Statement by
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Good morning Mr. Chairman and Members of the Senate Health, Education, Labor and Pensions Committee. My name is Jay Graham and I am a public health researcher at the Johns Hopkins Bloomberg School of Public Health. In addition, I was the co-author of a report for the Pew Commission on Industrial Farm Animal Production titled *Antibiotic Resistance and Human Health.* I appreciate the opportunity to speak to you today.

Antimicrobials are a critical defense in the fight against infectious bacteria that can cause disease and death in humans. Their value as a resource in human medicine is being squandered through inappropriate use in animals raised for food. The method that now predominates in food animal agriculture – applying constant low doses of antimicrobials to billions of animals – facilitates the rapid emergence of resistant disease-causing bacteria and compromises the ability of medicine to treat disease, making it clear that such inappropriate and indiscriminate use must end.

A wide range of antimicrobial drugs are permitted for use in food animal production in the U.S. (Sarmah et al 2006). These drugs represent most of the major classes of clinically important antimicrobials, from penicillin to third-generation cephalosporin compounds. In some cases, new drugs were licensed for agricultural use in advance of approvals for clinical use. In the case of quinupristin-dalfopristin – an analog of virginiamycin, which is used in food animal production – this decision by the FDA resulted in the emergence of resistance in human isolates prior to eventual clinical registration (Kieke et al 2006), thus demonstrating how feed additive use can compromise the potential utility of a new tool in fighting infectious disease in humans.

Agricultural use can also significantly shorten the “useful life” of existing antimicrobials for combating human or animal disease (Smith et al, 2002).

While discussion of the issue of declining effectiveness of antimicrobials often centers on the importance of ensuring the proper use of antimicrobials in human medicine, the fact is that most antimicrobials used in the U.S. are used as “growth promoters” in food animal production, not human medicine (Mellon et al 2001).   In North Carolina alone, the use of antimicrobials as a feed supplement has been estimated to exceed all U.S. antimicrobial use in human medicine. A relatively small percentage of antimicrobial use in food animal production is to treat sick animals, and much of what is needed for therapeutic purposes is the direct result of the animal husbandry practices of crowding large numbers of food animals in small confined spaces, thereby increasing the chance that diseases will spread through food animal populations.

Exposure of bacteria to sub-lethal concentrations of antimicrobial agents is particularly effective in driving the selection of resistant strains, and under conditions of constant antimicrobial use, resistant strains are advantaged in terms of reproduction and spread. Because of the rapidity of bacterial reproduction, these changes can be expressed with great efficiency.

Exacerbating the problem of using antimicrobials for growth promotion of food animals is the fact that bacteria can share genetic material that encodes resistance to antimicrobials. It is estimated that transferable resistance genes account for more than 95% of antibiotic resistance (Nwosu, 2001). These events have been frequently detected in resistant *E. coli* isolated from consumer meat products (Sunde and Norstrom 2006). At this point, most research has focused on specific patterns of resistance in selected disease-causing organisms – a “one bug, one drug” definition of the problem (Laxminarayan et al 2007). But this discounts the fact that it is the community of genetic resources that determines the rate and propagation of resistance (Salyers and Shoemaker 2006).

From a public health perspective, it clearly makes good sense to remove antimicrobials for growth promotion in food animal production. When this is done, resistance in disease-causing organisms tends to decrease significantly. Studies carried out in Europe have demonstrated a rapid decrease in the prevalence of antimicrobial resistant *Enterococcus faecium* recovered from pigs and broilers after antimicrobials were removed (from Aarestrup et al 2001). The prevalence of resistant enterococci isolates from human subjects also declined in the European Union (EU) over the same period (Klare et al 1999).

Addressing other animal agriculture practices, such as more thorough and frequent cleaning of animal feeding operation facilities, may also be needed in conjunction with cessation of using antimicrobials to eliminate reservoirs of antibiotic resistance bacteria from farms.

Recent studies call into question the assumed economic benefits of using antimicrobials in animal feeds. Historically, economic gains from using antimicrobials to promote growth have been thought to justify the expense of the drugs. Two recent large-scale studies – one with poultry and one with swine – found that the actual economic benefits were miniscule to nonexistent, and that the same financial benefits could instead be achieved by improving the management of the animals (e.g., cleaning out poultry houses) (Graham 2007; Miller 2003). Even when improvements from growth promoting antimicrobials have been observed, their benefits are completely offset if costs from increased resistance are considered: loss of disease treatment options in humans and animals, increased health care costs, and more severe and enduring infections. These costs are usually “externalized” to the larger society and not captured in the price of the meat and poultry sold to consumers.

