



LOUISE M. SLAUGHTER
CONGRESS OF THE UNITED STATES
28TH DISTRICT, NEW YORK

November 28, 2011

Dr. Margaret Hamburg
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Commissioner Hamburg:

It is with great disappointment that I write to you in order to address a number of growing concerns I have with the Food and Drug Administration (FDA), and the current approach it has taken with regard to antibiotic use in agriculture. FDA has not acted in the best interest of public health, and continues to postpone, prolong, and de-prioritize important measures that are necessary to protect the American people. The agency has a public mandate to protect public health – not to cater to the special interests of the agriculture industry.

I have three major concerns:

- 1) The finalization of Guidance #209, The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals, has been unacceptably delayed. In the past few months alone, 136 people were infected with the outbreak strain of antibiotic resistant *Salmonella* Heidelberg after consuming contaminated ground turkey. It is irresponsible to delay regulatory measures when public health is at stake.
- 2) FDA has consistently neglected to report critical information on antibiotic use in agriculture. At a time when antibiotic resistance is of growing global concern, reporting should be expanded, not limited.
- 3) FDA's rejection of two citizen petitions, asking for the withdrawal of approvals for the nontherapeutic uses of medically important antimicrobials in food animals, has demonstrated an inability to address safety concerns in an acceptable or timely manner. There are striking parallels with FDA's handling of the carcinogenic drug DES, an issue I spent a great deal of time addressing when I first came to Congress in 1986. As with nontherapeutic use of medically important antibiotics, DES was shown to be detrimental for human health, yet FDA waited years to take action. The American people deserve better.

Every year, two million Americans acquire bacterial infections during their hospital stay, and nearly 100,000 die from them. Seventy percent of these infections are resistant to the drugs commonly used to treat them. In a review study published last month, Tufts University School of Medicine researchers stated that, "There is no doubt that human misuse and overuse of antibiotics are large

contributors to resistance, particularly in relation to bacteria associated with human infection.” Despite clear warning signs, the U.S. has fallen behind as other countries, including Denmark, Germany, South Korea, and now China have implemented or announced bans on the use of antibiotics as growth promoters in food-animal production. Rather than follow a proactive “precautionary principle,” the U.S. continues to falter when it comes to regulation of antibiotic use, risking widespread and irreparable harm to the American people.

At my request, the Government Accountability Office (GAO) released a report in 2011 on antibiotic use in food-producing animals and antibiotic resistance. The GAO found that data collected by government agencies, such as FDA, “lack crucial details necessary to examine trends and understand the relationship between use and resistance.” Clearly this is a severe problem that must be addressed without delay. Therefore, I would like to elaborate further on my three concerns:

1) Finalization of Guidance #209, The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals

In August, 2011, I sent the FDA a letter urging rapid progress forward on the regulations and guidance for the use of antibiotics in agriculture, including Guidance #209, The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals, and the Veterinary Feed Directive. It has now been well over a year since Guidance #209 was first issued in draft form and FDA has yet to finalize this guidance. This unacceptable delay comes at a time when the European Parliament recently voted to extend the current Europe Union (EU) ban on antibiotic use for livestock growth promotion to include all prophylactic uses of antibiotics on farms. Just last week, the European Commission announced a five-year plan to address antibiotic resistance with twelve concrete actions to be implemented with Member States. Meanwhile, over 30 years have passed since the FDA first issued a warning call on agricultural usage of antibiotics, and still little to no regulatory action has taken place.

2) Transparency on Animal Drug User Fee Amendment Report

Section 105 of the Animal Drug User Fee Amendments (ADUFA 105) of 2008 directs the FDA to annually publish the quantity of antibiotics sold or distributed for use in food-producing animals. While ADUFA requires drug sponsors to report the target animals, indications for use, and dosage forms for which each drug sold is approved, FDA does not report these data publicly. For this reason, in December, 2010 – nearly a year ago – I recommended that FDA expand its tracking and reporting of antibiotic usage in three ways, specifically: 1) increase reporting on antibiotic classes used in agriculture that are critical to human medicine, 2) provide more information on the route of antibiotic administration in agriculture (therapeutic and non-therapeutic), and 3) provide data on the quantity of antibiotics used in human health. FDA provided much of this information after I made the request, which rendered the ADUFA report useful to both Congress and the general public.

In a letter responding to my request last year, Karen Meister, Supervisory Congressional Affairs Specialist at FDA stated that,

“In preparing the first ADUFA 105 summary report for 2009, FDA adhered closely to the reporting requirements set forth in the statute. However, FDA agrees there may be alternative approaches to summarizing ADUFA 105 sales and distribution data. Prior to making significant changes to the content and format of our annual summary reports, we intend to seek public comment on this issue when we publish

proposed implementing regulations for ADUFA 105. Such rulemaking would incorporate the new ADUFA 105 reporting requirements into existing records and reports regulations for new animal drugs, as well as the provisions for the Agency's annual summary report."

