raising cattle and swine from USDA surveys conducted over the last three decades. Much less information is publicly available on poultry production.

In the case of beef and swine production, this report relies on periodic surveys conducted by the USDA's Animal and Plant Health Inspection Service (APHIS). In estimating use in poultry, we draw primarily on reports from the National Academy of Sciences and the IOM. Although our estimates are based on limited data, they are generally consistent with published research reports over several years and enjoy a high level of agreement among experts.

### **Intensity of Use**

In general, it is much harder to accurately estimate the average intensity of use—the amount of antimicrobials fed during a given animal's lifetime or during a stage of growth—than to estimate the extent of use. The amount of antimicrobials fed to a given animal is a function of the dose fed at each growth stage and the duration over which antimicrobial supplements are fed. Total use for an animal is the sum of antimicrobials fed over all growth stages.

In calculating antimicrobial use during each stage of growth, our method first estimates the total pounds of feed consumed during the stage. Total feed consumed is a function of the average pounds of feed consumed per day and the average number of days it takes for animals to progress through each subsequent stage of growth.

Average pounds of gain during each growth stage were based on standard methods for reporting information on animal growth, caloric and nutrient intakes, feed additive rates, and overall feed efficiency. We calculated pounds of feed consumed from data in National Research Council reports on the nutrient requirements of various livestock species, USDA data on feed consumed per pound of gain, and other data sources. Data on average weight at slaughter for each species were obtained from the USDA.

This information on total feed consumed was coupled with estimates of the dose or feeding rate of supplemental antimicro-

*In 1998, cattle received more than 3.7 million pounds of antimicrobial drugs nontherapeutically.*

bials mixed into feed or water during each stage of growth. Antimicrobials are used at variable rates and time periods during a stage of growth. Thus we had to estimate an average dose or feeding rate for the period, as well as the number of days during the stage of growth on which antimicrobials were mixed with feed and/or water. Often, more than one drug is fed at a given time. Throughout this report, we have used industry averages for dose rates and duration of feeding, recognizing that in different operations antimicrobials will be used either more or less intensively.

When available, we have extracted and presented data on tetracyclines, a class of drugs that is extensively used in animal systems. We focused on tetracyclines for two reasons. First, these drugs are widely used in human medicine and increased resistance could undermine their efficacy. In addition, researchers have documented instances in which bacteria exposed to tetracycline have developed resistance to many unrelated drugs (Levy 1992). Thus, the continued use of tetracyclines is selecting not only for resistance to tetracyclines and their chemical relatives, but also for multidrug-resistant organisms.

## **Estimates of Nontherapeutic Antimicrobial Use in Beef and Veal Production**

### **Summary of Results**

As detailed below, we estimate that the over 29 million beef and veal calves moved through US feedlots in 1998 received more than 3.7 million pounds of antimicrobial drugs nontherapeutically. The greatest use of antimicrobial drugs comes in the last stage of cattle development, when approximately two-thirds of all drugs were administered. Over the last 15 years, total antimicrobial reliance in cattle has increased about 28 percent on a per-head basis. During the same time period, there has been a reduction in the use of and reliance on tetracyclines—falling from 50 to about 20 percent of the total pounds of antimicrobials fed to cattle.

### **Contemporary Estimates of Use**

Because we wanted to be able to compare our estimates with the data in the IOM report, we have calculated separate estimates for veal calves and beef cattle, which are the categories the IOM report uses. Veal calves come exclusively from the dairy industry

and account for virtually all nontherapeutic antimicrobial use in the dairy industry.

Our general methodology for estimating antimicrobial use in beef production was to

- determine which antimicrobials were given to cattle at various growth stages
- estimate the amount of antimicrobial delivered per day and the number of days the drug was likely to be given during each growth stage
- multiply that number by an estimate of the number of animals treated
- total the use across all the growth stages

Several information sources and assumptions are required to estimate antimicrobial use in beef cattle. We use “dosage per day” because this is the most common way pharmaceutical companies recommend dosage rates and it is also the way the Food and Drug Administration’s *Green Book* sets forth rates (FDA 1999c). Dosage rates are sometimes reported both as milligrams (or grams) per ton of feed and as average daily doses for animals within a given growth stage. In some cases, doses are reported per hundredweight of animal.

The antimicrobials approved for use in cattle production for growth promotion, feed efficiency, disease prevention, including coccidiosis, are given in Appendix A. Table A-1 lists the antimicrobials, the growth stage at which they are used, the indication for use, the average amount administered per day, and the duration of use. For example, monensin is used for all cattle in confinement in order to improve feed efficiency. For this purpose, animals are fed 50 to 360 mg daily. Monensin is also fed to calves at 0.14 to 1 mg per pound to prevent and control coccidiosis due to *Eimeria bovis* and *E. zuernii*. Table A-1 provides similar information for each antimicrobial used in calculating our estimate. The primary source of this information is the FDA *Green Book*.

The formula to estimate annual antimicrobial use during various stages of cattle growth is

$$U = N \times P \times T \times D$$

where

N = Number of animals in the stage

P = Percent of animals treated

T = Average duration of treatment in days

D = Average dose of antimicrobials delivered per treatment day

Estimates of use do not include every drug on the market for a specific use, nor every mixture. For example, we project use of two ionophores, monensin (Rumensin) and lasalocid (Bovatec), in beef cattle production. These two share most of the market, but there are some sales of laidlomycin propionate (Cattlyst) and other ionophores. For this reason, we have adjusted our estimates of the use of major products upward modestly to account for the limited use of other products for which we lack data on actual use.

**Number of Animals.** Recent USDA data on the number of cattle on farms suggest that there were 106.8 million cattle and calves in the inventory as of July 1, 1999 (NASS 1999c). There were 34 million beef cows and 9.15 million dairy cows in 1999. The total calf crop was 38.3 million.

The USDA publication “Livestock Slaughter: 1998 Summary” reports that the total number of cattle slaughtered in commercial facilities in 1998 was 35,637,000 (NASS 1999b).<sup>5</sup> In addition, 1,457,835 calves were slaughtered in commercial facilities; we assume all these are veal calves. Total slaughter included about 6.6 million animals consisting of

- 2.7 million dairy cows, or 7.5 percent of total slaughter
- 3.3 million other cows, or 9.3 percent
- 0.6 million bulls, or 1.7 percent

To calculate the number of animals passing through feedlots per year, we subtracted this 6.6 million number from the total number of animals slaughtered:

$$\begin{aligned}\text{Beef cattle entering slaughterhouses} &= 35,637,000 - 6,592,845 \\ &= 29,044,155\end{aligned}$$

In addition and separately, we estimated use in the approximately 1.4 million dairy calves also raised each year for slaughter.

In projecting antimicrobial use, we assumed that 29,044,155 cattle left the feedlot stage destined for market. But some death loss occurs as cattle age. We assumed a death loss of 0.5 percent from weaning to 250 pounds, a death loss of 0.5 percent in the stage from 250 to 500 pounds, and a loss of 0.3 percent during the backgrounder stage of growth (500 to 700 pounds). Using these estimates of death loss, we calculated that the post-weaning calf crop was 29,281,319. The assumed death loss over all growth stages is 0.81 percent.

<sup>5</sup> In addition to commercial slaughter, the USDA reports 172,000 head of cattle and 43,000 calves were slaughtered on farms in 1998. These and other minor adjustments account for the final estimate of slaughter.

Table 3 sets forth the results of our estimates of nontherapeutic antimicrobial use in cattle and veal production. The data represent best estimates of use in the late 1990s. The derivation of the numbers during each growth stage is described below.

**Table 3. Nontherapeutic Antimicrobial Use in Beef Cattle by Growth Stage and in Veal Calves**

Growth Stage	Antimicrobials Used (pounds)	Percent of Total Cattle Usage
Beef Cattle		
Birth to 250 pounds	45,511	1.2%
250 to 500 pounds	164,051	4.4%
500 to 700 pounds	1,421,277	38.5%
Feedlot stage	2,055,237	55.7%
Veal Calves	6,941	0.2%
<b>Total</b>	<b>3,693,017</b>	<b>100%</b>

Total cattle industry antimicrobial use is estimated at 3.7 million pounds in the late 1990s. This total includes antimicrobials fed to veal calves, as well as use with beef cattle during their four stages of growth.

#### ***Beef Cattle***

Stage 1: Calves (Birth to 250 pounds)

Modest feeding of antimicrobials is projected during the initial stage of growth: approximately 45,500 pounds, about 1.2 percent of total cattle use.

