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October 30, 2013

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-2012-N-0447 "Antimicrobial Animal Drug Sales and Distribution Annual Summary Report Data Tables"

Dear Commissioner Hamburg:

The Pew Charitable Trusts (Pew) thanks you for this opportunity to comment on the U.S. Food and Drug Administration's (FDA) revised information collection and reporting activities on antimicrobial animal drug sales under Section 105 of the Animal Drug User Fee Act (ADUFA). Pew commends the FDA for heeding public comments regarding the inadequacy of current reporting and issuing proposed changes to the annual sales data report. The revised content and format of data tables are important steps to enhance the public's understanding of antibiotic resistance and provide some useful information to the public and researchers about how medically important drugs are used in food animals. However, Pew would like to recommend additional improvements to the reporting format and content, including amending the definition of "therapeutic" antibiotic use to more clearly exclude inappropriate uses for so-called "disease prevention" purposes that, in practice, are similar or identical to growth promotion. Further, Pew would like to reiterate strong interest in additional data collection activities that can paint a fuller picture of antibiotic use in animal agriculture than ADUFA sales reporting can do alone.

According to a new report from the Centers for Disease Control and Prevention (CDC), *Antibiotic Resistance Threats in the United States, 2013*, two million Americans suffer antibiotic-resistant infections each year and at least 23,000 die. Resistant strains of two commonly foodborne bacteria—*Salmonella* and *Campylobacter*—are responsible for about 20 percent of the illnesses. The report noted: "antibiotic use in food animals can result in resistant *Campylobacter* that can spread to humans;" and "*Salmonella* spreads from animals to people mostly through food. Antibiotic use in food animals can result in resistant *Salmonella*, and people get sick when they eat foods contaminated with *Salmonella*."

By making agricultural antibiotic use more transparent, the U.S. Food and Drug Administration (FDA) can guide the development of precise policies that protect human and animal health.

Thank you for responding to public comments requesting additional information about the medical importance of data, as well as the route of administration for antibiotics. The newly proposed Tables 3 and 4 should enable the public to better understand how livestock and poultry producers are administering antibiotics, and whether they are medicines used commonly in human medicine to treat serious illness. This should help public health officials identify areas for concern (e.g., a scenario whereby a majority of antibiotics are given to animals through feed, and are from highly important drug classes used to treat dangerous human infections). The data may also show encouraging signs that certain antibiotics are not being fed in large quantities to animals, which could prompt researchers to look for other explanations for specific drug-resistant bacteria in meat or infections in people.

Also, Pew appreciates the FDA's inclusion of Table 6 in answer to requests for information about the marketing status of antibiotics used in agriculture. Pew expects this table to hold greater value after full implementation of finalized Guidance #213 and expansion of the Veterinary Feed Directive system. In fact, this table should help show whether the guidance plan is effective at moving medically-important antibiotics that are used in feed from the over-the-counter data category to the prescription/VFD category, in line with judicious use principles.

Pew understands that the agency's release of detailed data is constrained by 512(l) of the Federal Food, Drug, and Cosmetics Act (21 U.S.C. 360b(l)) and the Trade Secrets Act (18 U.S.C. 1905), designed to protect confidential business information. However, Pew would like to see greater explanation of confidentiality limitations caused by the "mosaic" effect, as it is not easily apparent what other sources of antibiotic sales or use data are publicly available to be layered onto data reported under ADUFA. This broad interpretation of confidentiality restrictions has so hampered data reporting in Table 5, for instance, that the information presented is of questionable additional value, particularly when based on definitions that only further muddle the intent of the agency's judicious use guidelines. If the FDA wishes to be transparent about implementation of judicious use policies and the data collected under ADUFA, there are further refinements that could be made to the tables to enhance public health.

Definitions Matter

Pew is very concerned that the data tables are based on flawed definitions of "therapeutic and production" uses. These terms are not exhaustive and not mutually exclusive. The FDA uses an overly broad definition of "therapeutic indications" that fails to take account of the range of antibiotic uses under current "disease prevention" label claims, some of which would not meet the judicious therapeutic use criteria posed by Guidance #209 and Draft Guidance for Industry #213. A more defensible approach would be to adopt the WHO-FAO-OIE definition of "therapeutic use": application of antimicrobials in curative doses in an adequate period of time to combat an established infection. This definition would necessarily exclude those uses for disease prevention that are at insufficient dosages and duration to kill bacteria, and do not occur in the presence of actual infection, i.e., uses the agency has deemed injudicious along with growth promotion and feed efficiency.

Likewise, the agency should refine its definition of disease prevention to exclude those same uses that do not meet the judicious use test. Using the agency's own reasoning, injudicious uses in healthy animals with no documentation of specific health risk should be included instead in the "production" category of use. If the division of data is impossible, the FDA should at minimum make clear in revised ADUFA data reports that its use of the term "therapeutic" to include all prevention does not signal that the agency accepts or condones all preventive uses, in line with the thinking presented in Guidance #209 and Draft Guidance #213.

Pew recognizes that drug applications and approvals have evolved over time with differing terminology, and that drawing a line between these terms may be difficult, especially when data presentation is limited by the number of drug sponsors. However, we expect the agency to uphold definitions in its data reports that, at minimum, adhere to the principles put forth by the guidance documents, which animal-drug sponsors have indicated they will soon implement. Failing this, the data would be more legitimately and clearly separated into "treatment" and "non-treatment" uses, perhaps based on dosages effective enough to kill bacteria.

More Could Be Reported

Data is collected from animal pharmaceutical manufacturers about the amounts sold every month. As such, there should be a table that reports sales by month for each drug class. FDA has collected data by monthly sales since at least 2008. The data may help researchers determine whether there is seasonality to sales linked to specific diseases and inspire novel treatment or prevention approaches.

Section 105 of ADUFA also requires that the FDA collect information pertaining to target animals and production classes. Pew urges the agency to add a table to the next ADUFA sales report that would present species-level information in the most detailed way that would still protect confidentiality, such as grouping sales first by medical importance. Should the data not adequately reflect antibiotic sales by species or production class, the agency should ask drug sponsors to produce estimates. If FDA does not believe that ADUFA is the appropriate vehicle, the agency should swiftly issue a proposed rule for alternate data collection methods that can answer the important question of which species and production classes of animals are getting medically-important antibiotics and the indications for administration.

In addition, the public's understanding of antibiotic use in animal agriculture is further challenged by the agency's inclusion of non-food animal data in the tables. Pew urges the agency to find ways to separate out companion and food animal data wherever possible, and to explain cases where the data cannot be separated.

The collection and public distribution of this information is critical to slow the spread of resistant infections. As the CDC's Dr. Steven L. Solomon recently said, "We want to get everyone in our society engaged in understanding the big picture of antimicrobial resistance, and that this is a very complex, holistic problem that we all need to be working together to solve… But let's not approach them one at a time. Let's turn our attention to the big picture and begin to solve that in a societal way."

Sincerely,

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