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The Campaign to End Antibiotic Overuse
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Keep Antibiotics Working

Statement for the Record

House of Representatives,
Health Subcommittee to the Energy and Commerce Committee
Hearing on the Public Health Risk from the Use of Antibiotics in Food-Producing Animals

Wednesday, July 14, 2010, 2:00 PM

Keep Antibiotics Working appreciates the attention that this committee is giving to the public health problem of antimicrobial resistance resulting from the use of antibiotics in food producing animals. Keep Antibiotics Working (KAW), a coalition of health, consumer, agricultural, environmental, humane and other advocacy groups, whose organizations have more than ten million members, is dedicated to eliminating this major cause of antibiotic resistance.

Antibiotic resistance has long been considered by the Centers for Disease Control (CDC) one of the "most pressing public health problems."[i] People already die from infections untreatable with existing antibiotics. More – perhaps many, many more – will die in years to come. This critical public health problem therefore requires a comprehensive approach that addresses *all sources* of resistance affecting human health.

Summarizing four decades of scientific research, the U.S. Food and Drug Administration recently identified an important part of the problem: the injudicious use of antibiotics in food animal production[ii].

The age of miracle antibiotics may be coming to an end. Before even more people die of resistant infections, KAW therefore advocates that Congress at long last address this crisis, and, in particular, support the scientifically sound approach found in H.R. 1549, The Preservation of Antibiotics for Medical Treatment Act (PAMTA).

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Yes, the FDA has identified the need to act. But it has failed to take any action steps, or, even to identify what steps it intends to take to address this critical public health problem. Because of the FDA's historic failure to act, Congress must step in and assure by passing PAMTA that FDA moves forward to protect public health.

Antibiotic-resistant infections: Major threats to food safety and public health

As is well known to the medical community, we face an urgent crisis of antibiotic resistance. Once considered miracle drugs, antibiotics are becoming less and less effective at treating infections and disease. Many Americans have died or fallen seriously ill due to antibiotic-resistant bacteria. When initial antibiotics don't work, it can mean several days of unnecessary pain and suffering while doctors figure out another drug is needed. Treating a patient with an ineffective drug also can give infections the chance to progress to more serious illness. For cases where none of the available antibiotics work, resistance becomes a matter of life and death. In addition to rendering drugs ineffective, resistant strains are often more virulent than their susceptible counterparts – causing more serious disease, longer hospitalizations, and driving higher healthcare costs.

Antibiotic resistance is particularly worrisome in terms of food safety. Half of all human Campylobacter infections are drug resistant, as are one in five Salmonella infections[iii]. Salmonella and Campylobacter, the most common sources of food borne illnesses in the United States, account for well over a million resistant infections in this country each year[iv]. It is not unusual for Salmonella to be resistant to many drugs at once, as was the case for several outbreaks linked to ground beef last year. Getting sick with multidrug resistant strains of Salmonella can "increase the risk of hospitalization or possible treatment failure in infected individuals"[v].

Antibiotic resistance is not a problem only for humans. The bottom line of antibiotic resistance—harder to treat diseases and higher medical costs—is also true for veterinary medicine.

Antibiotic resistance results from antibiotic use

Microorganisms exist in an interconnected ecosystem and travel back and forth among humans, animals, and other elements in the environment. Exposure to antibiotics selects for those bacteria that can withstand the drug. Resistant organisms are most encouraged in settings where antibiotics are heavily used—primarily human medicine, veterinary medicine, and food animal production. But antibiotic-resistant microorganisms generated in the guts of pigs in the Iowa countryside, for example, don't stay on the farm. They can be transmitted to humans in at least three ways: carried on meat or poultry; colonizing farm workers who transmit them into the community; or moving through water and soil, which can lead to the contamination of fresh produce.

When the antibiotics used in raising food animals such as pigs are the same (or more precisely, in the same classes) as those used in doctors' offices, bacteria from the pigs will be impervious to therapies based on the drugs[vi].

The fundamental approach to prolonging the effectiveness of drugs is to curb unnecessary uses. Every sector needs to accept responsibility and curb its own unnecessary antibiotic use.