Antimicrobial use is not heavy during the initial growth stage: only 5 to 10 percent of the animals are treated with the major antimicrobials that are used extensively in later stages of livestock production. In addition, the duration of feeding is limited: 15 days

**Table 4. Estimated Nontherapeutic Antimicrobial Use in Beef Calves (Birth to 250 pounds)**

Duration of Growth Stage: 90 days  
Number of Animals (1998): 29,281,319

Antimicrobial	Percent Cattle Treated	Average Days Fed	Average Antimicrobial per Day (mg)
chlortetracycline	5	30	20
monensin	10	20	100
oxytetracycline	5	20	25
amprolium	5	15	600

to 30 days, on average. These time periods reflect common feeding intervals intended to prevent shipping fever before weaned calves are moved to pastures or feedlots. On most ranches, a certain number of cows and calves are isolated in pastures or pens because of late births, signs of disease, or other problems. These animals are sometimes treated prophylactically for a variety of diseases.

Table 4 shows the numbers used in preparing the estimate for the initial growth stage and the results. Similar information is used in preparing estimates for the other stages. Table B-1 in Appendix B sets out the numbers used for all stages.

The average dose rate of tetracycline is estimated at 20 milligrams per day (mg/day), close to the maximum approved dose of 25 mg/day. The average 100 mg/day feeding rate of monensin is derived from the approved dose for calves of 0.14 to 1.0 milligram per pound (mg/lb), assuming an average 200-pound animal and an average rate of 0.5 mg/lb.

**Stage 2: 250 pounds to 500 pounds**

During the second stage of growth, supplemental antimicrobial use is estimated to be 164,051 pounds, or 4.4 percent of total cattle use.

There is great diversity across the industry in management practices and antimicrobial feeding during the stage of growth that takes the animal from 250 to 500 pounds. We project that less than half the animals are treated with common tetracycline-based products and that the average duration of treatment is limited to a few weeks to less than two months. Again, some cattle are probably treated for a much longer period during this growth stage, but others are treated for just a week or two either for shipping fever or when a problem arises in a particular herd.

During this stage of growth, use of the ionophore monensin (Rumensin) begins to grow, averaging 40 percent of animals treated for an average of 20 days. In most cases, the animals are treated

toward the end of this growth stage, possibly as part of an effort to prevent problems before shipment to the feedlot or to late fall or winter pasture.

**Table 4. Continued**

<b>Antimicrobial</b>	<b>Total Antimicrobial per Animal Treated (mg)</b>	<b>Total Antimicrobial All Treated Animals (mg)</b>
chlortetracycline	600	878,439,557
monensin	2,000	5,856,263,712
oxytetracycline	500	732,032,964
amprolium	9,000	13,176,593,353
<b>Total mgs</b>		<b>20,643,329,586</b>
<b>Total pounds</b>		<b>45,511</b>

### Stage 3: Backgrounder (500 pounds to 700 pounds)

**Total estimated antimicrobial use during the backgrounder growth stage is 1.4 million pounds, about 38 percent of the total fed to cattle during all stages of growth.**

As part of the National Animal Health Monitoring System (NAHMS), the USDA issued two 1995 reports entitled *Cattle on Feed Evaluation, Part I: Feedlot Management Practices* and *Part II: Feedlot Health Management Report* (APHIS 1995a,b). These key reports are based on a survey of 3,214 feedlots in 13 major cattle-feeding states accounting for 85.8 percent of the cattle on feed in January 1994. Estimates in the reports are statistically weighted to be representative of all cattle on feed in these states. Our estimates are based on the patterns of antimicrobial use described in these reports and are, in all likelihood, applicable to the other 15 percent of cattle in feedlots.

The NAHMS reports provide limited insight on the duration of antimicrobial use. About 40 percent of all lots surveyed reported “subtherapeutic” use of antimicrobials in feed for fewer than 15 days; about 18 percent fed antimicrobials for 15 to 89 days; and 42 percent fed them for 90 days or more. These data do not include ionophores and, in all likelihood, exclude some treatments at “subtherapeutic” levels that feedlot operators or veterinarians considered and reported as therapeutic treatments.

The USDA survey in the NAHMS reports does not state whether the data refer to all antimicrobials used in a lot or to any individual product. However, other data in these reports show that on average at least 2.6 antimicrobials were fed per feedlot reporting antimicrobial use (including ionophores). In some instances, for example, one product might be used for fewer than 15 days, while another was used for 120 days. Also, it is likely that at least one of the average 2.6 products used in surveyed lots was itself a combination product.

Most cattle destined for slaughter move into feedlots between 500 and 700 pounds in weight. Sometime during this stage and before they are shipped to feedlots, they are treated for shipping fever and the stress associated with being incorporated into the feedlot environment. The IOM report states that it is “common” for cattle to be fed a mixture of tetracycline and sulfamethazine for 4 to 6 weeks when animals are first incorporated in the feedlot population (IOM 1989).

Today, the commonly used mixtures contain chlortetracycline and sulfamethazine. We project that an average 50 percent of the 28.9 million animals entering feedlots are treated with an average

of 700 mg/day of a mixed chlortetracycline-sulfamethazine product for 28 days, the recommended duration of treatment. This combination accounts for the largest portion of antimicrobial use during this stage of growth (about 44 percent).

Part I of the NAHMS report projects that 98.2 percent of cattle on feed are treated with the ionophores monensin or lasalocid (APHIS 1995a, p. 13). During this background stage, we project that 80 percent were treated with these two ionophores (50 percent with monensin, 30 percent with lasalocid) for an average of 60 days, two-thirds of the days most cattle spend during this stage of growth. We also project minor use of bacitracin and erythromycin thiocyanate.

#### Stage 4: Feedlot (700 pounds to 1200 pounds)

**Total antimicrobial use during the feedlot stage of growth is estimated at 2.1 million pounds, about 55 percent of the total during all stages of growth.**

Part II of the NAHMS report contains tables reporting the percent of operations and the percent of cattle “given antimicrobials as a health or production management tool” (APHIS 1995b). The percent of animals treated during this stage of growth (see Table B-1) is based on the percent of operations reporting use of various antimicrobials as indicated in this report.

Ionophore use was reported on over 98 percent of animals. We assumed 95 percent were treated for an average 120 days out of a possible 145 days during this stage of growth. In estimating total ionophore use, we used an average feeding rate of 200 mg/day. The maximum approved rate for both monensin and lasalocid is 360 mg/day, so our estimate of ionophore use is substantially low if most animals are treated near the maximum rate during the feedlot stage. Ionophore use accounts for at least two-thirds of the total pounds of antimicrobial fed during the feedlot stage of production.

The next most heavily used antimicrobial was tylosin. The NAHMS report projects tylosin use in 43 percent of operations, which is the percent we used. We estimated an average treatment rate of 80 mg/day, somewhat below the maximum level of 90 mg/day for a period of 120 days. This duration of feeding represents about 83 percent of the time typically spent in this growth stage.

Tetracyclines and new drugs account for the remainder of use during this growth stage. Dosage rates were derived from the FDA

*Green Book* and the publication *Feed Additives for Beef Cattle* (Stock and Mader 1984). In general, average dosage rates were set equal to 80 to 100 percent of maximum allowed rates for feed efficiency and growth promotion. Feeding periods were generally about 80 percent of the maximum allowed, taking into account any required withdrawal period prior to slaughter.

### ***Veal Calves***

The total estimated antimicrobial use in raising veal calves is 6,941 pounds, only about 0.2 percent of total cattle use.

Few antimicrobials are approved for use in veal calves and most contain tetracyclines, of which oxytetracycline is by far the most widely used. Since treatment periods and dose rates vary little across various tetracycline-based products, we assumed that all treatments for disease prevention and growth promotion were done with oxytetracycline, and that 100 percent of the commercial veal crop was treated with a tetracycline product. This estimate is higher than other estimates because some calves are treated with more than one product, while some are not treated with any.

The average duration of treatment was estimated at 35 days—about one-third of their time on feed. We suspect a large deviation in the duration of treatment, with some calves on tetracycline products for a significant portion of their approximate 126 days on feed, and others on treatment for just one to three weeks.

Decoquinatate is a relatively new product for the prevention of coccidiosis in calves and veal. We projected that 20 percent of calves were treated with this (or perhaps another) coccidiostat. The approved duration of treatment is 28 days at a dose rate of 22.7 mg per 100 pounds. Since veal calves grow from under 100 to over 400 pounds, we assumed an average treatment rate of 70 mg per head, the proper dose for a 308-pound animal.

### **Changes in Use Since 1985**

The 1989 IOM report *Human Health Risks with the Sub-therapeutic Use of Penicillin or Tetracyclines in Animal Feed* includes data on use in 1985. This allows us to compare use levels from the mid-1980s with our estimates for the late 1990s.

The report contains a table summarizing USDA data on the number of animals produced for “marketing.” In 1987, the IOM reports there were 49,900,000 cattle produced for marketing and 10,564,000 calves. The “calves” represent predominantly dairy calves sold into the veal market. Total use of antimicrobials for disease

prevention and growth promotion in beef and dairy calves was reported as 1,440,000 kilograms, or 3,174,657 pounds (IOM 1989, Table IV-9). Therapeutic use was reported as 458,000 kilograms, or 24 percent of total cattle use.

