KEEP ANTIBIOTICS WORKING
The Campaign to End Antibiotic Overuse
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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20857

Docket No. FDA-2009-N-0512

The Food and Drug Administration ("FDA") has asked for public comments on how to improve the utility of the antimicrobial drug distribution data that the FDA will collect pursuant to section 105 of the Animal Drug User Fee Amendments of 2008 ("ADUFA"). 74 Fed. Reg. 55046 (October 26, 2009). Keep Antibiotics Working ("KAW") – a coalition of health, consumer, agricultural, environmental, humane, and other advocacy groups with more than nine million members working to protect public health through the promotion of the responsible use of antibiotics in animal agriculture – offers these comments on this important data collection effort.

I. Background

According to the FDA, animal drug sponsors are already required by the FDA to maintain and submit most of the data required by ADUFA. 74 Fed. Reg. at 55048. However, the data have not been submitted in a manner that allows the FDA to effectively track changes in antimicrobial use and thereby determine the impact of those changes on antimicrobial resistance. The collection of veterinary drug use data is widely recognized as being an important tool for the management of antimicrobial resistance and is included as a top priority for the Interagency Task Force on Antimicrobial Resistance's Public Health Action Plan (http://www.cdc.gov/drugresistance/actionplan/index.htm). The collection of these data is also recommended by the World Health Organization ("WHO") (http://whqlibdoc.who.int/hq/2000/WHO_CDS_CSR_APH_2000.4.pdf) and the OIE-World Organization for Animal Health (http://www.oie.int/eng/normes/Mcode/en_chapitre_1.6.9.htm). In 2007, during a review of the National Antimicrobial Resistance Program ("NARMS"), the FDA's Science Advisory Board recommended that drug use data be integrated with microbiological data and stated that the lack of drug use data "represents a critical barrier for NARMS to achieve its objectives and further utility."

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Congress enacted section 105 of ADUFA in 2008 because of its concern about antimicrobial resistance in people stemming from the use of medically important antimicrobials in food animals. As Representative Waxman put it during the debate on ADUFA, "We now have an overwhelming body of evidence showing that the overuse of antibiotics in industrial farm production is threatening to destroy the effectiveness of some of our most important antibiotics for human use...The ADUFA bill we are considering includes a provision to increase the availability and accessibility of data on the amount of animal antibiotics being distributed. This data will help us to determine how resistant bugs are developing and inform research on ways to stop those bugs from threatening human health." 154 Congressional Record H7540 (July 30, 2008).

ADUFA was passed unanimously by both the House of Representatives and the Senate.

Section 105 of ADUFA specifies that, beginning in 2010, by March of each year monthly drug distribution data for the previous year must be submitted to the FDA by the sponsor of each animal drug. By requiring all sponsors to submit data on a monthly basis, section 105 will enable FDA to monitor drug distribution on a calendar year basis -- something that was not possible before because each sponsor submitted data only once annually on the anniversary of the drug approval. The monthly data will also allow the FDA to determine if seasonal changes in drug use impact resistance. While the change in the reporting period mandated by section 105 will greatly improve the utility of drug distribution data there is much more that FDA could do on its own initiative to close this critical data gap.

In addition to requiring improved collection of drug distribution data, section 105 also requires that the FDA make public summaries of these data by antimicrobial class (provided that the class has at least three distinct sponsors). The method of submission of the data should be designed to facilitate public reporting requirements of section 105.

FDA has been mandated by Congress to both improve collection of antimicrobial drug use data and to make these data public. FDA should take this opportunity to develop a system to collect data in a manner that best meets the regulatory and public health protection needs and that allows for the greatest openness and transparency.

II. The FDA should acquire animal antimicrobial drug distribution and sales data needed for public health risk management in a format that will meet the needs of regulatory authorities, that can be readily integrated with other FDA databases, and that will lend itself to the creation of public summaries that provide the maximum amount of information to the public while meeting the confidentiality requirements of the legislation.

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A. The FDA should require manufacturers of medicated animal feed to supply sales data.

The data that the FDA proposes to collect will be useful for informing for the first time both the FDA and the public on how much of each class of antimicrobials is given to food animals and, over time, will show trends in this use. However, relying solely on these data, neither the FDA nor the public will learn how much of each class of antimicrobial is sold for use in different types of food animals. For example, the FDA permits the use of penicillin for weight gain and improved feed efficiency for swine (10 to 50 grams of penicillin per ton); for chickens, turkeys, and pheasants (2.4 to 50 grams of penicillin per ton); and quail (5 to 20 grams of penicillin per ton). 21 CFR 558.460. Data on the amount of penicillin sold by drug manufacturers will not reveal how much is sold for such use in swine, how much for such use in chickens, and how much for such use in turkeys.