The medical profession has stepped up to the plate and identified and attempted to address the issue by establishing guidelines against unnecessary uses, like treatment of viral diseases, and aggressively seeking to reduce prescriptions for those uses. Periodically, it evaluates the effectiveness of its initiatives.

To date, the veterinary and industrial agriculture communities lag far behind the human medical community in taking similar steps to reduce unnecessary use. Instead it has spent its energies in minimizing or denying the problem.

Production agriculture's contribution to the problem

As it turns out, food animal production uses the lion's share of the antibiotics in the United States—about 70 percent of the total. The estimates include drugs used in only three livestock sectors—poultry, swine, and beef cattle—and only for purposes other than treating sick animals—nontherapeutic purposes like growth promotion and routine disease prevention. All of these antibiotics, among them penicillins, tetracyclines, and erythromycin—are in classes of drugs used in human medicine[vii] Most of these drugs are delivered to animals mixed in their feed.

Why do animal producers use such huge quantities of valuable drugs when most of the antibiotics are not used to treat disease? In part, because growth promotion and feed efficiency uses are thought to improve the bottom line even in healthy animals. But also because drugs are needed to compensate for crowded, stressful, and unhygienic conditions characteristic of many animal production operations.

The link between animal production and reduced efficacy of human drugs

In light of the enormous use in production agriculture of exactly the same drugs used in human medicine, it is difficult to imagine a credible scenario under which resistant bacteria generated in the billions of animals we grow for food would not find their way to human populations and erode the effectiveness of our antibiotic arsenal. And indeed a mountain of scientific studies now demonstrates that that is the case.

The list of antibiotic-resistant pathogens originating in animals is long. It includes the foodborne illnesses mentioned above, caused by Campylobacter and Salmonella. Resistant urinary tract infections, which can be caused by a number of different animal-associated bacteria, including E. coli, have also been linked to animal sources. Microorganisms originating in animals are also often associated with bloodstream infections that affect hospitalized patients. Resistance in Campylobacter and Salmonella is associated with increased bloodstream infections, increased hospitalization, and increased death[viii]. And the list continues to grow.

We have only recently learned that livestock can be an important source of life-threatening methicillin-resistant *Staphylococcus aureus* (MRSA). In Europe, a strain of MRSA responsible for 20 percent of human MRSA infections in the Netherlands[ix] has been shown to be transmitted from pigs to farmers and their families, veterinarians, and hospital staff[x]. The pig-associated strain of MRSA has now been found in Canada[xi] and in the United States[xii].

Importantly, the list of resistant bacteria themselves traceable to animals does not convey the full scope of the problem. Bacteria are promiscuous. They can acquire bits of DNA, including resistance traits, from unrelated bacteria. This means that the traits that originate in animal guts might move through the microbial ecosystem to confer resistance on bacteria not of animal origin. In addition, bacteria are known to harbor large circles of DNA that carry ten or more resistance traits[xiii]. In these circumstances, the use of one antibiotic, say penicillin, can simultaneously drive up the levels of resistance to other antibiotics, like tetracycline, gentamicin, and cephalosporins.

The literature in this arena is voluminous and the conclusion is clear: antibiotic overuse in agriculture—just as in human medicine—is undercutting the efficacy of important human therapies and generating more virulent pathogens.

The recent FDA Draft Guidance Document #209 provides an overview of 40 years of studies on this topic[xiv] and finds that independent reviews of the data have consistently found a risk to public health and have repeatedly recommended reducing overuse.

Reducing antibiotic use

As long as the massive use of antibiotics continues, animals will remain an important source of resistant pathogens, dangerous to both animals and humans. The straightforward solution to the problem is to reduce the use of antibiotics in animal production and thereby diminish the pool of resistant organisms and traits.

Fortunately, the largest amounts of antibiotics in food animal production are used for growth promotion, feed efficiency, and routine disease control, uses that can be eliminated without damage to animal health or unacceptable increases in animal production costs or consumer meat prices.