These data were derived from testimony delivered before a December 1984 congressional hearing by R.H. Gustafson, a scientist working for the American Cyanamid Company. Gustafson's data were "derived primarily from industry sources" (IOM 1989, p. 74); the IOM committee considered them to be the most authoritative available. The IOM report presents no details on how these estimates were derived.

It is unclear from the IOM report whether Gustafson's beef and veal antimicrobial use estimates included ionophores. The question is important because these drugs have been used in large amounts for decades. Ionophores are a class of antimicrobials used both to treat diseases caused by protozoans and to promote growth and feed efficiency. These drugs are not used in human medicine because they are highly toxic. Because ionophores are not used in humans, they have not been well studied and there is little information on transferable resistance to these drugs.

Although the report is unclear on the issue, it is likely that Gustafson's antimicrobial use estimates probably did include these classes of antimicrobials, since his numbers were markedly higher than antibacterial use data provided by the Animal Health Institute to the IOM committee (because ionophores are directed against protozoa, they are considered to be antimicrobials but not antibacterials). Also the fact that recent NRC reports have considered ionophores as antimicrobials<sup>6</sup> lends some support to that interpretation of the 1989 report.

To assess changes in total antimicrobial use over the last 15 years on a per-cow basis, it is necessary to correct for changes in the size of the beef industry. In 1985, the beef industry was in the third year of marked contraction, having fallen from a peak of 115,444,000 cattle in 1982 to 109,582,000 in 1985 (NCBA 1999). The contraction continued for five more years before bottoming out in 1990 at 95,816,000 animals. In the 1990s, the numbers have rebounded to as high as 103,487,000 in 1996; and in 1998, the year of our estimate, the number of animals stood at 99,744,000.

<sup>6</sup> Two ionophores are approved as feed supplements for cattle in feedlots: monensin (Rumensin) and lasalocid (Bovatec). Both are clearly classified as beef cattle antimicrobials in the 1999 National Research Council report *The Use of Drugs in Food Animals: Benefits and Risks*.

The factor for adjusting the size of the industry in 1985 to reflect beef cattle numbers in the late 1990s is 0.91 (beef cattle herd size in 1998 divided by herd size in 1985). This adjustment indicates that a total of about 2.9 million pounds of antimicrobials would have been fed in 1985 if the size of the beef herd had been comparable to the late 1990s. On the basis of this correction, we calculate that total antimicrobial use has risen about 28 percent on a per-head or size-neutral basis. Table 5 summarizes these changes.

A second change evident in Table 5 is the drop in use of tetracycline-based products. As mentioned above, tetracyclines are important because they are used in human medicine and many multidrug-resistant bacteria carry tetracycline resistance (CDC 1999). Total tetracycline use fell from 50 percent of the total pounds of antimicrobials fed to about 20 percent. This appears to mark a true reduction in reliance and use, since the same ionophores and tylosin. No new products with markedly different dose rates have gained significant market share, and there have been no major changes in the average potency of drugs fed to cattle.

**Table 5. Changes in the Total Pounds of Antimicrobials Fed to Beef Cattle and Veal from 1985 to the Late 1990s and Percent Change on a Per-Head Basis**

	1985	1985 Adjusted for Change in Herd Size	Late 1990s	Percent Change 1985 to Late 1990s Adjusted for Change in Herd Size
All Antimicrobials	3,174,657	2,889,573	3,693,017	28%
Tetracyclines	1,585,124	1,442,780	731,520	-49%
Tetracyclines as Percent of Total	50%	50%	20%	

## Estimates of Nontherapeutic Antimicrobial Use in Swine Production

### Summary of Results

We estimate that over 10.4 million pounds of antimicrobial drugs were administered nontherapeutically to hogs in the United States in the late 1990s. Over 70 percent of these drugs were administered during the finishing growth stage. While overall reliance on nontherapeutic antimicrobial drugs by the swine industry has

declined just over 11 percent between 1985 and the late 1990s, the reliance on tetracycline drugs has risen from 33 percent to 48 percent over the same time period.

### Contemporary Estimates of Use

*In the late 1990s hogs were fed over 10.4 million pounds of antimicrobial drugs for nontherapeutic purposes.*

The method for calculating nontherapeutic drug use in hogs is different from that used to calculate nontherapeutic drug use in cattle. Industry sources and the FDA *Green Book* typically discuss antimicrobial feeding rates for hogs on the basis of grams of antimicrobial per ton of feed. Accordingly, we estimate antimicrobial use during each stage of growth by first projecting the pounds of feed consumed per day and the average number of days spent in each growth stage. These two numbers are then multiplied together to produce an estimate of the pounds of feed consumed per head during the growth stage.

This total is then multiplied by the dose: the projected grams of antimicrobial per pound of feed, which is the typical or recommended rate in grams per ton divided by 2,000. The result is the amount of antimicrobials consumed by treated animals during the growth stage.

Accordingly, the formula used to estimate annual antimicrobial use,  $U$ , during each stage of growth is

$$U = N \times F \times T \times D$$

where

$N$  = Number of animals in the stage

$F$  = Estimated feed consumed per day

$T$  = Average number of days in growth stage

$D$  = Average dose of antimicrobials (grams per pound of feed)

**Number of Animals.** Total commercial hog slaughter was just over 101,000,000 head in 1998 (NASS 1999b), almost 10 percent higher than slaughter the year before. The steep growth was caused by the sharp reductions in hog prices. The number of animals slaughtered in 1997 was about 92 million, levels of production comparable to 1996 and 1995 (NASS 1999b). The 1997 level of slaughter is, therefore, more representative of the size of the industry in the late 1990s.

Projections of antimicrobial use in the late 1990s in swine production are based on a herd size of 92,627,000 at the finishing stage of growth. This number is consistent with 1997 slaughter and

modest death loss during the finishing stage of growth. In estimating the average number of animals in the feeding and starting stages, we assumed a death loss of about 2 percent during the feeding stage and about 4 percent during the starting stage of growth.

**Estimating Feed Intake.** In estimating the average kilocalories (kcal) and feed intake required during each stage of production, we used USDA and university data, as well as NRC reports. The 1987 NRC report *Predicting the Feed Intake of Food-Producing Animals* estimates that the kcal needed per day vary within wide ranges during each growth stage of swine production:

- Starting stage (15 to 40 pounds): 1,000 to 3,200 kcal
- Feeding stage (40 to 100 pounds): 3,200 to 7,000 kcal
- Finishing stage (100 to 240 pounds): 7,000 to 10,000 kcal
- Breeding animals: 6,000 to 8,000 kcal

The lower limits apply to animals when they first enter the growth stage at the bottom end of the weight scale. The upper limits apply to the heavier animals when they are ready to move into the next stage of growth or to slaughter.

We used an average value of 1,450 kcal per pound of feed in estimating pounds of feed consumed per animal in each growth stage. This average is taken from the University of Minnesota Extension Service report *Formulating Farm-Specific Swine Diets* (Augenstein et al. 1997); it is very close to the number used in several other university publications and technical references (NRC 1987, 1999). Based upon an average of 1,450 kcal per pound of feed, we estimated ranges in the amount of feed consumed during each growth stage, as well as an average during the growth stage. The following results were used in calculating antimicrobials fed:

- Starting stage: 0.7 to 2.2 pounds per day; average used in calculations: 2 pounds
- Feeding stage: 2.2 to 5 pounds per day; average used in calculations: 4 pounds
- Finishing stage: 5 to 7 pounds per day; average used in calculations: 6.2 pounds
- Breeding: 4 to 6 pounds per day; average used in calculations: 5 pounds

**Antimicrobial Feeding Rates.** An overview of the major antimicrobials approved for nontherapeutic use in swine production appears in Appendix A, Table A-2. It includes the same type of information as provided for antimicrobials used for cattle. For

example, virginiamycin is used to increase the rate of weight gain and feed efficiency in swine at all growth stages. However, the average amount used during the starting and feeding stages is 10 mg per ton of feed, while for the finishing stage the dosage is 5 mg/ton.

The average antimicrobial feeding rates fell, we assumed, between 70 and 85 percent of the maximum allowed. Likewise, we adjusted the duration of feeding downward from the total number of days in the feeding period, taking into account withdrawal periods (if applicable) and the likelihood that some producers probably did not include antimicrobials in feed for the whole period allowed. We projected that most antimicrobials were fed on average 35 days during the 37-day starting stage, 38 days during the 40-day feeding stage, and 86 days during the 90-day finishing stage.

**Extent of Use.** We relied on several sources in estimating the percentage of hogs treated with antimicrobials at different stages of growth, but the key source was the USDA publication *Swine '95: Grower/Finisher, Part II: Reference of 1995 US Grower/Finisher Health and Management Practices* (APHIS 1996b). This covers a survey of 418 feeding-finishing operations with 300 or more market hogs. The survey was stratified to concentrate on major swine-producing states and covers 90.7 percent of the US swine industry.