It was therefore my hope that the ADUFA report would be the baseline for, rather than the extent of, antibiotic sales reporting. You can imagine my immense disappointment after seeing the recent 2010 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals. Once again, FDA has reported only on total sales and distribution of antibiotics in agriculture. I would like to know why the FDA refuses to be forthcoming with the data it has collected. Without additional information, this report is not useful in assessing the impact of antibiotic use in food-producing animals on public health.

I reiterate my request from last year for additional data from FDA:

- First, I would like monthly distribution data on: (1) fluoroquinolones and diaminopyrimidines combined, and (2) the combination of medications with less than three distinct sponsors used only in animal medicine.
- Second, I request data on the amounts of antibiotics sold in 2010 for administration to food-producing animals: (1) in feed, (2) in water, and (3) by injection. These data should be broken down by month and subdivided into the four groups of antibiotics that the FDA has established: critically important in human medicine, highly important in human medicine, important in human medicine, and not used in human medicine. Reporting ADUFA sales data by month would enable comparisons with resistance data from the National Antimicrobial Resistance Monitoring System, as suggested in the House Energy and Commerce Committee report on ADUFA.
- Third, I urge you to publicly report the quantity of antibiotics by class used in human medicine. These data are essential for obtaining a comprehensive understanding of antibiotic use associated with human medicine and animal agriculture.

In addition, I would like clarification from FDA on what specific error led the agency to revise its original report on the 2010 ADUFA sales data. The agency published the original report on October 28, and then published, without explanation or acknowledgement, a revised report on November 1. The revision included an egregious 700,000 kg reduction in total domestic sales of antibiotics for use in food-producing animals. After several days of silence, FDA issued the following statement:

"An earlier draft of the summary report was posted erroneously on 10/28/11. It did not contain the final results. We were still adjusting classifications and numbers including a late submission from a drug sponsor. The mistake was realized and we issued the final summary report which reflected the correct numbers on 10/31/11."

I ask that FDA explain how the inclusion of an *additional* submission could result in a reduction in the total. The lack of transparency in public reporting is indicative of a systematic problem within FDA that merits further investigation.

3) Withdraw Approval of Nontherapeutic Uses of Medically Important Antimicrobials in Food Animals

On November 7, 2011, FDA denied two citizen petitions, one from 1999 and the other from 2005, asking for the withdrawal of approvals for the nontherapeutic uses of medically important antimicrobials in food animals. In denying the petition, FDA did not question the need to address the problem, but instead stated that the formal withdrawal procedure is slow, cumbersome, and too costly. In a letter written by Leslie Kux, Acting Assistant Commissioner for Policy, prior examples of delays in the withdrawal process included the following,

“...the first [formal administrative hearing (NOOH)] for withdrawal of nitrofurantoin approvals were issued in 1971, but the final rule withdrawing the approvals was not issued until 1991. Withdrawal of diethylstilbestrol (DES) approvals became final in 1979, seven years after issuance of an NOOH. More recently, the withdrawal of approved uses of enrofloxacin in poultry took almost five years and cost FDA approximately \$3.3 million.”

This is a terrible excuse for the lack of action on antibiotic regulation. The fact that approval for carcinogenic drugs such as DES took years to withdraw only highlights a systemic problem with FDA. The seven year delay in DES withdrawal has disturbing parallels with our current situation. As with nontherapeutic use of medically important antibiotics, numerous studies on DES showed that the drug was detrimental for human health, yet no action was taken. For this reason, in 1992 I sponsored the DES Education and Research Amendment, which provided funding to NIH for research on the effect of DES on mothers and children. DES exposure has shown devastating effects on human health, including high risk pregnancies and miscarriage, higher rates of infertility, and higher rates of clear cell cancer and breast cancer. Shockingly, despite a public mandate to protect public health, FDA banned the use of DES in animal feed years before withdrawing this dangerous drug for human use. FDA is clearly not capable of addressing safety concerns in an acceptable or timely manner. The American people should be outraged by such failure to take action.

Antibiotics are a national resource that must be protected for the good of public health. Science tells us that the sub-therapeutic dosing of antibiotics in agriculture contributes to the rise in antibiotic resistance. We therefore need fast and effective action to ensure the dangers to public health do not continually rise at such a frightening pace. I hope that you will take measures to ensure that failures in action do not continue to occur. The FDA has a mandate to protect public health and establish science-based preventative controls throughout the farm-to-table continuum, not to protect the interests of the agriculture industry. I expect the FDA to deliver on this promise – the American public deserves no less.

Sincerely,



Louise M. Slaughter
MEMBER OF CONGRESS