As documented in the scientific literature, these uses can be reduced or eliminated with modern management practices. The viability of such practices has been demonstrated in a variety of different kinds of animal agricultural operations. On the more industrialized side, Tyson, Inc., a major poultry grower and retailer, was able to develop systems for all of its retail chicken that used no antibiotics at all. On the more niche side, cattle grown out-of-doors and fed primarily grass rarely need antibiotics at all. Many American producers, like Laura's Lean Beef, Niman Ranch, and Coleman Natural, are thriving in the marketplace selling beef and pork produced without antibiotics.

A 2009 report from the USDA Economic Research Service looking at changes in U.S. agriculture supported the notion that antibiotic use in agriculture could be reduced without

significant costs to producers[xv]. The USDA confirmed that large farms are more likely than small farms to use antibiotics in feed but noted that the benefits of this use is limited to certain stages of production, particularly pig nurseries. For other stages of production like finisher pigs, there were few benefits. The USDA also found that practices such as increased sanitation and vaccination could be substituted for antibiotics.

Data from Europe also support the feasibility of reducing antibiotic use even in intensely industrial poultry and swine systems. In 1999, Denmark, the world's leading pork exporter, ended all use of antimicrobial growth promoters without reducing the productivity of its livestock sector[xvi].

Policy recommendation

Because as mentioned above, reductions in the use of antibiotics can often be achieved by managing animals and their feeds better, production agriculture represents a golden opportunity to reduce the pressure driving up resistance traits in the microbial ecosystem.

A sensible and protective two-part policy would:

a) Reduce antibiotic use wherever possible in animal production by establishing and enforcing clinical practice guidelines in veterinary medicine

b) Review, and where supported by the evidence, cancel the use of those antibiotics also used in human medicine (so-called medically important drugs) in animal agriculture for non-therapeutic purposes like growth promotion, feed efficiency, and routine disease prevention. The classes of medically important drugs are penicillins, tetracyclines, sulfonamides, lincosamides, streptogramins, aminoglycosides, and macrolides.

Such a policy would lead to substantial reductions in antibiotic use without depriving producers of antibiotics to treat sick animals. It is important to point out that a number of antibiotic-like drugs are not used in human medicine, and that, under this approach, these drugs would be available to producers for any purpose including feed efficiency or routine disease prevention.

To accomplish public health and food safety goals, the policy needs to be effective across the board. A level playing field will force innovation in the industry and enable producers to resist temptation to fall back on antibiotics to compensate for sloppy management practices.

Reduce through PAMTA

The FDA has the authority to cancel antibiotics that are no longer safe from a resistance point of view, but so far has used it only in the case of fluoroquinolones in poultry.

While FDA has correctly identified the problem of antibiotic overuse in its new Draft Guidance Document #209, the document gives no indication that FDA is taking steps to actually prohibit antibiotic overuse. There is nothing in the new draft policy by the FDA that

even suggests that the FDA has overcome the legal and institutional barriers that have long blocked action on this important public health issue. The policy itself falls short because it only recommends reduction of antibiotics used for growth promotion. The FDA guidance does describe a vision of appropriate preventative use but the FDA has no authority to regulate veterinary practice to the extent that would be necessary to require that this vision be followed. {Once drugs are on the market, and there are many more existing approvals for disease prevention than growth promotion, the FDA has very little ability to change how they are being used.}

So even if the current policy were to be implemented sometime in the future, the public health impact could be limited because it fails to recognize that drugs used for growth promotion can often be used in the exact same manner as drugs used for disease prevention. There is no benefit to be gained from continuing to use the same drugs in the same manner but calling it disease prevention instead of growth promotion. The FDA's push for voluntary changes by drug manufacturers is highly likely to result in only this type of cosmetic change and is unlikely to lead to real reductions in use and the subsequent reductions in resistance.

The failure of the FDA to move gave impetus to the Preservation of Antibiotics for Medical Treatment Act (PAMTA) and Draft Guidance #209 does nothing to diminish the need for legislative action. This legislation would require the FDA to review antibiotics used in animal agriculture to determine whether they put public health at risk by leading to increased resistance and to withdraw from the market in a timely manner those drugs that cannot be shown to be safe.