In that report, the section titled "Preventive Antimicrobials/Growth Promotants" states that in late 1994 and early 1995 an estimated 92.7 percent of hogs in the growing-finishing stages were fed antimicrobials in feed and another 4.5 percent received them through water (APHIS 1996b). The growing stage in the USDA report corresponds to what we have called the "feeding" stage. These two stages of growth last, on average, about 130 days.

The USDA publication includes a table showing the percent of operations reporting use of 14 specific antimicrobials and a category labeled "other" (APHIS 1996b, p. 6). The most widely used antimicrobial was bacitracin, used on 52 percent of the operations. By summing the percent of operations reporting use of antimicrobials across the 15 categories of drugs listed in the table, it is clear that, on average, at least two antimicrobials were used on each operation for an average duration of at least 62 days during the feeding and finishing stages. There are 130 days in these two stages, so if two products were used in succession, each for 62 days on average, it would result in almost continuous use of an antimicrobial during these stages of growth on essentially all operations.

In addition, over 15 percent of the operations reported use of

combination products containing two antimicrobials for an average of over 50 days each. Over 13 percent of operations reported use of products containing three antimicrobials. Accordingly, it is likely that the majority of hogs in the feeding and finishing stages was treated continuously with one antimicrobial for most of the 130 days in those two stages, and that they were also treated with a combination product containing two or three antimicrobials for 25 to 60 days.

**Antimicrobial Use by Product.** We used the results of the 1995 USDA survey in estimating the percent of hogs at each stage treated with a given antimicrobial. However, the survey reported that 10.4 percent of operations used a neomycin-oxytetracycline combination product. We could not identify such a product in the FDA *Green Book* and assumed it has been withdrawn from the market. We also assumed that the operations reporting use of this product in 1995 are now either using more oxytetracycline and/or one of the newer products not included in the USDA's 1995 survey.

Table 6 shows estimates of subtherapeutic antimicrobial use in swine production during the late 1990s. The 90-day finishing stage accounts for 7.3 million pounds out of total industrywide use of 10.4 million pounds—about 70 percent of total use. Tetracyclines account for 4.9 million pounds—about 48 percent of total use.

Table 7 shows the numbers used in preparing the estimate for the starting growth stage and the results. Similar information was used in preparing estimates for the other stages. Table B-2 in Appendix B sets out the numbers used for all stages, as well as for breeding animals.

### Changes in Use Since 1985

The IOM report offers the only credible quantitative estimate of antimicrobial use in the 1980s. According to information provided to the IOM committee by industry sources, an estimated 10,955,000 pounds of antimicrobials were fed to 86.6 million hogs.

**Table 6. Nontherapeutic Antimicrobial Use in Swine by Growth Stage**

Growth Stage	Antimicrobials Used (pounds)	Percent of Total Swine Usage
Starting (15 to 40 pounds)	1,254,943	12.1%
Feeding (40 to 100 pounds)	1,757,249	17.0%
Finishing (100 to 240 pounds)	7,279,080	70.3%
Breeding animals	57,324	0.6%
<b>Total</b>	<b>10,348,596</b>	<b>100%</b>

Tetracyclines accounted for one-third of total pounds applied (IOM 1989, Table IV-9).

In 1985, 31.9 million pounds of antimicrobials were produced in the United States (IOM 1989, Table IV-4) and almost 11 million pounds were fed to hogs (IOM 1989, Table IV-9).

The IOM report states that in 1985 about two pounds of antimicrobials were fed for disease prevention for every pound fed for growth promotion. There were 3.64 million pounds of tetracyclines used subtherapeutically. In 1985, 86.6 million hogs were marketed (IOM 1989, Table IV-2). Given that 10,954,771 pounds of antimicrobials were fed to hogs, the average hog marketed received 0.1265 pounds of antimicrobials, or 57.4 grams per hog.

The number of hogs slaughtered increased from 86.6 million in 1985 to about 92.6 million in the late 1990s. To estimate changes in reliance on a per-head basis, it is necessary to correct estimates of industrywide use in the late 1990s for change in the size of the industry since 1985. Antimicrobial use in 1985 was adjusted by a factor of 1.069. Using this conversion factor, total antimicrobial use for swine in 1985 is estimated as 11.7 million pounds and tetracycline use as 3.89 million pounds (33 percent). Table 8 summarizes trends in antimicrobial use between 1985 and the late 1990s.

Between 1985 and the late 1990s antimicrobial reliance on a per-hog basis declined 11.6 percent, but relative reliance on tetracyclines rose from 33 percent to 48 percent—a significant jump. It is difficult to sort out the factors accounting for the decline in overall antimicrobial use despite an increase in reliance on tetracycline-based product use. The generally lower costs of tetracycline products in comparison with new products no doubt played a role.

Recent USDA survey data and other sources suggest that major tetracycline-based products are fed during the finishing stage at dose rates between 40 grams per ton (oxytetracycline, 30 percent of animals treated) and 70 g/ton (chlortetracycline, 55 percent of animals treated). Both feeding rates are substantially higher than the rate of 25 g/ton that the IOM reported as typical in 1985 for tetracycline-based products.

These higher feeding rates for tetracyclines may be the result of many factors. Among them are lower prices per unit of antimicrobial fed, slippage in product efficacy as a result of resistance, increased sensitivity to the risk of disease loss given the larger scale of operations, faster rates of gain, and/or increased disease pressure and animal stress.

**Table 7. Estimated Nontherapeutic Antimicrobial Feed Use in Swine—Starting Growth Stage (15 to 40 pounds)**

**Duration of Growth Stage: 37 days average**  
**Number of Animals (1998): 98,258,722**

Antibiotic	Percent Animals Treated	Feed per Day per Animal (lb)	Average Days Fed	Avg. Antimicrobials per Day (g per ton of feed)	Avg. Antimicrobials per Day (g per lb of feed)
chlortetracycline sulfathiazole penicillin	20	2	35	200	0.1
chlortetracycline sulfamethazine penicillin	20	2	35	200	0.1
tylosin	40	2	35	50	0.025
virginiamycin	4	2	35	8	0.004
chlortetracycline	50	2	35	80	0.04
oxytetracycline	40	2	35	50	0.025
apramycin	10	2	14	130	0.065

## Estimates of Nontherapeutic Antimicrobial Use in Poultry Production

### Summary of Results

There has been phenomenal growth in the US production of poultry over the past 15 years along with a dramatic rise in the use and reliance on nontherapeutic antimicrobial drugs. An estimated 7.8 billion chickens received over 10.5 million pounds of antimicrobials in the late 1990s. Since the mid-1980s there has been increased reliance on antimicrobial drugs in poultry production, with usage increasing over 300 percent on a per-bird basis. While the total share of tetracycline drugs used has remained nearly constant over the past 15 years, overall nontherapeutic use of this class of antimicrobials continues at very high levels.

**Table 8. Changes in the Total Pounds of Antimicrobials Fed to Swine from 1985 to the Late 1990s**

	1985	1985 Adjusted for Herd Size	Late 1990s	Percent Change 1985 to Late 1990s
All Antimicrobials	10,954,771	11,710,650	10,348,596	-11.6%
Tetracyclines	3,639,832	3,890,980	4,972,213	27.8%
Tetracyclines as Percent of Total	33.2%	33.2%	48%	

**Table 7. Continued**

Antibiotic	Total Anti-microbials per Animal (g)	Total Anti-microbials All Treated Animals (g)
chlortetracycline sulfathiazole penicillin	7.00	137,562,211
chlortetracycline sulfamethazine penicillin	7.00	137,562,211
tylosin	1.75	68,781,105
virginiamycin	0.28	1,100,498
chlortetracycline	2.80	137,562,211
oxytetracycline	1.75	68,781,105
apramycin	1.82	17,883,087
<b>Total grams</b>		<b>569,232,428</b>
<b>Total pounds</b>		<b>1,254,943</b>

**Contemporary Estimates of Use**

Data on antimicrobial use in the poultry industry are even harder to come by than data for the beef and swine industries. As a result, this report resorts to a different method to estimate antimicrobial use in poultry from the one we used in the other two cases. Since there are no recent, publicly available survey data on which feeds are used in different poultry operations, there was no way of knowing how much of each approved antimicrobial was being used in poultry operations. So we drew upon the literature, university websites, and pharmaceutical company literature to develop six repre-

sentative mixtures of approved antimicrobials that would typically be fed to poultry. These mixtures include one or two antimicrobials, most have an arsenical, and all contain one coccidiostat. These mixtures reflect the antimicrobial use patterns described in the 1999 NRC report *The Use of Drugs in Food Animals: Benefits and Risks*.

