Statement of

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Antibiotic Resistance and the Use of Antibiotics in Animal Agriculture

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Mr. Chairman and Members of the Subcommittee:

Thank you for the opportunity to submit written testimony on the crisis of antimicrobial resistance and to make recommendations for Congressional action.

Antimicrobials are a critical defense against infectious bacteria that can cause disease and death in humans. However, this precious resource in human medicine is being wasted through inappropriate use in animal agriculture, which contributes to the increased prevalence of pathogenic bacteria resistant to antibiotics.

A common and widespread occurrence in today's food animal agriculture is the administration of constant, low doses of antimicrobials to billions of animals across the country. This practice facilitates the rapid emergence of antimicrobial resistance among potentially disease-causing bacteria and compromises our ability to treat disease in humans with antibiotics, making it clear that such inappropriate and indiscriminate use of antibiotics in food animal production must end.

Antimicrobial Resistance

The use of antimicrobials in any context, veterinary or human, appropriate or otherwise, creates environmental pressure that selects for resistance. This has been well established; indeed, the statement reflects the most basic understanding of evolutionary biology. The eventual emergence of resistance in pathogens to current antimicrobial drugs is accepted as a *fait accompli* within public health and human medicine (Spellberg, et al., 2008). Effective antimicrobials are analogous to nonrenewable resources: their eventual depletion is assumed. Nevertheless, overuse and misuse of antimicrobials can accelerate the evolution of resistance, outpacing the development of new antimicrobial drugs by biomedical researchers in academia and the pharmaceutical industry.

Accordingly, regulatory agencies and the medical community have developed rules and recommendations to ensure appropriate use of antimicrobial products, extending their efficacy to future generations. These best practices often receive scant attention in food animal production, making the industry a leading contributor to the evolution of resistant bacteria (Mellon, et al., 2001). These bacteria can spread through food and environmental pathways to human populations, threatening the public's health with pathogens incurable by standard treatment regimens (Silbergeld, et al., 2008).

Food Animal Production

The relationship between food animal production and antimicrobial resistance extends beyond one or two particular drugs; almost every major class of medically important antimicrobials, from penicillin to third-generation cephalosporin compounds, has been approved for use in animal agriculture (Sarmah, et al., 2006). In some cases, new drugs were licensed for agricultural use before their approval in human medicine. Resistance to these drugs was then detected before they became available to physicians for treatment of human patients, further suggesting a causal relationship between animal agriculture and resistance (Kieke, et al., 2006). Indeed, researchers have consistently found that using antimicrobials in food animal production shortens the "useful life" of existing drugs to treat both human and veterinary diseases (Smith, et al., 2002).

The current discussion of antimicrobial resistance has focused on the inappropriate prescription of drugs by physicians, and noncompliance with treatment regimens by patients. The animal agricultural industry asserts these factors as the primary cause of resistance. However, it is estimated that food animals consume as much as 70 percent of antimicrobials administered in the United States — almost 25 million pounds per year (Mellon, et al., 2001). In North Carolina alone, the quantity of antimicrobials consumed by food animals exceeds the quantity utilized in human medicine throughout the United States (Florini, et al., 2005). The use of antimicrobials in animal agriculture clearly exceeds their prescription in human medicine, suggesting the importance of food animal production's contribution to resistance.

The use of antimicrobial drugs as growth promoters in food animal production is of special concern. In these cases, drugs are typically added to feed and water at levels below those used to treat clinical infection in animals. The exposure of bacteria to lower concentrations of antimicrobial agents selects for resistance. Under these conditions, resistant strains are more likely to survive and reproduce, and, given that most bacteria reproduce every 20-30 minutes, an entire population will quickly express resistance as the susceptible strains of the bacteria are eliminated by the low-dose antibiotics (Spellberg, et al., 2008).

Furthermore, the industry asserts that, beyond growth promotion, antimicrobial drugs remain necessary for treatment, prevention, and control of pathogenic bacteria, often conflating these purposes and collectively labeling them "therapeutic use." Very few antimicrobials used in agriculture are administered as treatment for infection (Mellon, et al., 2001). Nevertheless, food animals should receive treatment for clinical disease. Furthermore, using antimicrobial drugs to control the outbreak of specific, diagnosable pathogens also merits consideration, with proper regulatory and veterinary oversight.

Nonspecific prevention, however, is not justifiable. Many infections requiring antimicrobial drugs for prevention or control result primarily from the overcrowding and poor sanitation common in concentrated food animal production (Gilchrist, et al., 2007; McEwan and Fedorka-Cray, 2002). Under these conditions, pathogens spread quickly, and producers administer drugs to prevent or control infections they have essentially provoked through overcrowding and poor sanitation. The "need" for antimicrobial drugs claimed by industry is largely self-generated and better animal husbandry would protect animal health without stimulating antimicrobial resistance.

Beyond the evolution of resistance at production facilities, bacteria share genetic material that likewise encodes resistance to antimicrobials — that is, genes transferred from resistant bacteria to susceptible bacteria in the environment can make the recipients similarly resistant to multiple antimicrobial drugs. Transfer of resistance genes was observed in *Escherichia coli* (*E. coli*) isolated from consumer meat products (Sunde and Norstrom, 2006). Researchers estimate that 95 percent of genes that encode resistance are transferrable to other organisms (Nwosu, 2001). Although most research on antimicrobial resistance has focused on specific pathogens and individual drugs, this "one bug, one drug" approach misrepresents the problem. Resistance that evolves in food animal production facilities can later spread to pathogen and commensal bacteria through gene transfer. Thus, irresponsible practices in food animal production have dire consequences beyond the producers' property lines.

