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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ATTN: Comment Docket No. FDA-2011-D-0889; "Draft Guidance for Industry on New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions With GFI 209; Guidance 213"

Dear Commissioner Hamburg:

On behalf of The Pew Charitable Trusts (Pew), I commend the U.S. Food and Drug Administration (FDA) for issuing Draft Guidance 213 for industry on antibiotics in animal feed and water and respectfully urge the agency to consider improvements that would better protect public health. The guidance document constitutes an important step in limiting the overuse of antibiotics in food animal production, and should help address the growing problem of antibiotic-resistant bacteria, especially if strengthened. 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 However, with appropriate strengthening measures described below, we believe FDA Draft Guidance 213 can help make progress toward reducing the development and spread of antibiotic-resistant bacterial infections in people. Although the guidance is a positive development, we have three significant concerns about the draft document as it is currently written.

RISK OF CHANGE IN NAME ONLY

First, Section VI of Draft Guidance 213, "Supplemental New Animal Drug Applications" would allow sponsors of antibiotics currently approved for growth promotion and other uses in food animal feed or water (i.e., "production purposes") to submit supplemental new animal drug applications (NADAs) to replace currently-approved labeling with veterinary feed directive (VFD) or prescription drug (Rx) labels for disease prevention purposes. This could mean little more than strategic relabeling, whereby antibiotic approvals that have been withdrawn for growth promotion would be approved for "disease prevention." Under such a scenario, the disease prevention use would have the same effect as a growth promotion use—continuous or low-dose drug administration to an animal that often exhibits no disease, has a disease or condition with multiple causes that may or may not respond to antibiotics (e.g., bovine

respiratory disease), or resides on a farm where disease does not directly threaten the animal's health. Such changes in name only would fail to reduce non-disease treatment (or non-therapeutic) uses of antibiotics, which are known to select for antibiotic resistance.[ii]

It also is important to note that many antibiotics approved currently for disease prevention, just like antibiotics for growth promotion, are often administered to all animals on a farm for long periods of time. We ask that Draft Guidance 213 include steps designed to eliminate this type of preventive use as it leads to increased risk of antibiotic resistance.

CONSISTENT METHOD FOR EVALUATING SAFETY

If FDA is willing to approve new preventive uses or changes in marketing status to VFD or Rx for a supplemental NADA submitted under Draft Guidance 213, Pew recommends the agency use the existing methods to evaluate the microbial safety of the claims as detailed in Guidance 152. Specifically, as discussed below, Guidance 152 requires a detailed risk assessment of the potential impact of a proposed new antibiotic use on the safety of the food produced. If Draft Guidance 213 is not clarified, it would create an entirely separate system for approval of new uses that does not clearly require such an assessment—a new approach that is untested and has no public health advantages over the existing system, but could cause confusion in the public and the industry, since there would presumably be two conflicting processes for approval.

Thus, in Draft Guidance 213, FDA states that it will not require a drug sponsor that submits supplemental NADAs to conduct a qualitative risk assessment to evaluate the microbial food safety of the proposed use. In contrast, such a risk assessment is obligatory under Guidance152. Specifically, Draft Guidance 213 recommends, "in lieu of a complete, qualitative, microbial food safety risk assessment [as outlined in Guidance152], firms should discuss with CVM [FDA's Center for Veterinary Medicine] the type of information to submit with their application."[iii] While limited in scope since it only addresses foodborne bacteria, Guidance 152 has been finalized and successfully implemented; it provides a transparent and effective process for decision making. This well-established process should be utilized in Draft Guidance 213 for all amended approvals.

EVALUATING SUCCESS

Equally important, FDA does not lay out a plan to track, evaluate, and report on whether Draft Guidance 213 succeeds in reducing antibiotic use or antibiotic resistance. Nothing in the document suggests how the agency will determine whether sponsors have followed the voluntary guidelines, whether there is any change in antibiotic use patterns, or whether the proposed changes have had the desired effect of decreasing antibiotic resistance in food animals, meat and poultry, or people. Pew urges FDA to track and publish a detailed report on animal drug sponsors' voluntary changes to drug labels made under Draft Guidance 213. This will allow verification of progress by both FDA and independent assessors of these changes.

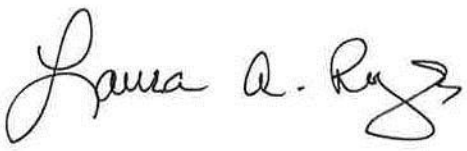
FDA should also evaluate whether Draft Guidance 213 results in meaningful reductions in actual use of antibiotics in food animal production. The annual reports released publicly under the Animal Drug User Fee Act (ADUFA) provide only minimal information on antimicrobial sales for food animal purposes. While FDA appears to have the authority to report more than just total volume of sales by drug class, the

agency is choosing not to provide additional information within those class distinctions. For example, ADUFA allows public reporting of summary data on the quantity of each drug class approved for different uses, such as growth promotion and feed efficiency. Pew also encourages FDA to obtain actual on-the-ground or end-user drug use data in collaboration with industry and other federal agencies to best assist in determining the success of the voluntary Draft Guidance 213.

In addition, the agency should regularly assess intermediate and long-term outcomes of antibiotic resistance in pathogens and associated public health implications. While the existing National Antimicrobial Resistance Monitoring System is designed to track a few foodborne bacteria, it lacks a comprehensive and coordinated approach to assess the total burden of antibiotic resistance. In Draft Guidance 213, the section titled, "Impact on Human Intestinal Flora," mentions public health effects but merely indicates that FDA expects that change-in-use patterns will reduce overall human exposure to residues of antimicrobial new animal drugs. This section does not address human exposure to antibiotic-resistant bacteria.

We believe the voluntary measures in Draft Guidance 213 combined with the recommendations outlined above should begin to protect human health by addressing some overuse and misuse of medically important antibiotics on industrial farms. However, Pew also urges FDA to continue to move forward with additional steps to exercise its authority to issue binding regulations that will further restrict the way antibiotics are used in food animal production.

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 25, 2012>

ii Tello A, Austin B, Telfer TC 2012. Selective Pressure of Antibiotic Pollution on Bacteria of Importance to Public Health. *Environ Health Perspect*:-. http://dx.doi.org/10.1289/ehp.1104650.

[iii] Draft Guidance 213 p. 11.