The formula used to estimate annual nontherapeutic antimicrobial use, U, in poultry for each of the combination drugs during the two growth stages is the product of four variables,

$$U = N \times P \times F \times D$$

where

N = Number of animals in the stage

P = Estimated percent of the birds treated

F = Feed consumed per animal (pounds)

D = Average dose of antimicrobials per day (grams per pound of food)

A list of antimicrobials currently approved for poultry production appears in Appendix A as Table A-3. This table includes eight antimicrobials, two arsenicals, and ten coccidiostats. The table includes the stage at which the antimicrobials are administered, the indication for use, the dose rate, and the duration of use. Some of

these drugs are approved for use through the full production cycle, while others are restricted to chicks under a certain age or birds at least 16 weeks old. For example, zoalene is used with chickens in both the starting and growing stages to enable them to develop active immunity to coccidiosis. During the starting stage, it is fed at a rate of 75.4 to 113.5 g per ton of feed. During the growing stage, the rate is 36.3 to 75.4 g/ton. But zoalene is also used for all broilers, again to prevent and control coccidiosis at a rate of 113.5 g/ton.

Table 9 shows an example of one of the six mixtures we used in projecting late 1990s antimicrobial use in poultry production. All the mixtures for the starting stage and for the growing/finishing stage are shown in Table A-4 of Appendix A. These tables show the combination of drugs as well as the recommended dose ranges for each in grams per ton of feed. In the third column, the high dose rates are summed across the drugs in each mixture. The fourth column shows the average dose rates used in estimating the volume of use. These rates are equal to 80 percent of the maximum allowed.

**Table 9. Representative Antimicrobial/Coccidiostat Combinations Used for Poultry Production**

Combinations (Mixtures)	Antimicrobial Dose per Ton of Feed (g)	Average Dose per Mixture (g)	80% of Mixture Dose (g)
<b>Starting Stage</b>			
<b>Combination #1</b>			
bambermycin	2-3		
amprolium	113.5	154.2	123.36
ethopabate	3.6		
roxarsone	22.8-34.1		

**Feeding Rates.** Antimicrobial use is projected in two stages of growth for broilers typically produced in six weeks: the starting stage, and the growing and finishing stage. Mississippi State University provides information on the typical range of feed required in each growth stage (Mississippi State Univ. 1998). We used the midpoint of each range in calculating total antimicrobial use, after taking account of any required withdrawal periods:

- Starting Stage: 2 to 3 pounds, with a midpoint of 2.25 pounds
- Growing/Finishing Stage: 5 to 7 pounds, with a midpoint of 6 pounds

**Number of Chickens.** For the total number of broilers, we used the USDA estimate of 7.8 billion slaughtered in 1997 (NASS 1998c).

Estimates of antimicrobial use in the starting and growing/finishing stage of production are shown in Table 10. One-quarter of total antimicrobial use occurs in the starting stage and three-quarters in the growing/finishing stage.

**Table 10. Nontherapeutic Antimicrobial Use in Poultry by Growth Stage**

<b>Growth Stage</b>	<b>Antimicrobials Used (pounds)</b>	<b>Percent of Total Poultry Usage</b>
Pre-starting and Starting	2,658,081	25.2%
Growing and Finishing	7,877,845	74.8%
<b>Total</b>	<b>10,535,926</b>	<b>100%</b>

Table 11 shows the numbers we used in preparing the estimate for the pre-starting and starting growth stages and the results. Similar information was used in preparing estimates for the growing/finishing stages. Table B-3 in Appendix B sets out the numbers used for all stages. We assume that nearly all broilers would be treated with one of the six mixtures. A small percentage is not treated with any antimicrobials, while another small portion is likely treated with two or more combinations of drugs.

Our research confirms the conclusion of the 1999 NRC report that “by 1951, the addition of growth-promoting antimicrobials to [poultry] feed throughout the birds’ lives had become standard practice” (NRC 1999, p. 31).

One nontherapeutic use of antimicrobials in poultry deserves special mention even though it does not involve a food or water route of delivery: the ubiquitous injection of chicks and eggs with either gentamicin or ceftiofur. Virtually all of the 7.8 billion broilers produced are injected either in the egg or as one-day-old chicks with a combination of an antimicrobial and a vaccine. We estimate that for about 80 percent of the flock the antimicrobial is gentamicin and for the remaining 20 percent ceftiofur. Both of these drugs are important in human medicine, especially ceftiofur, a so-called third-generation cephalosporin valued by physicians for broad-spectrum activity. Based on the common dose rate of 0.1 mg per chick or egg, we estimate that the quantity used for the entire 7.8 billion national broiler flock would be on the order of 1,700 pounds per year. Although small against the background of the millions of pounds of other antimicrobials used in poultry, such uses are notable because of the medical importance of these particular drugs.

**Table 11. Estimated Nontherapeutic Antimicrobial Use in Poultry Production Pre-starting and Starting Growth Stage**

Number of Animals (1998): 7,800,000,000

Antimicrobial Combination Number	Percent Broilers Treated	Feed per Stage per Broiler (lb)	Average Antimicrobial per Stage (g/ton of feed)	Average Antimicrobial per Day (g/lb of feed)
#1	25	2.25	123.36	0.06168
#2	25	2.25	144.24	0.07212
#3	5	2.25	436.32	0.21816
#4	5	2.25	133.68	0.06684
#5	15	2.25	132.8	0.0664
#6	25	2.25	88.32	0.04416

Combination #1: bambermycin, amprolium, ethopabate, roxarsone

Combination #2: BMD, roxarsone, monensin

Combination #3: chlortetracycline, roxarsone

Combination #4: penicillin, amprolium, ethopabate

Combination #5: lincomycin, roxarsone, amprolium, ethopabate

Combination #6: virginiamycin, roxarsone, salinomycin

### Changes in Use Since 1985

Statistics compiled by the USDA document the phenomenal growth in US consumption and production of chicken. In 1971, 2.9 billion broilers were raised (IOM 1989). By 1985, the number had risen to 4.5 billion. A decade later, the number of broilers produced had reached 7.3 billion (NASS 1998c). Production has continued to rise, reaching 7.8 billion in 1997 (NASS 1998c).

Antimicrobial use in broiler production has increased dramatically since 1985, as shown in Table 12. The IOM report estimated total 1985 antimicrobial use in poultry at 1.97 million pounds. Just 15 years later, our estimates indicate that use had risen almost six-fold to 10.6 million pounds. Growth in the number of birds produced accounted for about 40 percent of the increase. The balance reflects greatly increased usage on a per-bird basis (i.e., heavier reliance). On a per-bird basis, usage of antimicrobials in poultry since the mid-1980s has increased by a dramatic 307 percent.

Table 12 also shows that the share of total use in poultry accounted for by tetracyclines has remained nearly constant. This is somewhat surprising in that industry sources report that these mixtures are not as heavily used as they once were. Because of the reported downward trend, we project that just 10 percent of birds are now treated with them. In addition, we have included chlortetracycline and penicillin in only two of the six mixtures we used in making the late 1990s estimates. Nevertheless, significant quantities of these two drugs, both of which are important in

**Table 11. Continued**

Antimicrobial Combination Number	Total Combination Used per Broiler (g)	Total Combination All Treated Animals (g)
#1	0.034695	270,621,000
#2	0.0405675	316,426,500
#3	0.024543	191,435,400
#4	0.0075195	58,652,100
#5	0.02241	174,798,000
#6	0.02484	193,752,000
<b>Total grams</b>		<b>1,205,685,000</b>
<b>Total pounds</b>		<b>2,658,081</b>

human medicine, are still used in poultry production.

While our estimates were based on limited solid data, the IOM’s 1985 estimates support the assertion that nontherapeutic uses of drugs like tetracycline and penicillin have long been important in the poultry industry. The IOM committee received information from the

National Broiler Council based on a survey of 30 companies representing 77.8 percent of industry output in 1984 (IOM 1989, p. 71). While no antimicrobial use for growth promotion or feed efficiency was reported, there was extensive use for disease prevention, with 60 percent of the companies reporting using penicillin, 93 percent reporting chlortetracycline use, 77 percent oxytetracycline, and 33 percent tetracycline. Some industry experts consulted for this report consider these estimates of nontherapeutic uses of these two classes of antimicrobials to still be an accurate reflection of industrywide usage patterns.

