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July 10, 2012

The Honorable Margaret A. Hamburg, M.D.
Commissioner
c/o Division of Dockets Management (HFA–305)
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

ATTN: Comment Docket No. FDA-2010-D-0094; "The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals; Guidance 209"

Dear Commissioner Hamburg:

On behalf of The Pew Charitable Trusts (Pew), I am writing to commend the U.S. Food and Drug Administration (FDA) for issuing final Guidance 209 and thank you for the opportunity to comment. As reinforced by recent court decisions[i], Pew believes the best course for protecting public health would be for the Administration to issue regulations ending injudicious uses of antibiotics in food animal production. However, with appropriate strengthening measures described below, we believe FDA Guidance 209, along with accompanying Draft Guidance 213, can help begin the process of making progress toward reducing the development and spread of antibiotic-resistant bacterial infections in people.

We applaud FDA for acknowledging in Guidance 209 the scientific evidence showing that it is inappropriate to use antibiotics to make animals grow faster, i.e., for "growth promotion" purposes. There is no health-based justification for this practice, which contributes to the emergence of disease-causing, drug-resistant bacteria that threaten the public health. In this regard, we welcome the Guidance document's inclusion of key highlights from the peer-reviewed scientific literature published over the course of several decades.

Today, too many antibiotics of critical importance in human medicine are available over-the-counter, which facilitates overuse and misuse in food animal production. Therefore, Pew also commends the agency for calling for greater veterinary involvement in the dispensing of antibiotic medicines and ensuring the drugs are available only under a veterinary order, akin to a doctor's prescription in human medicine.

For the reasons stated above, we appreciate the principles advanced through Guidance 209. Still, we believe there are two important gaps that must be addressed in order to assure the public that FDA's action will result in meaningful protections for public health.

DISEASE PREVENTION VS. THERAPY

As currently written, the guidance does not clearly define categories of antibiotic use, especially disease "prevention" and how it differs from legitimate "therapeutic" uses of antibiotics. As a result, Pew remains very concerned that drug makers could make minor label changes to allow prevention uses, or take advantage of existing prevention uses already on their labels, resulting in little on-farm change. It appears that some within the pharmaceutical industry are preparing to avoid the principles outlined in Guidance 209 and its blueprint for implementation, Guidance 213, by exploiting ambiguity on the issue of disease prevention. On April 11, 2012, for example, *FDA Week* paraphrased Richard Carnevale, a vice president at the Animal Health Institute (AHI), the trade association representing animal drug manufacturers, as saying, "Manufacturers will likely seek to make the voluntary label changes by applying for a new prevention indication for these low dose formulations."[ii]

FDA should clarify that, along with growth promotion, disease prevention is an inappropriate use of antibiotics unless they are administered in the presence of a known or expected bacterial disease, at levels that are effective to treat that disease, and are limited in scope (in terms of duration and the number of animals). For instance, FDA has listed use of antibiotics to manage necrotic enteritis in broiler chickens as a judicious use of the drugs. However, if use of antibiotics is required over multiple production cycles, there are no other attempts to manage concurrent disease or underlying husbandry problems are not addressed, this should not be considered a judicious prevention use of the drugs. Addressing underlying production problems is consistent with the FDA document "Judicious Use of Antimicrobials for Poultry Veterinarians" developed in cooperation with the American Veterinary Medical Association. [iii] Further, although Guidance 209 does list two examples where prevention uses are necessary and judicious, it would also be useful to give examples where the agency believes prevention uses of the drugs are not necessary or judicious.

The prevention guidelines originally presented in the July 2010 draft of Guidance 209 are far preferable, and Pew urges that, at minimum, FDA restore them to the final Guidance. The July 2010 draft established factors that should be considered in determining the appropriateness of preventive use. Those factors include whether there is: (1) evidence of effectiveness, (2) evidence that such a preventive use is consistent with accepted veterinary practice, (3) evidence that the use is linked to a specific etiologic agent, (4) evidence that the use is appropriately targeted, and (5) evidence that no reasonable alternatives for intervention exist.[iv]

Prevention uses of antibiotics must be even more narrowly defined, however. In addition to following the guidelines above, prevention labeling must indicate the maximum duration of use in groups of animals, as is the case with time limits established in the FDA's Guidance for Industry #152 "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern." Veterinary orders for prevention should also limit the number of refills available without further inspection of animals and facilities. Furthermore, repeated prevention uses should signal a problem with a facility's animal health maintenance and trigger additional supportive and/or corrective measures by the veterinarian to improve animal husbandry, cleanliness, or other production practices.