This legislation has been endorsed by over 350 organizations, including the American Medical Association, American Academy of Pediatrics, American Nurses Association, American Public Health Association, and Infectious Diseases Society of America.

Delay on antibiotics: a disadvantage in the marketplace

The European Union (EU) now has an EU-wide ban on non-therapeutic uses of antibiotics[xvii]. New Zealand[xviii], Thailand[xix], and Korea[xx] also have either enacted or will soon enact bans on certain non-therapeutic antibiotic use.

As warned in a Government Accountability Office (GAO) report from 2004[xxi], these countries also represent potential challenges to U.S. products in the global marketplace. Under the trade rules, countries can restrict imports that do not conform to certain rules, provided they adhere to those rules themselves. For example, Korea could potentially restrict imports that relied on medicated feed not allowed in Korea. The greater the number of export partners that adopt such bans, the more vulnerable our meat exports in the global marketplace. As further noted in the GAO report, if a major importer were to restrict trade from the United States because of the use of nontherapeutic antibiotics, that action would override any economic benefits of this practice.

The U.S. animal agriculture industry is at risk of following the example of the U.S. auto industry and failing to see where the market is going. Increasingly, consumers are seeking

meat from animals raised without these antibiotics. International competitors are beginning to meet this demand. In addition to protecting public health, minimizing antibiotics use in livestock can help U.S. producers add consumer value to their products, and position themselves advantageously in the global marketplace. American producers should be supported in reducing their antibiotics use.

Conclusion

Antibiotic-resistant infections are making more people sick, and keeping them sick for longer. Longer hospital stays to treat these infections are also increasing the nation's health costs—by one recent estimate adding well over $24 billion per year to the health care tab in the United States[xxii]. And, of course, more time away from work is a drag on our economy.

We have waited far too long for action to reduce the unnecessary uses of antibiotics in food animal production. While we have dithered, drugs have stopped working, new resistant diseases have emerged, old diseases have gotten worse, and people have died.

Neither can we rely on the arrival of new drugs. The unhappy truth is that there are virtually no new classes of antibiotic drugs in the pipeline[xxiii]. The discovery of new classes of antibiotics, once almost a predictable occurrence, has become frustratingly difficult in recent decades.

Even if we were able to develop a portfolio of new antibiotic drugs, we'd risk bacteria becoming resistant to them too, unless we take steps to assure they are used judiciously. We must act to preserve the continued effectiveness of today's antibiotics, or risk the age of the miracle antibiotics coming to an end.

While FDA in Guidance #209 has recognized the problem and the solution, there is nothing in the document that indicates it is ready to tackle this problem head on.

There is simply no reason to continue the profligate use of valuable antibiotics for economic purposes or to compensate for the stressful, crowded animal production facilities. The improved management practices necessary to reduce, if not avoid, antibiotic use are available and feasible. Yet, production agriculture has been unwilling to acknowledge, much less act on, this problem. We cannot tolerate this situation any longer. To protect our food supply and the public health, we must pass PAMTA.

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[i] Centers for Disease Control (CDC). 2004. Background on antibiotic resistance. Online at www.cdc.gov/getsmart.

[ii] Food and Drug Administration (FDA). Draft Guidance #209. The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. Online at:http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM216936.pdf

[iii] Centers for Disease Control (CDC). 2009. National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria: Human Isolates. Final Report. 2007. Atlanta, GA: U.S. Department of Health and Human Services, CDC.

[iv] Total number of illnesses from USDA (www.ers.usda.gov/Data/FoodBorneIllness) is multiplied by data from footnote 3 to obtain totals for resistant illness

[v] USDA/FSIS. 2009. California Firm Recalls Ground Beef Products Due to Possible Salmonella Contamination. Online at: http://www.fsis.usda.gov/News_&_Events/Recall_041_2009_Release/index.asp

[vi] McEwen S, and Fedorka-Cray P. 2002. Antimicrobial use and resistance in animals. Clinical Infectious Diseases 34:S93-106.