### Trends in Agricultural Antimicrobial Use from the Mid-1980s to the Late 1990s

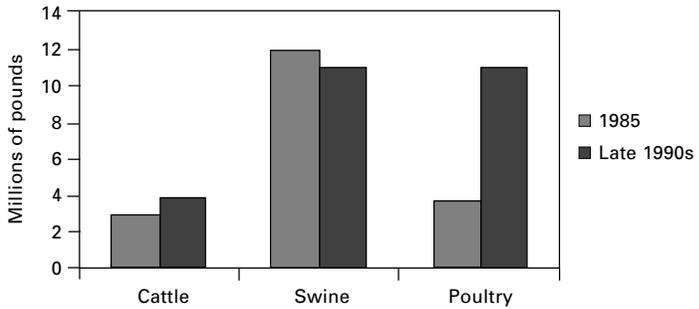
Figures 1 and 2 show estimates of feed and water antimicrobial use in beef, swine, and poultry production in 1985 and the late 1990s. The data in Figure 1 are for all antimicrobials, while Figure 2 focuses specifically on tetracycline-based products. The data for

**Table 12. Changes in the Total Pounds of Antimicrobials Fed to Poultry from 1985 to the Late 1990s**

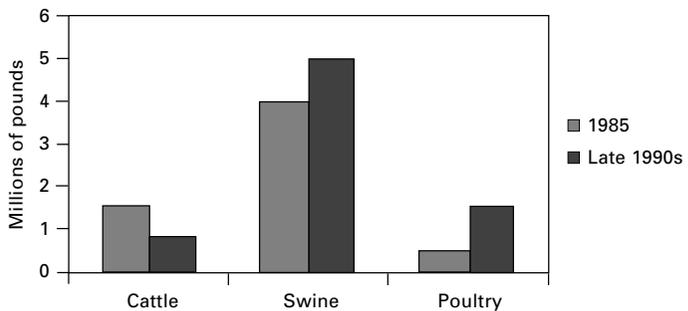
	1985	1985 Adjusted for Change in Industry Size	Late 1990s	Percent Change 1985 to Late 1990s
Size of industry (# of broilers)	4.5 billion		7.8 billion	
All Antimicrobials	1,973,138	3,436,140	10,535,925	307%
Tetracyclines	278,885	485,667	1,418,675	92%
Tetracyclines as Percent of Total	14%	14%	14%	

1985 are derived from estimates of what antimicrobial use would have been in 1985 if the number of cattle, swine, and poultry produced in 1985 were the same as in the late 1990s. These size-adjusted estimates provide insights into changes in the relative reliance on antimicrobials.

**Figure 1. Changes in Nontherapeutic Antimicrobial Use in Cattle, Swine, and Poultry from 1985 to the Late 1990s**  
(1985 data are adjusted for changes in the size of the industry)



**Figure 2. Changes in Nontherapeutic Use of Tetracyclines in Cattle, Swine, and Poultry from 1985 to the Late 1990s**  
(1985 data are adjusted for changes in the size of the industry)



Several surprising and significant findings are evident in these two figures:

- Total quantities of antimicrobials used for nontherapeutic purposes in the three major species of farm animals have risen 53 percent in just 15 years, driven by the explosive growth in use in poultry production.
- In 1985, poultry production accounted for just 12 percent of total quantities of antimicrobials used for nontherapeutic purposes across the three species and now it accounts for almost half.
- Modest progress has been made in reducing overall reliance on tetracyclines as a percent of all antimicrobials used. The beef industry did the best of the three sectors—reducing reliance per animal by almost half. Reliance on tetracycline in swine systems actually increased.





## CHAPTER 5 **ANTIMICROBIALS AS PESTICIDES**

Antimicrobials are also used as pesticides in agriculture, particularly in fruit orchards where they are used to combat fire blight,<sup>7</sup> a disease caused by *Erwinia amylovora*, a bacterium related to *Escherichia coli*. Modest amounts are also sprayed on a variety of vegetable crops. Use is highly variable and tends to be driven by weather conditions that trigger certain diseases.

The antibiotics involved—oxytetracycline and streptomycin—are of concern because they are used in human medicine. Use in fruit orchards accounts for less than 50,000 pounds annually, as shown in Table 13, according to information provided by the US Department of Agriculture and the National Agricultural Statistics Survey (NASS 1995, 1996, 1997, 1998a, 1999a, 2000). Total use in vegetable production accounts for less than another 5,000 pounds annually.

While the amounts are relatively small and deal with crops not animals, we have presented the pesticide data in this report because unlike the animal data, they are taken from government information on fruit use collected through producer surveys. Data are collected on fruit production in odd years, vegetable production in even years, and field crop production annually. Data categories include the percent of acres treated (by state and nationally), the number of applications, the average rates of application, and the total pounds applied.

The supply and quality of publicly available pesticide data demonstrate that the antimicrobial-use information needed for public health research can be obtained without unduly burdening either agricultural producers or the pharmaceutical industry. Moreover, Table 13 illustrates one of the many advantages of having data compiled over the years: trend analysis. Table 13 provides a picture of

<sup>7</sup> It is interesting to note that in 1994 the EPA received an application to approve another antibiotic, gentamicin, as a pesticide because the fire blight pests are evolving resistance to oxytetracycline and streptomycin (61 Fed. Reg. 41153, 1996).

**Table 13.**  
**Antibiotic Pesticide Use on Fruit Crops (pounds)**

<b>Active Ingredient</b>	<b>1991</b>	<b>1993</b>	<b>1995</b>	<b>1997</b>	<b>1999</b>
oxytetracycline	13,300	15,800	13,700	26,800	21,700
streptomycin	29,000	24,800	25,000	39,800	21,500
Total	42,300	40,600	38,700	66,600	43,200
Percent Increase 1991 to 1999					2.1%

Note: Use data in 1999 on sweet cherries not published by NASS/USDA because less than one percent of national acres were treated.

Source: Compiled by Benbrook Consulting Services based on *Agricultural Chemical Usage: Fruit and Nut and Vegetable Summaries, National Agricultural Statistics Survey, Economic Research Service, multiple years.*

how antimicrobial pesticide use in fruit crops has changed over the last decade. Similar information on annual usage is critical to evaluate the success of new initiatives to curb antimicrobial use. As this report demonstrates, we have virtually no basis on which to analyze antimicrobial use trends in animal agriculture. If, for example, livestock users were to claim that they had reduced antimicrobial use as called for in a new government or private initiative, there would be no basis on which to evaluate those claims.



# ANTIMICROBIALS IMPORTANT TO HUMAN MEDICINE

The antimicrobials of greatest concern from a resistance standpoint are those that are used in human medicine and those that are chemical relatives (or analogs) of those used in human medicine. Animal drugs chemically related to human drugs are important because microorganisms often develop resistance to whole families of drugs. Thus, the use in livestock production of a close chemical relative of an antimicrobial used in humans may result in resistance to the medically important drug. As a result of cross-resistance, bacteria may become impervious to a drug without ever having been exposed to it. An example is the case of Synercid and its chemical relative virginiamycin, which were discussed in Chapter 1.

The other important factor is whether alternative therapies are available in case the bacteria become resistant to a drug used to treat a disease. The drugs of greatest importance in human medicine are those for which therapeutic alternatives are limited.

Of course, such classifications are moving targets. Uses of antimicrobials are not static. New disease agents can emerge and scientists and physicians can come up with new uses for existing drugs. Moreover, as resistance evolves, drugs not previously used in human medicine may be pressed into service. Such was the case of Synercid. This drug was long thought too toxic for human use, but the Food and Drug Administration recently approved it, in large part because the rest of the arsenal had lost efficacy as a result of resistance (Stolberg 1999). Nevertheless, classifications along these lines are useful and the Food and Drug Administration is employing them in developing its antimicrobial resistance policy.

Table 14 presents an estimate of the quantities of antimicrobial by product used for nontherapeutic purposes in agriculture. This classification is based on a review of the literature and consultation with experts (see Appendix C). The antimicrobials are grouped into three categories corresponding to their importance to human medicine. At the top of the list are drugs or analogs of drugs used

**Table 14. Nontherapeutic Antimicrobial Use in Livestock by Relative Importance in Treating Human Diseases**

	Cattle	Swine	Poultry	Total
<b>Class I: Used to Treat Human Diseases, Few or No Alternatives</b>				
Erythromycin	18,181		381,753	399,934
Virginiamycin		7,492	192,682	200,174
<b>Total Class I</b>	<b>18,181</b>	<b>7,492</b>	<b>574,435</b>	<b>600,108</b>
<b>Class I as % of Total</b>	<b>0.5%</b>	<b>0.1%</b>	<b>5%</b>	<b>2%</b>
<b>Class II: Used to Treat Human Diseases, Alternatives Exist</b>				
Chlortetracycline	588,042	4,007,632	1,418,675	6,014,349
Bacitracin	25,885	1,894,450	96,728	2,017,063
Tylosin	356,999	943,635		1,300,634
Oxytetracycline	143,478	964,581		1,108,059
Sulfathiazole		901,251		901,251
Sulfamethazine	344,400	455,434		799,834
Penicillin		528,777	141,867	670,644
Lincomycin		53,685	25,794	79,479
Apramycin		39,425		39,425
<b>Total Class II</b>	<b>1,458,804</b>	<b>9,788,870</b>	<b>1,683,064</b>	<b>12,930,738</b>
<b>Class II as % of Total</b>	<b>39.5%</b>	<b>95%</b>	<b>16%</b>	<b>53%</b>
<b>Class I and II as % of Total</b>	<b>40%</b>	<b>95%</b>	<b>21%</b>	<b>55%</b>
<b>Class III: Not Currently Used to Treat Human Diseases</b>				
Monensin	1,343,900		1,923,723	3,267,623
Lasalocid	841,823		2,238,514	3,080,337
Roxarsone			1,972,443	1,972,443
Amprolium	29,049		789,299	818,348
Zoalene			702,631	702,631
Arsanilic acid		169,440	371,435	540,875
Carbadox		299,135		299,135
Salinomycin			232,147	232,147
Ethopabate			25,072	25,072
Efrotomycin		42,953		42,953
Oleandomycin		33,156		33,156
Bambermycin		7,550	23,163	30,713
Decoquinat	1,260			1,260
<b>Total Class III</b>	<b>2,216,032</b>	<b>552,234</b>	<b>8,278,427</b>	<b>11,046,693</b>
<b>Class III as % of Total</b>	<b>60%</b>	<b>5%</b>	<b>79%</b>	<b>45%</b>
<b>Total All Classes</b>	<b>3,693,017</b>	<b>10,348,596</b>	<b>10,535,926</b>	<b>24,577,539</b>

in human medicine today for which there are few or no alternatives. In Class II are drugs or analogs of drugs used in human medicine for which alternatives currently exist. Class III includes drugs not currently used in human medicine. Many of these are not well studied and it is not clear whether or not they might induce crossresistance to current or future drugs.