Data on use by species would, however, be of more utility to researchers and policy-makers than merely aggregate data. As the Government Accountability Office determined in 2004, "Although federal agencies have made some progress in monitoring antibiotic resistance, they lack important data on antibiotic use in animals to support research on human health risks. *These data, such as the type and quantity of antibiotics and purpose for their use by species, are needed to determine the linkages between antibiotic use in animals and emerging resistant bacteria. In addition, these data can help assess human health risks from this use and develop and evaluate strategies for mitigating resistance*." (emphasis added). *Antibiotic Resistance Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals* GAO-04-490 (April 22, 2004) at Summary. http://www.gao.gov/products/GAO-04-490. The FDA's Science Advisory Board in 2007 also acknowledged that drug distribution data alone is not adequate to meet the needs of regulators and risk assessors. Similarly, collecting drug distribution data alone is not consistent with the recommendations of the international organization's WHO and OIE. In order to get at least some data on antimicrobial use by species and animal class, KAW recommends that in addition to drug distribution data FDA collect antimicrobial drug sales data from manufacturers of medicated animal feeds. Because feeds are specific to animal species and animal class, these data would contain much more detail than the drug distribution data required by section 105.

The FDA has long recognized that medicated feeds may create greater public health risks because they are fed to large groups of animals often over long periods of times at low doses. Medicated feed sales data would be complementary to the drug distribution sales data and would create an opportunity for determining at least to the level of species what antimicrobials are being fed to food-producing animals.

The FDA already requires medicated animal feed manufacturers to maintain records on their sales of animal feed and to make them available to FDA on request. 21 CFR 225.110; 21 CFR 225.202. These data would show, for example, how much animal

feed containing penicillin is sold for use in different food animals, such as swine, chickens, and turkeys. At a meeting in November 2009, FDA staff informed KAW that FDA has the legal authority to require the animal feed manufacturers to routinely supply these data.

Accordingly, the FDA should acquire these data as soon as possible and make them public.

B. The FDA should require drug sponsors and feed manufacturers to supply data in a form that makes it easy to enter these data into other FDA databases.

The FDA's Science Advisory Board review of the NARMS program recommends that drug use data be integrated into a single database that also includes information on resistance levels in human, retail meat, and slaughter isolates. In addition the FDA has created a publically accessible database of approved veterinary drugs (http://www.accessdata.fda.gov/scripts/animaldrugsatfda/). FDA should require sponsors and medicated feed manufacturers to provide data in a form that will make the integration with these other sources of data easier.

Because information on target animals, indications, and production classes that are specified on the approved label of the product is already known by the FDA for each NADA, KAW believes that the most important information to collect is the amount of active ingredient distributed on a monthly basis. Where combination products are reported, then each active ingredient should be reported separately.

KAW recommends that FDA require all data to be submitted electronically through a web based application directly into a form created by the FDA. The form should be linked to a relational database that contains the information on indication, target species, and dose form associated with each label.

C. The FDA should require drug sponsors and feed manufacturers to supply these data in a form that will lend itself to the creation of public summaries that provide the maximum amount of information to the public while meeting the confidentiality requirement of the law.

For KAW, the most important change under section 105 is the requirement that the FDA make public summaries of the data. The public disclosure of the data will allow outside researchers to test hypothesis related to antimicrobial use and resistance and will lend greater credibility to FDA's risk management activities related to antimicrobial resistance. Because of this, KAW recommends that the data be collected in a way that makes summarizing the data most easy. We strongly recommend that FDA create a publically accessible database that would allow searches by drug class (or combined classes when required for reasons of confidentiality), dose form, and marketing status. The submission method should be designed from the outset to allow submitted data to be entered into such a database.

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III. Conclusion

FDA should expand its request for animal drug sales data in order to comply with the Congressional purpose of helping to "determine how resistant bugs [bacteria] are developing and inform research on ways to stop those bugs from threatening human health." This means collecting data on medicated feeds and designing the method of submission in a manner that ensures that it can meet the needs of regulatory authorities and external researchers. The method of submission should be created in conjunction with the creation of a database designed to meet the two goals for collecting data: to create a better understanding of the relationship between antimicrobial drug use and the development of resistance and to improve transparency and openness of FDA's risk management decision making. If time does not allow the creation of such a database, then FDA should require the data to be submitted in a form that anticipates the future creation of just such a database.

Respectfully submitted,

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