[vii] Mellon M, Benbrook C, and Benbrook K. 2001. Hogging it!: Estimates of Antimicrobial Abuse in Livestock. Cambridge, MA: Union of Concerned Scientists. Online at www.ucsusa.org/food_and_agriculture/science_and_impacts/impacts_industrial_agriculture/hogging-itestimates-of.html

[viii] Helms M, et al. 2005. Adverse health events associated with antimicrobial drug resistance in Campylobacter species: a registry-based cohort study. Journal of Infectious Diseases 191:1050-5; Varma JK, et al. 2005. Antimicrobial-resistant nontyphoidal Salmonella is associated with excess bloodstream infections and hospitalizations. Journal of Infectious Diseases 192:554-61.

[ix] van Loo I, et al. 2007. Emergence of methicillin-resistant Staphylococcus aureus of animal origin in humans. Emerging Infectious Diseases [serial on the Internet] December. Online at www.cdc.gov/EID/content/13/12/1834.htm.

[x] Huijsdens X, et al. 2006. Community-acquired MRSA and pig farming. Annals of Clinical Microbiology and Antimicrobials 5:26. Online at www.ann-clinmicrob.com/content/5/1/26.; Voss A, et al. 2005. Methicillin-resistant Staphylococcus aureus in pig farming. Emerging Infectious Diseases 11:1965–6.

[xi] Khanna T, et al. 2008. Methicillin resistant Staphylococcus aureus colonization in pigs and pig farmers. Veterinary Microbiolgy 128:298–303.

[xii] Smith T, et al. 2008. Paper presented at the International Conference on Emerging Infectious Diseases, Centers for Disease Control and Prevention, Council of State and Territorial Epidemiologists, Atlanta, GA, March, and personal communication.

[xiii] Partridge SR, et al. 2009. Gene cassettes and cassette arrays in mobile resistance integrons. Federationof European Microbiological Societies (FEMS) Microbiological Reviews 33:757-84; Akwar HT, et al.2008. Associations of antimicrobial uses with antimicrobial resistance of fecal Escherichia coli from pigs on 47 farrow-to-finish farms in Ontario and British Columbia. Canadian Journal of Veterinary Research 72:202-10; Gillings M, et al. 2008. The evolution of class 1 integrons and the rise of antibiotic resistance. Journal of Bacteriology 190:5095-100.

[xiv] Food and Drug Administration (FDA). Draft Guidance #209. The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. Online at:http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM216936.pdf

[xv] USDA Economic Research Service. 2009.The Transformation of U.S. Livestock Agriculture: Scale, Efficiency, and Risks. Online at www.ers.usda.gov/Publications/EIB43/EIB43e.pdf.

[xvi] Aarestrup, F et al. 2010. Changes in the use of antimicrobials and the effects on productivity of swine farms in Denmark. Am J Vet Res. 71(7):726-33.

[xvii] European Commission. 2005. Ban on antibiotics as growth promoters in animal feed enters into effect, IP/05/1687. Online at: http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/1687&format=HTML&aged=0&language=EN&guiLanguage=en.

[xviii] Government Accountability Office (GAO). 2004. Antibiotic Resistance: Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals, GAO-04-490, April 22.

[xix] Brooks E. 2008. Reconciling scarcity and demand through innovation. Food Business Asia, Issue 21, July/August. Online at www.efeedlink.com/ShowDetail/03c885e3-7852-439a-9ef0-a8a0b66a749c.html.

[xx] Pig Progress. 2008. Korea to ban antibiotics in feed. Online at: http://www.pigprogress.net/news/korea-to-ban-antibiotics-in-feed-id1914.html

[xxi] GAO. 2004. Antibiotic Resistance.

[xxii] Foster. 2010. Economic Consequences of Antibiotic Resistance. Presented at 2010 Annual Conference on Antimicrobial Resistance. February 1-3. Bethesda, MD.

[xxiii] Infectious Diseases Society of America. 2003. Bad bugs, no drugs: Defining the antimicrobial availability problem. Backgrounder. Online at www.idsociety.org/badbugsnodrugs