As Table 14 indicates, the two highest categories (Classes I and II) account for over half the nontherapeutic antimicrobials used in animals. All the antimicrobials in these two classes—accounting for more than 13 million pounds of antimicrobials—have already been banned from use for growth promotion and other nontherapeutic purposes in the European Union.<sup>8</sup>

<sup>8</sup> As international organizations move to draft global strategies to slow the spread of antimicrobial resistance, the United States and other countries will be under pressure to follow the lead of the Europeans in cutting back high-risk agricultural uses of antimicrobials.





## **This Report's Estimates**

Our estimates—based on calculations from numbers of animals, recommended uses, and dose—place total contemporary non-therapeutic use of antimicrobials in cattle, swine, and poultry at 24.6 million pounds. Cattle account for 3.7 million pounds, swine for 10.3 million pounds, and poultry for 10.5 million pounds.

We also used prescription information and reasonable assumptions to estimate human medical use at about 3 million pounds.

## **The Institute of Medicine's 1985 Estimates**

Drawing on US International Trade Commission reports, the Institute of Medicine estimated total antimicrobial production in the United States at 31.9 million pounds in 1985 (IOM 1989). The report estimated total subtherapeutic use in beef, swine, and poultry production at 16.1 million pounds, well over half the total US production. The total antimicrobial production number, although dated, is still the most credible estimate available.

## **The Animal Health Institute's 2000 Estimates**

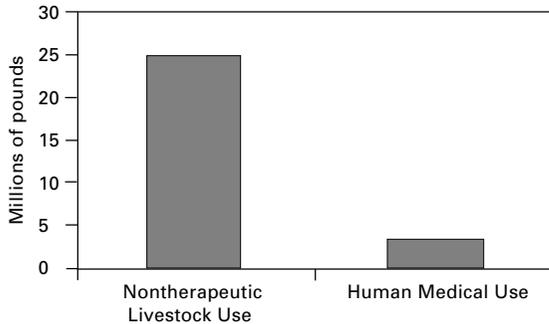
The Animal Health Institute (AHI) issued a press release in 2000 on antimicrobial production based on a 1998 survey of AHI members (AHI 2000a). Although the absence of detail in terms of methodology hampers interpretation, AHI reported 17.8 million pounds of antimicrobial production, apparently for all animal uses, therapeutic and nontherapeutic. Of the 17.8 million pounds, 14.7 million were attributed to therapeutic use and disease prevention and 3.1 million pounds were attributed to growth promotion.

AHI used the 50-million-pound figure for total antimicrobial production and calculated that animal agriculture accounts for only 35 percent of total antimicrobial usage. AHI did not directly estimate the usage in humans, but simply subtracted its 17-million-pound figure for animal use from the 50 million total.

## Comparison of UCS's Estimates for Medical and Nontherapeutic Agricultural Use

Our estimate for the amount of nontherapeutic use of antimicrobials for the three major livestock sectors—24.6 million pounds—is 8 times the 3 million pounds that we estimate are annually used in human medicine (see Figure 3). Since our estimate includes only cattle, swine, and poultry, and leaves out aquaculture and minor species, it is likely an underestimate of the degree to which agricultural use of antimicrobials swamps use for human medicine.

**Figure 3. Comparison of Antimicrobials Used in Livestock and Human Medicine**



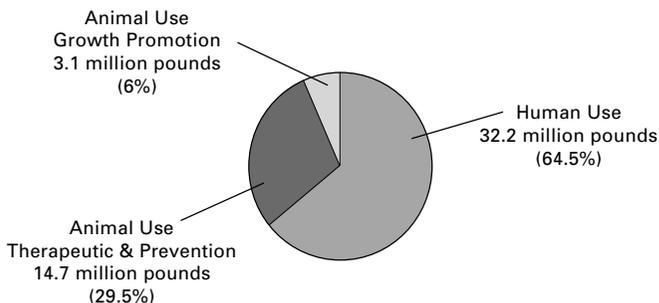
## Comparison of UCS's Estimates with AHI's Estimates

Industry's estimate for the total animal antimicrobial use—17.8 million pounds—is far less than ours. We estimate 24.6 million pounds just for nontherapeutic uses in the three livestock sectors, while AHI's 17.8-million-pound estimate apparently includes *all* animal uses—therapeutic and nontherapeutic, livestock, aquaculture, and companion animals (see Figure 4).

If AHI's number is correct, the trend in antimicrobial use is dramatically downward. AHI's 17.8 million pounds is just above the 16.1 million pounds IOM estimated as being used in 1985 for subtherapeutic use alone in only three species. That would suggest that total use had held steady for 15 years despite the huge increases in poultry production and the modest increases in swine and beef production documented in this report—a major accomplishment, if true.

It is difficult to compare our estimate for human medical use with AHI's extrapolated 32-million-pound number. In theory, this

**Figure 4. Percent of Antibiotics Used in the United States in 1998 as a Reported by the Animal Health Institute 2000 (AHI 2000)**



estimate includes consumer uses, like soaps, in addition to human, aquacultural, and pet uses. Our number for human use (3 million pounds) is an estimate based on solid numbers for courses of antimicrobial prescribed by physicians. But even using AHI's lower figure for animal antimicrobials—17.8 million—the use of antimicrobials in animal agriculture far outstrips our 3-million-pound estimate for human medical use.

We also cannot compare estimates of nontherapeutic use (including uses for both growth promotion and disease prevention) with AHI's because AHI reported its data differently, lumping together disease prevention and therapeutic uses. As we discussed in Chapter 3, we think that considering growth promotion and disease prevention together is justifiable from a public health standpoint. In any case, there is no indication in the AHI survey of how respondents made the distinction between growth promotion uses and disease prevention uses. So, even if we attempted to break out our estimates into those categories, it would remain difficult to compare them with AHI's estimates.

Estimates of the animal vs. human share of antimicrobial production and use depend on the accuracy of data and on projections of use within each sector and across the whole industry. As we have discussed, the oft-cited 50-million-pound number is not based on hard data and should no longer be used for share calculations.

Better ballpark estimates can be made with information now in hand. We can start with our estimates of 24.6 million plus 3 million pounds for nontherapeutic animal use and human medical use, respectively, and make educated guesses for the remaining categories of antimicrobial use. Our breakdown for the remaining

categories is as follows: over-the-counter use (1.5 million pounds), nontherapeutic use in minor species (3 million pounds), therapeutic use in all species (2 million pounds) and in companion animals (1 million pounds). The total based on these educated guesses—35 million pounds—seems reasonable when compared with the 32 million pounds IOM estimated for total use in 1985.

Using 35 million pounds as the total, the nontherapeutic use of antimicrobials in the three livestock sectors comes to 70 percent of the total, as shown in Table 15. All agricultural uses (livestock, nontherapeutic and therapeutic, plus pesticides) represent 84 percent of the total. All nonhuman uses (livestock, pesticides, and companion animals) are 87 percent of the total.

By contrast, AHI's report indicates that currently *all animal uses*—therapeutic and nontherapeutic, including minor livestock species and companion animals—account for a mere 35 percent of the total antimicrobial production.

**Table 15. Human, Agricultural, and Companion Animal Antimicrobial Use**

	Total Pounds	Percent of Total
<b>Human Uses</b>		
Treatment of Human Diseases*		
Inpatient Use	900,000	
Outpatient Use	2,100,000	
<b>Total for Disease Treatment</b>	<b>3,000,000</b>	<b>9%</b>
Other Human Uses		
Topical creams, soaps, disinfectants	1,500,000	
<b>Total All Human Uses</b>	<b>4,500,000</b>	
<b>Livestock Uses</b>		
Nontherapeutic—Cattle, Swine, Poultry*	24,577,539	<b>70%</b>
Nontherapeutic—Other Species	3,000,000	
Therapeutic—All Species	2,000,000	
<b>Total All Livestock Uses</b>	<b>29,577,539</b>	<b>84%</b>
<b>Pesticide Uses*</b>	50,000	
<b>Total All Agricultural Uses</b>	<b>29,582,539</b>	<b>84%</b>
<b>Companion Animal Uses</b>	1,000,000	
<b>Total Nonhuman Uses</b>	<b>30,582,539</b>	<b>87%</b>
<b>Total Antimicrobial Use</b>	<b>35,127,539</b>	

\*Estimates based on data reported or cited in this report. The other estimates in the table are educated guesses.