As FDA and the American Veterinary Medical Association have pointed out, antimicrobial use should not be viewed in isolation from the disciplines of animal management, animal welfare, husbandry, hygiene, nutrition, immunology, and vaccination. The objective is to prevent disease to the extent possible so that antimicrobial treatment is not required. In food animals, antimicrobial use should be part of, and not a replacement for, integrated disease control programs.[v]

MONITORING AND EVALUATING SUCCESS

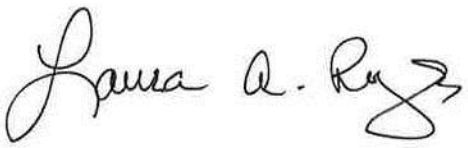
We call on FDA to establish a plan for evaluating how well the guidance is meeting its objectives. First and foremost, FDA should develop a process or system with stakeholder input to enable verification that progress is being made. FDA's accounting of drug sales through the Animal Drug User Fee Act (ADUFA) is not sufficient to produce the detailed information the agency needs to determine the extent to which antibiotic use on industrial farms has decreased. At present, the agency reports antibiotic sales by class only and does not track the purpose for which antibiotics are used (e.g., for growth promotion, feed efficiency, disease prevention, control, or treatment), nor does it report such usage by species of animal. If FDA cannot work with the Department of Agriculture to establish a system to track on-farm antibiotic use, it should call on Congress, as Pew will, for additional authority to collect the data needed to track specific uses, by species of animal.

In the meantime, FDA should develop additional measures including reporting through the Veterinary Feed Directive and further analysis of National Antimicrobial Resistance Monitoring System data, which measures rates of selected drug-resistant bacteria in animals, on meat, and in people. In addition, the agency should establish goals that include timetables and targets for reducing levels of antibiotic-resistant bacteria in food animals and meat, whereby failure to reach goals triggers additional actions by the agency. We elaborate on our suggestions in this area in our comment letter regarding Guidance 213, submitted to the docket.

Guidance 209 is a welcome step toward protecting human health and addressing the overuse and misuse of vital antibiotics on industrial farms, and can be a valuable tool if strengthened and adopted by the pharmaceutical industry. We believe the recommendations suggested above will improve the document from a public health and consumer perspective, and could help to curb antibiotic resistance. Furthermore, Pew urges FDA to continue to move forward with additional steps as necessary to exercise its authority to issue formal regulations barring non-therapeutic uses of medically important antibiotics in food animal production.

Thank you for your consideration.

Sincerely,



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[i]U.S. Court for the Southern District of New York, case 1:11-cv-03562-THK. March 22, 2012. http://docs.nrdc.org/health/files/hea_12032301a.pdf <accessed June 21, 2012>; and case 1:11-cv-03562-THK. June 1, 2012, http://www.nylj.com/nylawyer/adgifs/decisions/060612katz.pdf <accessed June 21, 2012>

[ii]Nanci Bompey, *FDA Week*, "Animal Antibiotic Label Changes Hinge on FDA Finalizing Rule, Industry Says," April 20, 2012. Attribution based on an AHI press call with the National Pork Producers Association and the American Veterinary Medical Association.

[iii]Judicious Use of Antimicrobials for Poultry Veterinarians. U.S. Food and Drug Administration, Center for Veterinary Medicine, publication date not listed. http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/UCM095575.pdf. <accessed June 21, 2012>

[iv]The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Veterinary Medicine, June 28, 2010.

[v]Judicious Use of Antimicrobials for Poultry Veterinarians. U.S. Food and Drug Administration, Center for Veterinary Medicine, publication date not listed. http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/UCM095575.pdf, <accessed June 21, 2012>