Exposure Pathways

While industry groups argue that using antimicrobials in food animal production does not threaten public health, many studies have shown the opposite (Silbergeld, et al. 2008). Resistant bacteria move through food and environmental pathways to infect humans, who then suffer clinical disease with fewer treatment options.

Food: In the United States, numerous resistant bacteria have been isolated from consumer meat products, including bacteria resistant to broad-spectrum antimicrobials such as penicillin, tetracycline, and erythromycin (Johnson, et al., 2005; Simjee, et al., 2002). Higher prevalence of multidrug-resistant *E. coli* has been reported in animals receiving antimicrobials in feed than animals raised without these drugs (Sato, et al., 2005). Likewise, products derived from animals raised without antimicrobials contain fewer resistant bacteria (Price, et al., 2005; Luantongkum, et al., 2006).

Environment: The excretion of resistant enteric bacteria in animal waste likewise creates exposure pathways between food animals and human populations. Each year, according to USDA, confined food animals produce 335 million dry tons of waste, more than 40 times the mass of human biosolids generated by publicly owned treatment works (7.6 million dry tons were generated in 2005, for example).

When applied to farmland as fertilizer, typically without any pretreatment, animal waste contaminates surface and groundwater. Resistant *E. coli* and resistance genes have been detected in groundwater in North Carolina, Maryland, and Iowa (Anderson and Sobsey, 2006; Stine, et al., 2007; Mackie, et al., 2006). Resistant bacteria have also been isolated in air samples collected downwind of production facilities, while fewer bacteria were identified in samples collected upwind (Gibbs, et al., 2006).

Given the ability of bacteria to exchange resistance genes in the environment, and the numerous environmental pathways that connect food animal production with human populations, no method of controlling the spread of pathogens can substitute for ending the practices that have accelerated the development of antimicrobial resistance. Just one resistant bacterium that "escapes" can quickly reproduce, creating countless opportunities for human exposure.

Rural Communities: Rural communities and farmworkers face especially high risks of infection with antibiotic resistant bacteria and suffer disproportionately from the use of antimicrobial drugs in food animal production. Researchers have repeatedly documented this disproportionate risk (Van den Bogaard and Stobberingh 1999; Price, at al., 2007; Ojeniyi 1998; Saenz 2006; Smith, et al., 2005; and KE Smith, et al. 1999).

Policy Responses

There is consensus within public health and human medicine that the administration of antimicrobial drugs as growth promoters in food animal production should end. The American Public Health Association has called for banning non-therapeutic use of antimicrobials in food animal production (APHA, 2003). The World Health Organization, the American Medical Association, and the Infectious Diseases Society of America have made similar recommendations (WHO, 2003; Fryhofer, 2010; Spellberg, 2008).

The WHO has stated, "In the absence of a public health safety evaluation, [governments should] terminate or rapidly phase out the use of antimicrobials for growth promotion if they are also used for treatment of humans." In 2002, three years after Denmark banned the use of antimicrobials as growth promoters, the WHO wrote,

> "…the termination of antimicrobial growth promoters in Denmark has dramatically reduced the food animal reservoir of enterococci resistant to these growth promoters, and therefore reduced a reservoir of genetic determinants (resistance genes) that encode antimicrobial resistance to several clinically important antimicrobial agents in humans" (WHO, 2003).

The WHO also reported no significant differences in animal health or producer income with these changes.

Following Denmark's lead, the European Union issued a ban on using antimicrobial drugs as growth promoters beginning in 2006. Repeated studies have shown that legal prohibitions on such use cause resistance in bacteria isolates from humans and food animals to decline significantly. In Europe, the prevalence of antimicrobial resistant *Enterococcus faecium* in swine and poultry declined significantly when antimicrobial growth promoters were removed (Aarestrup, et al., 2001). The prevalence of resistant enterococci in human patients also declined in Europe over the same period, reflecting the causal relationship (Klare, et al., 1999).

In the United States, the indiscriminate use of antimicrobial drugs in food animal production continues, threatening the public's health. Recent actions by Congress have received attention throughout the public health community. Most notably, the "Preservation of Antibiotics for Medical Treatment Act" (HR 1549) would strictly regulate using antimicrobial drugs for growth promotion and "routine disease prevention."

Economic Arguments

Recent studies contradict the food animal industry's claims that the use of antimicrobials for growth promotion brings animals to market weight in less time, and therefore justifies the expense of the antimicrobial drugs. However, two large-scale studies that examined poultry and swine production have concluded that economic gains are minimal or nonexistent, and that identical benefits could be attained through better animal husbandry, especially improved sanitation (Graham 2007; Miller 2003). Even if producers derive an economic benefit from antimicrobial drugs, however, the harm to society — fewer treatment options, increased health care costs, and heightened virulence of bacterial infections — more than offsets these supposed benefits. Nevertheless, producers and integrators ignore these health costs, which have been externalized to the larger society, and are not captured in the retail price of consumer meat products (Osterberg and Wallinga, 2004).

Conclusion

The Food & Drug Administration recently released a draft "guidance document" that reviewed the evidence linking antimicrobial resistance to food animal production. FDA concludes, "Using medically important antimicrobial drugs for production purposes is not in the interest of protecting and promoting public health" (FDA, 2010). FDA clearly supports the conclusions of public health researchers discussed here, and has begun taking action in response to antimicrobial resistance accelerated by animal agriculture. No *scientific* debate exists on these issues — only political questions remain.

I commend members for their leadership on this topic, and urge further action to fully prohibit using antimicrobial drugs for growth promotion and prophylaxis. Preserving the efficacy of antimicrobials in human medicine requires immediate action, and I urge Congress to move quickly in taking steps to protect the public's health.

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