# CONCLUSIONS AND RECOMMENDATIONS

## Conclusions

Publicly available, verifiable data on antimicrobial use and production in the United States are shockingly incomplete. Such information as we have is an extrapolation from decades-old data, inferences from sales data, or brief reports from industry surveys done with unknown methodology. No government agency collects or compiles comprehensive data on antimicrobial use for any purpose.

Such data are vital for the understanding of and response to the problem of antimicrobial overuse and the loss of drugs due to resistance. Without such information, the government cannot devise rational plans for the phase-out of antimicrobials nor can it evaluate the effectiveness of policy milestones as they are implemented. Industry data on antimicrobial use in livestock production almost certainly underestimate usage and are far too general to help scientists explore the linkages between various types of farm use and the emergence and spread of resistance.

Under these circumstances, our government, our public health agencies, and the public are flying blind.

This report produces estimates that ought to be readily available to the public. Although the methods depend on numerous assumptions and expert judgments, our estimates are the best we know of on the quantities of antimicrobial used in livestock and human medicine.

The implications of the report are sobering:

- Tetracycline, penicillin, erythromycin, and other antimicrobials that are important in human use are extensively used in the absence of disease for non-therapeutic purposes in today's livestock production.

*Without data on use, the government cannot devise rational plans for phasing out antimicrobials in livestock production.*

Cattle, swine, and poultry are routinely given antimicrobials throughout much of their lives. Many of the antimicrobials given to livestock are important in human medicine.

- **The overall quantity of antimicrobials used in agriculture is enormous.**

Many consumers will be surprised to find that tens of millions of pounds of antimicrobials are used in livestock systems. Our estimates are that every year livestock producers in the United States use 24.6 million pounds of antimicrobials in the absence of disease for nontherapeutic purposes: approximately 10.3 million pounds in swine, 10.5 million pounds in poultry, and 3.7 million pounds in cattle. The tonnage would be even higher if antimicrobials used therapeutically for animals were included.

- **Previous estimates may be drastic underestimates of total animal use of antimicrobials.**

Our report suggests that a study recently released by the Animal Health Institute (AHI) may have severely underestimated animal use of antimicrobials. Our estimate of 24.6 million pounds for animal use is almost 40 percent higher than industry's figure of 17.8 million pounds—and ours includes only nontherapeutic uses in the three major livestock sectors. AHI's covers all uses—therapeutic and nontherapeutic—in all animals, not just cattle, swine, and poultry.

- **Approximately 13.5 million pounds of antimicrobials prohibited in the European Union are used in agriculture for nontherapeutic purposes every year by US livestock producers.**

The European Union has prohibited the nontherapeutic use of antimicrobials in agriculture that are important in human medicine, such as penicillins, tetracyclines, and streptogramins. Total US agricultural use of these antimicrobials is enormous.

- **Driven primarily by increased use in poultry, overall use of antimicrobials for nontherapeutic purposes appears to have risen by about 50 percent since 1985.**

According to our estimates, total nontherapeutic antimicrobial use in animals has increased from 16.1 million pounds in the mid-1980s to 24.6 million pounds today.

Since the mid-1980s, nontherapeutic antimicrobial use in cattle has risen 16 percent from 3.2 to 3.7 million pounds in absolute terms.

In swine, nontherapeutic use has declined slightly (from 10.9 to 10.3 million pounds), although there is growing reliance on tetracycline-based products.

In poultry, nontherapeutic use since the 1980s has increased by over 8 million pounds (from 2 million to 10.5 million pounds), a dramatic 307 percent increase on a per-bird basis. Growth in the size of the industry accounted for about two-fifths of the overall increase.

- **The quantities of antimicrobials used in livestock in the absence of disease for nontherapeutic purposes dwarf the amount of antimicrobials used in human medicine.**

Our estimates of 24.6 million pounds in animal agriculture and 3 million pounds in human medicine suggest that eight times more antimicrobials are used for nontherapeutic purposes in the three major livestock sectors than in human medicine. By contrast, industry's estimates suggest that two pounds of antimicrobials are used in human medicine for every pound used in livestock.

Livestock use accounts for the lion's share of the total quantity of antimicrobials used in the United States. Our estimates suggest that nontherapeutic livestock use accounts for 70 percent of total antimicrobial use. When all agricultural uses are considered, the share could be as high as 84 percent. This estimate is far higher than the 40 percent figure for the agricultural share of antimicrobial use commonly encountered in the literature.

- **The availability of data on antimicrobial use in fruit and vegetable production demonstrates that credible use information can be obtained without unduly burdening either agricultural producers or the pharmaceutical industry.**

The report presents several years of data on the quantity of antimicrobials used as crop pesticides. These easily accessible data were compiled by the US Department of Agriculture, which uses producer surveys to gather information on pesticide use annually.

## Recommendations

There is an urgent need for solid, reliable information on antimicrobials used in agriculture. Production and usage data on antimicrobials are essential to understanding the role agricultural use plays in the evolution of bacterial resistance and to responding to the overuse and misuse of antimicrobials. This report strives to meet that need.

Our estimates of antimicrobial use are based on numerous assumptions, guidance from experts, and NASS and IOM reports.

*We invite the livestock and pharmaceutical industries to bring better data to the public arena.*

Let those who can refute and correct our estimates do so—the sooner the better. We invite the pharmaceutical industry, which holds the production data, and the animal livestock industry, which holds and could compile usage information, to bring better data to the public arena. For the public to have confidence in the data, the meth-

odology on which the numbers are based will have to be transparent and verifiable.

Fundamentally, however, the responsibility for gathering, compiling and disseminating antimicrobial production and use information must rest with the federal government. Only the government has the authority to comprehensively collect data in a way that is useful to the public health community, serves the needs of the interested public, and protects the legitimate needs of companies and producers. Only the government can ensure that public health officials have access to information they need.

Our recommendations are as follows:

1. *The Food and Drug Administration (FDA) should establish a system to compel companies that sell antimicrobials for use by food animals or that mix them in animal feed or water to provide an annual report on the quantity of antimicrobials sold. The information should be broken out by species and by antimicrobial. It should also include the class of antimicrobial, indication, dosage, delivery system, and treatment period.*

The FDA should work with the Centers for Disease Control and Prevention (CDC) to assure that all valuable information is collected and reported in ways that facilitate ease of use by public health scientists. Over time, the industry should work with the government to produce a retrospective series of data that provides more detail and reliable information on patterns of use by major sectors from 1960 to the present.

Usage data can then be assessed alongside historical data on the emergence and spread of resistant bacteria.

2. *The US Department of Agriculture (USDA) should improve the completeness and accuracy of its periodic surveys of antimicrobial use in livestock production.*
  - Cooperation in providing survey data should be mandatory, and methods should be put in place to verify compliance with rules governing accuracy and completeness.
  - Data should be collected at two levels in the agricultural production chain: the animal feed industry should supply data on the pounds mixed in feed and put into other supplements, and livestock producers should report the tons of feed used and the concentration of antimicrobials in this feed or delivered through drinking water.
  - All data collected should be in the public arena and available in appropriate forms to scientists or research institutions.
  - Estimates from different sources should be compared to identify possible gaps in survey coverage or methodological problems.
3. *The FDA, CDC, and USDA should speed up implementation of Priority Action 5 of A Public Health Action Plan to Combat Antimicrobial Resistance, the US government's recently published action plan on antimicrobial resistance.*

Priority 5 of the action plan recommends the establishment of monitoring systems and the assessment of ways to facilitate collection and protect confidentiality of usage data. New federal authority will likely be needed to establish adequate data-collection systems. The probable need for legislation highlights the urgency of beginning this work as soon as possible.

The plan indicates that the effort should begin within the next two years, but government should get on with this fundamental task immediately. The planned agricultural monitoring would allow the linkage of drug-use data to species and usage patterns. Having the ability to monitor use will enable the government to wisely plan and manage the phase-out of the use of the most troubling drugs.

This report is not meant to end the debate about usage but to start it. Our hope is that it will provide a useful framework for refining the accuracy of the estimates. We hope the report will stimulate those who have the data—mostly industry—and those

who have the power to get the data—the government—to get on with the job of compiling comprehensive, accurate data on antimicrobial use and production and making it available to the public.

The price of complacency on this important issue could be a return to an era where untreatable infectious diseases are regrettably commonplace. Doctors and the medical community will continue to innovate and eventually probably find new drugs and therapies. But the costs—human and economic—of dealing with infectious disease could rise far, far above what we have become accustomed to over the past thirty years.