There are industry trade groups that argue that using antimicrobials in the food animal production process does not pose a threat to public health. But, numerous studies support a strong link between the introduction of an antimicrobial into animal feeds and increased resistance in disease-causing organisms isolated from humans (Silbergeld et al. 2008). Resistant disease-causing organisms can affect the public through food routes and environmental routes.

Food routes: In the U.S., antimicrobial resistant disease-causing organisms are highly prevalent in meat and poultry products, including disease-causing organisms in meats that are resistant to the broad-spectrum antimicrobials penicillin, tetracycline and erythromycin (Johnson et al 2005; Simjee et al 2002). Animals given antimicrobials in their feed contain a higher prevalence of multidrug-resistant *E. coli* than animals produced on farms where they are not exposed to antibiotics (Sato et al 2005), and the same disparity shows up when one compares the meat and poultry products consumers purchase from these two styles of production (Price et al 2005; Luantongkum et al 2006).

Environmental routes: Waste disposal is the major source of antimicrobial resistant disease causing organisms entering the environment from animal feeding operations. Each year, confined food animals produce an estimated 335 million tons of waste (dry weight) (USDA), which is deposited on land and enters water sources. This amount is more than 40 times the mass of human biosolids generated by publicly owned treatment works (7.6 million dry tons in 2005). No treatment requirements exist in the U.S. for animal waste before it is disposed of, usually on croplands – even though levels of antimicrobial resistant bacteria are present at high levels.

Antimicrobial resistant *E. coli* and resistance genes have been detected in groundwater sources for drinking water sampled near hog farms in North Carolina (Anderson and Sobsey 2006), Maryland (Stine et al 2007), and Iowa (Mackie et al 2006). Groundwater provides drinking water for more than 97% of rural U.S. populations. In addition, antibiotics used in food animal production are regularly found in surface waters at low levels (Sarmah et al 2006).

Resistant disease-causing organisms can also travel through the air from animal feeding operation facilities. At swine facilities using ventilation systems, resistant disease-causing organisms in the air have been detected as far away as 30 meters upwind and 150 meters downwind (Gibbs et al 2006).

Farm workers and people living near animal feeding operations are at greatest risk for suffering the adverse effects of antimicrobial use in agriculture. Studies have documented their elevated risk of carrying antibiotic-resistant disease-causing organisms (Van den Bogaard and Stobberingh 1999; Price et al 2007; Ojeniyi 1998; Saenz 2006; Smith et al 2005; and KE Smith et al 1999).

The rise of antimicrobial resistance in bacteria, in response to exposure to antimicrobial agents, is inevitable as all uses of antimicrobial agents drives the selection of resistant strains. Thus, there is the potential to lose this valuable resource in human medicine, which might well be finite and nonrenewable – once a disease-causing organism develops resistance to an antimicrobial, it may not be possible to restore its effectiveness. Declining antimicrobial effectiveness can be equated with resource extraction. The very notion of antimicrobial effectiveness as a natural resource is a new concept, so it is not surprising that there has been very little public discussion about the ethical implications of depleting this resource for non-essential purposes, such as for growth promotion in food animal production.

In 2003, the American Public Health Association (APHA), in its policy statement, said "the emerging scientific consensus is that antibiotics given to food animals contribute to antibiotic resistance transmitted to humans." APHA, the world's largest public health organization, also remarked that "an estimated 25–75 percent of feed antibiotics pass unchanged into manure waste."

For its part, the World Health Organization (WHO) has recommended that "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."

For an industry that has become accustomed to using antimicrobials as growth promoters, the idea of stopping this practice might seem daunting. But, consider the case of Denmark, which in 1999 banned the use of antimicrobials as growth promoters. In 2002, the World Health Organization reported that:

> "…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."

The World Health Organization also reported there were no significant differences in the health of the animals or the bottom line of the producers. The European Union has followed suit with a ban on growth promoters that took effect in 2006.

Finally, prudent public health policy thus indicates that nontherapeutic uses of antimicrobials in food animal production should be ended. Economic analyses demonstrate that there is little economic benefit from using antimicrobials as feed additives, and that equivalent improvements in growth and feed consumption can be achieved by improved hygiene.

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